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# From Dyspepsia to Helicobacter: A History of Peptic Ulcer Disease

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A thesis submitted in fulfilment of the requirements for the degree of MD to the University of Glasgow.

School of Medicine

Centre for the History of Medicine

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## Abstract

This thesis is a historical study of peptic ulcer disease from the sixth decade of the eighteenth century until the end of the twentieth. Symptoms of dyspepsia or indigestion have affected more than twenty percent of the British population for most of that period and attracted the involvement of many medical practitioners and others with the provision of health care. Within this group of symptomatic dyspeptic patients were to be found gastric and duodenal ulcers which were capable of causing serious health problems. However the prevalence of stomach and duodenal peptic ulcers has declined markedly during the time course of this thesis and now they are relatively uncommon. Although peptic ulcers may still have a fatal outcome, they now are considered to be curable conditions for the majority of patients who suffer from them in the developed world.

This thematic history of gastric and duodenal ulcer examines how medical practitioners worked in a changing climate of novel ideas about disease, often aided or driven by technological developments, from the nineteenth century onwards. It begins with a humoral approach to the understanding of disease, which concentrated upon a patient's personality, lifestyle choices and circumstances but this was gradually displaced from the end of the eighteenth century by the clinico-anatomical approach, which sought to identify a specific lesion as the 'seat' of the disease. In the nineteenth century, the discoveries of pathology, physiology, chemistry and bacteriology became incorporated in clinical medical practice, involving the laboratory in the investigation and treatment of many diseases. In the twentieth century, medical research became rooted in experimentation using scientific technology and engineering to equip investigators with new methods which changed the ways in which diseases were understood and treated. Although there were many innovations in theoretical concepts of disease aetiology and empirical treatments, many were subsequently rejected for reasons of ineffectiveness or possible harm to the patient, sometimes after long periods of use.

In its first part, the thesis draws upon publications from 1769 until 1950, mostly in the form of scientific articles and books. In the second part, the oral testimonies of health care professionals involved with the management and treatment of gastric and duodenal ulcers are added. The recorded testimonies of 28 witnesses have been preserved in written form as a supplement to this dissertation.

Peptic ulcer disease was initially perceived as a whole-body ailment which was centred on the stomach as its symptomatic location and its treatment was intended to alter humoral

imbalance or relieve symptoms. However after post-mortem examinations were increasingly performed from the seventeen-nineties, medical practitioners could see its complications in death and combine their findings with the clinical presentations of what was becoming recognised as a relatively common disorder. In the nineteenth century, physiologists investigated the workings of the stomach using vivisection and chemistry to analyse the stomach contents. The acid produced by the stomach was seen to play a part in ulcer genesis but there was no agreement as to what its precise contribution was for many years thereafter. Bacteriologists who found micro-organisms in the stomach assumed that they were pathogenically involved and subsequent experiments confirmed this.

As a result of effective anaesthesia and antisepsis in the last decades of the nineteenth century, surgeons intervened increasingly in life-threatening complications of gastric and duodenal ulcers and their observations changed their perceptions of the diseases. In the twentieth century, opaque meal X-ray techniques began to allow doctors to see lesions inside the living stomach, as did improved endoscopes. In 1952, research suggested that stomach bacteria played no part in causing ulcers and further bacteriological research in the stomach was abandoned. By this time, surgeons had designed operations to reduce stomach acid production which healed most gastric and duodenal ulcers. Good therapeutic results were also achieved using medication and dietetic regimens, but it was recognised that only the surgeon could help patients who had failed to respond to medical treatments. In 1962 it was noted that deaths rates for gastric and duodenal ulcer were falling and fewer people were suffering from them, but they remained a serious cause of morbidity and mortality. A new acid-reducing operation was devised in 1969 that offered the hope that surgery could adequately treat ulcers without causing iatrogenic damage, and in 1976, a new drug was marketed which healed them if continuously taken. Then in 1983 it was asserted that peptic ulcers were caused by a bacterium which was later called *Helicobacter pylori*. In time and in the face of much opposition, it was shown that if this organism was eradicated in the stomach by medication then gastric ulcers and duodenal ulcers could be cured for the first time.

This account of the history of peptic ulcer disease shows how medical practitioners adapted the theoretical basis of their medical practice as its evolved under the influence of scientific or societal changes and later abandoned concepts and therapeutic regimens which no longer were in accord with current thinking. Important issues which have arisen out of the testimonies include: medical involvement with the pharmaceutical industry, how doctors co-operate in the care of patients and how they respond to new theories and

equipment and techniques as they became available. The history of peptic ulcer disease over the past two hundred years as described in this thesis follows a broadly similar course to that of other diseases such as tuberculosis, syphilis and chronic renal disease which once dominated the lives of those who suffered from them and have largely become curable in recent years. This thesis is offered as an account of an equally fascinating and complex disease.

## Dedication

This thesis is dedicated to the memory of my mother and father, Jean and William Pollock of Motherwell, Lanarkshire.

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Dr Darryll Green is thanked for his practical help with computer issues as is my fellow student Dr Kenneth Macaulay for his friendship and availability to discuss practical issues which concerned the production of the thesis.

Finally to my long-suffering and loving wife Dr Myra Pollock, I say 'thank you' for your patient support during the years taken for my academic project.

## Author's declaration

I declare that this dissertation is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Alexander Chapman Pollock

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# Chapter 1. A history of gastric and duodenal ulcer in Britain: methodology, nosology and philosophy.

## Introduction to thesis

People have always suffered from painful stomach complaints. They generally found ways to live with their symptoms, which were amenable to treatment by various means, but on occasions, their condition would worsen and a sufferer might die from a stomach disorder. One of the earliest examples of a death caused by a gastric ulcer is found in the 1984 autopsy report of the exhumed body of a Chinese man who died in 167 BC.<sup>1</sup> Although ulcers may be found in the oesophagus, the stomach and the duodenum, this thesis is concerned only with the history of gastric (or stomach) and duodenal ulcers. When discussing these collectively, the term ‘peptic ulcers’ may be used. The word ‘peptic’ is derived from the Greek ‘peptein’ which means ‘to digest’ and there is an implication by its conjunction with ‘ulcer disease’ that the digestive processes themselves play a part in the formation of an ulcer.

The thesis begins in the late eighteenth century, when aspects of the clinical presentations of gastric and duodenal ulcers began to be recognised. The history continues to the end of the twentieth century by which time a cure had been found for most gastric and duodenal ulcers. The thesis uses both primary and secondary sources throughout, and in the last three chapters the evidence of oral history testimonies is incorporated in the text.

Concepts of how health and disease were perceived and treated began to change at the end of the eighteenth century, leading over the next half century to the development of what is now considered to be ‘scientific medicine’. This was based upon the observations, measurements and experiments of those who practised medicine and who were initially barely distinguishable from ‘irregular practitioners’ with whom they were in competition both in terms of their disease hypotheses and treatment regimens. The events and developments in medicine described in this historical account will be examined within their contemporaneous contexts.

The history of medicine is often portrayed today in the media as a march of progress from darkness to light but the reality is very different. This history will discuss the experiments

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<sup>1</sup> Cheng T O, ‘Glimpses of the past from the recently unearthed ancient corpses in China’, *Annals of Internal Medicine*, Nov 1<sup>st</sup> 1984, vol. 101, 714-5. The man died as a result of a perforation of the stomach which is a hole through the stomach at the site of an ulcer which allows the spillage of stomach contents into the sterile peritoneal cavity.

and observations which led to better understanding of the disease, as well as some of those which ended in futility but which were considered to be of major importance at the time. It will be seen how chance occurrences and planned procedures influenced many aspects of the history and it will also be seen how medical research in the laboratory and the hospital became well established as the main driver for the introduction of new treatments and investigations from the mid nineteenth century and continued throughout the twentieth century. Despite these new treatments, for most of the period, medical input in the management of the condition was at best palliative and the alternative of surgery, which helped many, produced a burden of morbidity in a few. The introduction of the National Health Service (NHS) into the UK in 1948 was a significant milestone in this history when, for the first time, British patients had a right of access to medical services free of charge to them. In the second half of the twentieth century the pharmaceutical industry emerged as an important player in the history as companies competed with one another for larger market shares of their products becoming the locus for most medical research. In the last two decades of the century, a new hypothesis as to the aetiology of peptic ulcers was proposed which in time proved to the profession that the cause of most peptic ulcers was an infection which could be treated medically. This important discovery changed the way in which peptic ulcers were dealt with and gradually a serious disease became a relative rarity in the UK mainly affecting the elderly.

This thesis will show that while peptic ulcers historically killed a relatively small number of the population in any year, they existed within a society where between twenty and forty percent of the population were affected with similar symptoms. At first when doctors became confident of making a diagnosis of peptic ulcer, it was clinically based from a combination of history-taking and physical examination until the means became available for visualisation of the lesions causing them. Not all peptic ulcers were symptomatic and some presented with serious life-threatening complications without prior warning. For nearly two centuries medical practitioners treated peptic ulcers using the same medication regimens on the pragmatic basis that they worked better than any available alternatives.

In the nineteenth and twentieth centuries, the nature of this particular disease was repeatedly reconceived as a consequence of scientific experimentation of many kinds which changed the nature of the understanding of this and many other contemporary diseases. Medical practitioners amassed a vast literature about the disease without coming to any conclusion as to its actual cause which was only revealed as a consequence of a return to a scientific concept which had been discarded a generation previously. The thesis

discusses these changes in a thematic manner which is set within a contemporaneous societal framework and it will answer two questions. The first is, ‘What were the significant ideas and discoveries which played a part in the evolution of the understanding of this disease over the two hundred year period covered by the thesis?’ The second question is, ‘To what extent does analysis of these changes challenge received understanding of the history of peptic ulcer disease?’

## Introduction to chapter one

The thesis relies upon two sources for its substance; the published record and the testimonies of witnesses who were involved with the management and treatment of the problems caused by peptic ulcer. An early diagnostic term, ‘dyspepsia’ will be discussed and the nosology of its clinical presentation examined in its historical context.<sup>2</sup> Dyspepsia will then be reviewed in the light of modern understanding, revealing its continuing ambiguity. The chapter includes a section on the philosophies of health and illness before considering the main authors who have written about the history of peptic ulcer.

### 1. 1: The published record

The research described in the first part of the thesis relies on the published record of the period from 1769 until 1950, largely extracted from scientific articles and books, being both primary and secondary in nature. It describes the British experience but includes, where relevant, research undertaken in Europe and the USA. Articles in medical journals are a fruitful source of information. Some describe a single case, others series of cases and the observations of researchers who made important first descriptions of illnesses and those of investigators who confirmed or refuted their findings. Contributions of seminal importance which are still remembered today are to be found alongside those which have passed into obscurity. Books reviewed for the research may be those devoted solely to diseases of the stomach or to peptic ulcer disease as one symptomatic condition among many. Journals and books on various relevant topics by authors who are historians have been consulted as secondary sources. Government statistical information, parliamentary publications and newspaper articles have also been used where helpful. Librarians have assisted with finding primary sources, usually in journals. The internet has been an

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<sup>2</sup> Nosology in the medical context is the classification of diseases

invaluable resource for data topic searches, increasingly so as the volume of online publication increases.

## 1. 2. 1: Oral history as a tool for the historian

In the second part of the thesis, the testimonies of health care professionals who were involved with the management and treatment of gastric and duodenal ulcers have been examined to enrich the background history of the period. These recorded testimonies extend from the beginning of the NHS and describe the circumstances and work of a group of professionals from different disciplinary backgrounds actively involved in the management and treatment of both types of ulcer.

Lisa Jardine, a well-known historian and broadcaster on BBC Radio Four says of oral history,

*Nothing could bring home to me more sharply the importance of memory for history. Nothing more strongly reminds me of the responsibility that those of an historical temperament have, to document and record events in the present as they unfold, lest future generations forget.*<sup>3</sup>

She was speaking of her mother's life experience and of her father's involvement with significant world events; in his case the aftermath of the atomic bomb explosions in Japan, which he witnessed as an official observer, and about which he never spoke to her.

Oral history is a validated means of recovering history and recording experiences which would otherwise be lost. In 1960 the Malian writer and ethnologist Amadou Hampâté Bâ said, '*En Afrique, quand un vieillard meurt, c'est une bibliothèque qui brûle*'. — 'In Africa, when an old man dies, a library burns.'<sup>4</sup> Writing about oral history, Samuel Schragger of the University of Pennsylvania says, 'Talk about events is much more than data for the derivation of history: it is also a cultural production in its own right, a mode of communicating, a surfacing of meaningfulness that binds past and present together.'<sup>5</sup> The historian Paul Thompson said, 'Oral history is a history built around people. It thrusts life into history and widens its scope.'<sup>6</sup> An historian contemporary of Paul Thompson, George Ewart Evans, described his interview subjects as 'walking books' and he developed an

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<sup>3</sup> Jardine L, 'A point of view', (London. Feb 26<sup>th</sup> 2010, BBC Radio 4)

<sup>4</sup> Bâ A H, Speech at l'UNESCO, 1960

<sup>5</sup> Schragger S, 'What is social in social history?', *International Journal of Social History*, Jun 1983, vol. 4, 76-98

<sup>6</sup> Thompson P, 'The voice of the past: oral history', in Perks R, Thomson A, *The Oral History Reader*, 2<sup>nd</sup> ed, (London and New York, 2006, Routledge), p31

immense respect for their accurate powers of recall.<sup>7</sup> In another paper, Thompson analyses the sources which historians use in original research and points to the inherent difficulties presented by each kind of archival source, be it government report, autobiography, newspaper, personal correspondence or any other written source. It is naïve to assume that something is historically more correct or accurate simply because it exists in a physical form. Thompson's paper discusses one of the objections to the validity of oral history namely the accuracy of memory.<sup>8</sup> Thompson is one of many respected historians who champions oral history and there is now a large body of academic research which depend on memory recall and its preservation as a tool.

Alessandro Portelli in writing about the tensions surrounding the acceptance of oral history as a discipline in its own right, covers many of the objections to its acceptance as a valid source of data. He places the narrator (witness) in the heart of the history,

*Traditional writers of history present themselves usually in the role of what literary theory would describe as an 'omniscient narrator'. They give a third party account of events of which they were not a part, and which they dominate entirely and from above (above the consciousness of the participants themselves). They appear to be impartial and detached, never entering the narrative except to give comments aside, after the manner of some nineteenth-century novelists. Oral history changes the writing of history much as the modern novel transformed the writing of literary fiction: the most important change is, that the narrator is now pulled into the narrative and becomes part of the story.<sup>9</sup>*

Most modern medical research is quantitative, that is to say that it uses statistics to express results which allow comparisons between different series of studies thereby providing a scientific review in an agreed setting. Qualitative research differs insofar that it does not use mathematics as its main tool of comparison and its subject is human behaviour.

*The differences between what are commonly called quantitative and qualitative research run deeper than the presence and absence of numbers. In general, quantitative research focuses on answering the questions 'What?' and 'How much?' whereas qualitative research focuses on answering the questions, 'Why?' and 'How?' Qualitative research also allows for the generation of rich data and*

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<sup>7</sup> Evans G E, 'Approaches to interviewing', *Oral History*, 1972, vol. 1, no. 4, 56-7

<sup>8</sup> Thompson P, 'Problems of methodology in oral history', *Oral History*, vol. 1, no. 4, 1972, 1-47

<sup>9</sup> Portelli A, 'The peculiarities of oral history', *History Workshop*, no. 12, Autumn 1981, p105

*the exploration of 'real life' behaviour, enabling research participants to speak for themselves.*

*Many quantitative researchers in the health sciences work from the assumption that there is an absolute truth, a 'reality', which they are trying to discover. For these researchers, knowledge is objective and neutral. This belief about knowledge has been called, 'objectivism' and the theoretical framework it implies is called 'positivism'. However the relevance of this objectivist belief about knowledge has been the subject of challenges since the end of the 19<sup>th</sup> century. Many of the challenges have come from studies of social phenomena, such as individual or group behaviour. Most qualitative researchers today share a different belief about knowledge, called 'constructivism', which holds that the reality we perceive is constructed by our social, historical, and individual contexts.<sup>10</sup>*

The oral history used in this thesis includes qualitative research tools used in interviews, such as semi-structured questions, open questions, verbal recording and in two instances iterative interviews. The witness data were incorporated in the thesis to amplify specific issues which were germane to the history, which might not be so effectively elucidated in other approaches. This allowed the voices of participants to be heard describing their experiences and contributing to the history in their own words, raising issues of importance which otherwise might be concealed and thereby enriching the narrative. The data were obtained by interviewing 28 participants in two periods of time, 2003 and 2010-11 and a history was constructed which addresses some of the important background events of the topic under examination, which are not to be found elsewhere, except sometimes in sources such as published autobiographies. As part of the taught curriculum for Master of Philosophy degree in History, the author was trained in the techniques of oral history. The first five testimonies, (T1-T5), were recorded in 2003 as part of a piece of research for a Master of Philosophy degree dissertation. The remaining testimonies (T6-T28) were recorded between 2010 and 2011.

Before proceeding with this project, the research proposal was discussed with supervisors for approval and advice. An application was then submitted to the University of Glasgow, Faculty of Medicine's Research Ethics Committee. Part of the consent involved the production of an information sheet for the participants and a consent form which met with the approval of the Ethics Committee. The application was agreed, (FM00508), and

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<sup>10</sup> Kuyper A, Reeves S, Levinson W, 'Qualitative research: An introduction to reading and appraising qualitative research', *British Medical Journal*, Aug 16<sup>th</sup> 2008, 404-7

recorded interviews were arranged. The project was undertaken subject to the ethical guidelines of the Oral History Society.<sup>11</sup> A strategy for recruitment was devised and the recordings made using a digital recorder over the period of almost a year and not in any particular order. The interviews were transcribed by a medically trained typist. The testimonies generally required light editing to remove repetition or unhelpful speech mannerisms. Each testimony was then returned to its witness who was invited to make changes or corrections where necessary and to supplement his or her testimony if unclear.

## 1. 2. 2: The participants

The witnesses who participated worked in the community and in the hospital service. Two pharmacists were interviewed who had trained in the 1950s and spent their professional lives mainly working as pharmaceutical retailers. Two drug company representatives were interviewed, one who worked in the general practice sector and one who covered hospitals, both employed by what became GSK (GlaxoSmithKline), one of the world's largest pharmaceutical companies. A major part of GSK's economic growth came from the sales of 'Zantac' which was an anti-ulcer drug and at one time had the largest sales of any prescription drug in the world. Four general practitioners were interviewed, and six hospital-based gastroenterologists who had begun their careers at a time when this medical specialty was being established in the UK, three of whom were involved in peptic ulcer research. Five surgeons were interviewed, who had spent a large part of their professional lives treating patients with gastric and duodenal ulcers. One radiologist and two pathologists added their experiences. Peptic ulcer remains a problem in the elderly and two geriatricians were interviewed. Ulcers of the stomach and duodenum are less common in childhood, but interviews with two paediatricians shone light on other aspects of this particular disease with quite unexpected results. Finally two senior nurses were interviewed and graphically described their experiences of peptic ulcer as a 'hands-on' problem. All the witnesses worked in Scotland for at least some part of their careers but no attempt has been made to suggest that there was a particular local dimension to their experience which made the disease somehow different here, other than the fact that it was very common in Scotland. There would have been merit in seeking the testimonies of patients who had suffered from peptic ulcer disease to place alongside the testimonies of those who were involved in treating their illness. A conscious choice was made not to

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<sup>11</sup> The ethical guidelines of the Oral History Society may be found at [www.oralhistory.org.uk/ethics/index.php#eg](http://www.oralhistory.org.uk/ethics/index.php#eg), Oct 20<sup>th</sup> 2011.

undertake this task because of limitations on time and resources, but it was recognised that that this could be a useful line of enquiry for future research. Medical understandings of the complications of peptic ulcer disease at a symptomatic level are well described in the thesis both in the text and in articles which were used in references.

The author's professional experiences played a part in recruitment, having worked as a general practitioner from 1974 until 2007. Knowing 'how things worked' helped selection of participants and a medical background opened the door to introductions to witnesses. Recruitment was mainly by the process known as 'snowballing', whereby witnesses who participated in the project made suggestions of the names of those known to them who might also contribute. Recruitment began with a telephone call to the proposed witness, and in the majority of cases an enthusiastic response was obtained. A formal letter with an information sheet was then sent to them and a date arranged for the interview. Most interviews took place in the homes of the witnesses but in a few exceptions public places were used. Using a semi-structured format with some pre-planned questions, the interviews centred around the professional development of the participants and out of this the questions were directed to peptic ulcer and their experience of the disease.

Part of the richness of the data obtained is found in the background history provided by first-hand descriptions of professional activities which describe a now-lost world. One witness (T6), wrote an essay about his early training as a pharmacist and others added one or more written paragraphs to the end of their oral testimonies. Two witnesses were re-interviewed to answer a number of questions which had arisen in their testimonies that required clarification or expansion. Another witness gave further clarification by letter. The transcripts of the testimonies are stored in a bound record in the library of the Royal College of Physicians and Surgeons of Glasgow and will in due course be accompanied by this MD thesis. It is a volume of over 216,000 words in 446 pages and may be seen subject to normal restrictions applied to such research material.

### 1. 3. Dyspepsia and the problem of diagnosis

In the eighteenth century, 'dyspepsia' was regarded as a disorder of nervous function, later changing in the minds of practitioners to one whereby the whole body was affected by the disordered stomach in a process called 'sympathy', of which more is written in chapter

three.<sup>12</sup> James Rhymer, an eighteenth-century surgeon, wrote about it in his *Treatise upon Indigestion and the Hypochondriac Disease*,

*That derangement of health termed dyspepsy and indigestion or morbid affection of the stomach; and the hypochondriac disease, the vapours or low spirits; are distempers generally blended with each other, and with the atonic or flying gout; and also with every affection of the system purely nervous ... The stomach is an organ of the first importance in the animal body. If it be in the slightest degree disordered, the affection is felt more or less throughout the system.*<sup>13</sup>

A contemporary physician, Robert Squirrell, described the symptoms of indigestion as follows; ‘Diminution or total loss of appetite, sometimes vomiting, especially in the morning, bad taste in the mouth, foul tongue, distension, and pain in the stomach and bowels, particularly after meals, eructations, etc.’<sup>14</sup> Squirrell, along with most of his contemporaries, also contended that there were causal links to gout and ‘debility of the nerves in general’ among many other features.<sup>15</sup> By the nineteenth century, ‘dyspepsia’ had become virtually synonymous with ‘indigestion’ and many books were written on the subject.<sup>16</sup> After accounts of William Beaumont’s experiments on gastric digestion were published in 1838, the workings of the stomach could be seen to have a psychic input, (psychological) of which more is written in subsequent chapters.<sup>17</sup> ‘Indigestion’ is another vague term used to describe symptoms referable to the stomach which was commonly linked to the term dyspepsia in the nineteenth century. Gastric and duodenal ulcers would be found amongst other causes of dyspepsia.

‘Biliousness’ was a term which became fashionable in the nineteenth century and Thomas Carlyle claimed to suffer from it all of his life and used the term interchangeably with dyspepsia.<sup>18</sup> John Gibson included the symptoms of biliousness with the symptoms of

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<sup>12</sup> Gibbs D, ‘The demon of dyspepsia: some nineteenth-century perceptions of disordered digestion’ in *Gastroenterology in Britain: Historical Essays*, ed Porter R, (London, 1997, Wellcome Institute for the History of Medicine), pp29-42

<sup>13</sup> Rhymer J, *A Tract upon Dyspepsy or Indigestion, and the Hypochondriac Disease*, (London, Paternoster Row, 1795, Thomas Evans), pp1-2

<sup>14</sup> Squirrell R, *An Essay upon Indigestion and its Consequences*, (No. 7 Denmark Street, London, 1795, sold by the author), pp1-2

<sup>15</sup> Squirrell R, *An Essay*, *ibid*, pp8-9

<sup>16</sup> Gibbs D, ‘The demon’, *op cit*, p34

<sup>17</sup> Beaumont W, *Experiments and Observations on the Gastric Juice and the Physiology of Digestion*, *Reprinted from the Plattsburgh Edition*, (Edinburgh, 1838, Maclachlan and Stewart) pp100-07, 298-302,

<sup>18</sup> Porter R, ‘Biliousness’, in *Gastroenterology in Britain: Historical Essays*, ed Porter R, (London, 1997, Wellcome Institute for the History of Medicine), pp7-28

indigestion in his treatise of 1879 and treated them both with the same medicaments.<sup>19</sup> There was a strong link with perceived malfunction of the bowels in some cases of dyspepsia. ‘Great costiveness’ is listed as one of the features of dyspepsia as well as ‘profuse evacuations’ in a long list of symptoms extracted by historian Denis Gibbs from the thirteenth edition of John Quincey’s *Lexicon Physico-Medicum*, suggesting that perhaps the symptoms being described might now be classified as ‘irritable bowel syndrome’.<sup>20</sup> The process of linking particular abdominal symptoms with abdominal diseases was especially problematic.

John Abercrombie began the process of clarifying some causes and symptoms of abdominal pain with his published studies on peptic ulcer and other related conditions in 1824 and 1828.<sup>21</sup> This is discussed at length in chapter two. Doctors became more confident of making a correct diagnosis, usually of gastric ulcer, on the basis of agreed symptoms. Another term in use in the nineteenth century which presented with dyspeptic symptoms was ‘gastritis’. This is particularly interesting since it was a non-fatal condition in which there was no autopsy evidence of peptic ulcer. It was much written about by Abercrombie who believed that it preceded gastric ulcer. In 1828 he wrote, ‘We have every reason to believe that the mucous membrane of the stomach is liable to inflammation in a chronic form which also advances so slowly and insidiously that the dangerous nature of it may be over looked until it has passed into ulceration or has even assumed the characteristics of organic and hopeless disease.’<sup>22</sup>

## 1. 4: Nosology of gastric and duodenal ulcers in the nineteenth and twentieth centuries

The word ‘nosology’ means the study of disease, but in the eighteenth century it referred to the classification of diseases according to their symptoms.<sup>23</sup> In 1836, the UK Parliament passed an act creating the post of Registrar General for Births, Marriages and Deaths for England and Wales. Scotland followed in 1856 with its own office. William Henry Lister

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<sup>19</sup> Gibson J, *A Treatise on Bilious Diseases and Indigestion*, (London, 1799, Murray and Highley, J Harding and J Cuthill), pp3-5

<sup>20</sup> Gibbs D, ‘The demon’, op cit, p31

<sup>21</sup> Abercrombie J, ‘Contributions to the pathology of the stomach, the pancreas and the spleen’, *Edinburgh Medical and Surgical Journal*, Jan 1<sup>st</sup> 1824, 1-14 and Apr 1<sup>st</sup> 1824, 243-9 and Abercrombie J, *Pathological and Practical Researches of Diseases of the Stomach, the Intestinal Canal, the Liver and other Viscera of the Abdomen*, (Edinburgh, 1828, Waugh and Innes)

<sup>22</sup> Abercrombie J, *Pathological and Practical*, ibid, p17

<sup>23</sup> Rosner L, *Medical Education in an Age of Improvement*, (Edinburgh, 1991, Edinburgh University Press), p52

was the first Registrar General for Births, Marriages and Deaths for England and Wales, and an early problem which he faced, when he started to accumulate data for publication, was how to establish a working nosology. William Farr the chief statistician to the Registrar General office produced the mortality statistics, which were published in its first annual report.<sup>24</sup> His policy was to use diagnoses then in common use which were a mixture of symptomatic terms and what could be called pathological terms. Later in the century in 1847, 1853 and 1881 he amended his diagnostic terms in response to changes in medical terminological usage. The Registrar General's annual returns recorded diseases with fatal outcomes. With reference to fatal stomach diseases, the first, very limited, report for the year 1838 included 'peritonitis', 'gastric fever', 'gastritis', 'pyrosis', 'ulceration of the stomach' and 'dyspepsia', in the appendix which dealt with nosology. By 1857, 'gastritis', 'ulceration of the intestines', and 'diseases of the stomach, etc.' were the main diagnoses in the Causes of Death table of the Registrar General Report which could be interpreted today as being due to upper gastrointestinal diseases which were not of an infective origin. In 1881, 'gastric ulcer' was included alongside 'gastritis', 'other diseases of stomach' and 'ulceration of the intestines' with the other categories discarded. The disease nomenclature remained unchanged until 1911 when 'ulcer of the duodenum' was added.<sup>25</sup> Today, two of the diagnoses, 'gastritis,' and 'dyspepsia', used by the Registrar General in 1839, continue in general medical usage as diagnoses of non-fatal stomach disorders but the term 'pyrosis', which equates to 'indigestion', was no longer used in the second half of the twentieth century.

Chapter two of this thesis describes how it took the published works of John Abercrombie in Edinburgh from c1824, and of Jean Cruveilhier in Paris from c1828, to begin to change our understanding of stomach disorders, in particular gastric and duodenal ulcer, and how they presented symptomatically and their clinical outcomes.<sup>26</sup> Monographs on stomach-related subjects began to be published around 1850. Charles Evans Reeves was one such early author with *Diseases of the Stomach and Duodenum*, but possibly the most frequently quoted text was that written by William Brinton: *Lectures on the Diseases of the Stomach*.<sup>27 28</sup> In these books the authors followed the traditions of medical writing of half a century or more as they described stomach diseases and classified them, offering

<sup>24</sup> Farr W, *Appendix to the First Annual Report of the Registrar General of Births, Deaths and Marriages in England*, (London, 1839, H.M.S.O), p69

<sup>25</sup> This data was extracted from Annual Reports of the Registrar General of Births, Deaths and Marriages in England for the respective years stated.

<sup>26</sup> Cruveilhier J, *Anatomie Pathologique du Corps Humaine*, (Paris, 1829-33, JB Bailliere)

<sup>27</sup> Reeves C E, *Diseases of the Stomach and Duodenum*, (London, 1856, Simpkins Marshall & Company)

<sup>28</sup> Brinton W, *Lectures on the Diseases of the Stomach*, (Philadelphia, 1865, Lea and Blanchard)

explanations for their occurrences and suggestions for treatments. These books relied heavily on case examples described by their authors for pedagogical purposes. Later, textbooks began to be produced with chapters that discussed the clinical presentations of different individual pathologies to bring comprehensive order to them.

Another early example of a textbook of stomach diseases which followed this pattern was written by Wilson Fox in 1872.<sup>29</sup> Fox divided his book into two parts, with chapters on ‘symptomatology of the stomach’ and on ‘special diseases’. His chapters described four particular clinical conditions in detail as well as others which included chronic ulcer of the stomach and duodenum and cancer of the stomach. His book reflected the writings and opinions of a clinician of his time. The diagnostic labelling of these four conditions was based upon patients’ symptoms, for there had not been any invasive techniques used to make them. Some nineteenth-century medical practitioners believed that they could assess the degree of muscular activity of the stomach and attributed certain diseases to malfunctions of gastric motility. They asserted that gastric ulcer was associated with slow gastric emptying and duodenal ulcer with fast emptying. At this time, it was believed that these conditions were due to one of four possible causes: the stomach’s motility as a muscular organ was defective, the mind affected the function of the stomach, it was inflamed, or it was producing too much secretion. They are briefly described as follows:

## 1. 5: Fox’s classification

### 1. 5. 1: Atonic dyspepsia

The diagnosis of atonic dyspepsia was based on four clinical observations. The first was the minor degree of gastric uneasiness and the absence of epigastric tenderness. The second was simple lack of appetite and thirst. The third was the absence of pyrexia, and the fourth was the condition of the tongue ‘which exhibits no sign of irritative action of the gastrointestinal tract but is pale, broad and flabby’.<sup>30</sup>

### 1. 5. 2: Neurosis of the stomach

The symptoms of neuroses of the stomach were; pain, vomiting and what was called ‘certain forms of hypersecretion’. The diagnosis was based upon five main features:

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<sup>29</sup> Fox W, *Diseases of the Stomach*, (London, 1872, Macmillan & Co). Another which follows a similar pattern was written by Samuel Habershon, *On Diseases of the Stomach, the Varieties of Dyspepsia, their Diagnoses and Treatment*, 3<sup>rd</sup> ed (London, 1879, J&A Churchill). There are many more such books, including in the French language.

<sup>30</sup> Fox W, *Diseases of the Stomach*, *ibid*, p59

1. 'The constitutional state which predisposed to nervous excitability and in particular the presence of great exhaustion or the hysterical diathesis'. 2. 'The presence of the causes of sympathetic irritation'. 3. 'The disproportion observed between the severity of the gastric symptoms and the general state of the patient'. 4. 'Frequent complete remissions of pain'. 5. 'Pain occurring when the stomach is empty and relieved by food', which Fox said was, 'almost distinctive of its nervous origin'.<sup>31</sup>

### 1. 5. 3: Acute gastritis or acute gastric catarrh

Fox defined acute gastritis or acute gastric catarrh as 'an acute disorder of the stomach characterised by depression and prostration, with or without pyrexia, by anorexia, nausea and vomiting and severe cases by pain after food and depending on an inflammatory condition of the mucous membrane'.<sup>32</sup>

### 1. 5. 4: Chronic gastritis or obstinate chronic dyspepsia

Of chronic gastritis or obstinate chronic dyspepsia Fox said, 'The symptoms of this disorder are primarily those of indigestion of an aggravated kind but they are often varied and very irregular in their course'. Fox included 'hypochondriasis' and 'nervous derangement', describing it as, 'being difficult to distinguish from chronic catarrh which tended to cause more vomiting'. The symptoms of hypochondriacal affections were often simultaneously present with chronic catarrh.<sup>33</sup>

Fox's classifications based on symptoms did not last long because other authors chose to regroup symptoms under different headings. William Pepper's textbook included them in the chapter, 'Functional and inflammatory diseases of the stomach'.<sup>34</sup> Its author, Samuel Armour, retained the diagnoses of 'atonic dyspepsia', 'gastralgia', 'acute gastritis' and 'chronic gastritis'. All of these conditions had different characteristics and were assumed to be individually treatable. Many of these diagnostic labels persisted over the succeeding decades, although some disappeared or diminished in importance. William Osler devoted eleven pages to dyspepsia and from an examination of his and others writings it appears

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<sup>31</sup> Fox W, *Diseases of the Stomach*, *ibid*, pp77-92

<sup>32</sup> Fox W, *Diseases of the stomach*, *ibid*, p97

<sup>33</sup> Fox W, *Diseases of the Stomach*, *ibid*, p139

<sup>34</sup> Armour S G, 'Functional and inflammatory diseases of the stomach', in *A System of Practical Medicine by American Authors*, ed Pepper W, vol. 2, (London, 1885, Sampson Lowe, Marston, Searle and Rivington), pp436-79

that the symptoms described are similar to those of gastric ulceration without the typical pain which was thought characteristic of gastric ulcer.<sup>35 36</sup>

Despite its ambiguity, the word ‘dyspepsia’ continues in use today because of its usefulness, for medicine still needs shorthand terms for conditions that are not understood. The term was revived in the twentieth century as ‘non-ulcer dyspepsia’ or ‘functional dyspepsia’. It has been redefined many times, but all definitions retain much of what Squirrell wrote in 1792.<sup>37</sup> A working party set up in 1988 to tackle the problem decided on the following definition: ‘upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptom considered to be referable to the proximal alimentary tract’. The inherent difficulties in the consideration of dyspepsia were addressed:

*Dyspepsia may be an early symptom of a serious illness, such as peptic ulceration, cholelithiasis<sup>38</sup> or gastric carcinoma, but often no organic cause is found. Dyspepsia has considerable implications for individual suffering, medical workload and financial cost. Nearly half the gastroenterological workload involves the management of patients in whom no organic lesion can be identified: many have dyspepsia<sup>39</sup>. The majority are treated in General Practice. No agreement has yet been reached on the definition, classification or management of dyspepsia. Even the term ‘dyspepsia’ is not universally understood ... dyspepsia defies definition.<sup>40</sup>*

The task for a historian is to make sense of a disease which was until the twentieth century only understood in life from its symptoms which were not easily correlated with its pathology. The first advances in understanding the nature of peptic ulcer disease, or at least some of it, came by relating the findings at autopsy to the symptoms in life of those who had died. Until the medical profession had the means of ‘seeing into the body’ by X-rays or by direct visualisation of the stomach by instruments in life or indirectly by test meals, the only tools available to doctors were history-taking from the patient and thorough physical examination. These clinical skills proved successful for the doctors in making

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<sup>35</sup> Osler W, *The Principles and Practice of Medicine*, (Edinburgh and London, 1892, Young J Pentland), pp348-359

<sup>36</sup> Brinton W, *Lectures on the Diseases of the Stomach*, op cit, pp554-5

<sup>37</sup> Squirrell R, *An Essay*, op cit, pp1-2

<sup>38</sup> Cholelithiasis is the medical term for gallstones.

<sup>39</sup> A lesion is any abnormality in the tissue of an organism usually caused by disease or trauma

<sup>40</sup> Colin-Jones D G, ‘Management of dyspepsia: report of a working party’, *The Lancet*, Mar 12<sup>th</sup> 1988, 576-9

diagnoses of peptic ulcer disease in most situations and their confidence grew with experience.

Until the end of the nineteenth century surgeons had had poor outcome results when they operated for the acute life-threatening complications of peptic ulcer disease but when they eventually began to experience successes, albeit initially few in number, they were able to directly visualise disease processes in life. They became increasingly aware that there were many abdominal conditions which could mimic the symptoms of peptic ulcer disease. Newly invented instruments for investigating peptic ulcer disease are described in an article published in 1898 most of which have passed into obscurity.<sup>41</sup> However, included in this list of instruments was an early gastroscope with moving parts which illuminated the inside of the stomach by an electrically-powered lamp.

Other successful inventions were developed further in the twentieth century including test meals to assess gastric acidity, and bismuth meal X-rays to outline the upper gastrointestinal tract and thereby visualise ulcers of the stomach and duodenum indirectly. Direct visualisation of the inside of the stomach, via the gastroscope, began to become part of some doctors' diagnostic armamentarium in the 1930s.<sup>42</sup> Peptic ulcer was diagnosed mainly at the bedside or in the clinic and for the most part it was treated medically. Today's doctors still rely on history-taking and physical examination and have access to a number of well validated tests and procedures to make the diagnosis. It is these tests and procedures, most notably endoscopy, which have led to accurate diagnosis. This new perspective on peptic ulcer disease raises questions about much of that which has been written about peptic ulcer disease before these tests were available.

## 1. 6: Dyspepsia revisited

Gerald Crean and his colleagues in 1994 published a comprehensive thirteen year prospective study of 1540 patients with dyspepsia in Glasgow.<sup>43</sup> It reveals what a complicated matter it was for a doctor to make an accurate diagnosis on clinical grounds alone. The terms 'functional' and 'non-ulcer' were applied to symptomatic conditions where there was no underlying lesion found in that proportion of the patients sufficiently ill to be seen by doctors. Indeed one third of emergency admissions with dyspeptic

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<sup>41</sup> Turck F B, 'A demonstration of intragastric instruments', *British Medical Journal*, Dec 24<sup>th</sup> 1899, 1865-8

<sup>42</sup> Witts L J, 'Haematemesis and melaena', *British Medical Journal*, Apr 24<sup>th</sup> 1937, 847-2

<sup>43</sup> Crean G P, Holden R J, Knill-Jones R P, et al, 'A database on dyspepsia', *Gut*, Feb 1994, vol. 35, issue 2, 191-202

symptoms in the study were found to have no ‘organic’ cause, i.e. no lesion was found, to explain their symptoms, which had been sufficiently severe to necessitate hospitalisation.

Crean and his co-workers had hoped that they would be able to make accurate differential diagnoses on symptoms alone and the purpose of this computer-based study was to devise a way to ‘weight’ symptoms to increase their diagnostic sensitivity. They adopted the term ‘indicants’, coined by Card and Good in a paper on the logical foundations of medicine which analysed how doctors made decisions based on complex information including experience managing the condition. An ‘indicant’ was a symptom which might point more strongly to one or other disease.<sup>44</sup> Doctors had hitherto sought the ‘pathognomonic’ sign to confirm a diagnosis.<sup>45</sup> The study’s outcome did not yield any diagnostic indicants and served to reinforce the view that dyspepsia was an extremely complex syndrome which was difficult to unravel without the aid of tests. A major strength of the paper was that it contained an extensive database of all the symptoms and presentations of dyspepsia and one of its ultimate conclusions was that 39% of those patients in the study with dyspeptic symptoms did not have demonstrable peptic ulcer disease or any other organic disease.

If it is as difficult as this for today’s doctor to make an accurate clinical diagnosis in patients with dyspepsia, how much harder was it for his forebears who had only what they believed were ‘indicants’ and physical examination from which to make their diagnosis? The implications of this are clear; that what has been written before, where the diagnosis was based upon clinical diagnostic methods alone, has to be treated by a historian with some reserve. Crean’s research was not a new revelation. In 1857 William Brinton discussed the difficulties of distinguishing between the symptoms of dyspepsia and gastric ulcer. He was confident that there was a particular presentation of three symptoms which made for a definitive diagnosis of gastric ulcer. These were a pain pattern initially, perhaps mild but ultimately assuming a gnawing nature and accompanied by vomiting and bleeding from the stomach. He conceded that, ‘an absolute enforcement of this rule of diagnosis would lead us to overlook a vast number of cases’. Brinton accepted that distinguishing between dyspepsia and gastric ulcer ‘is by no means easy’, in a lesser number of cases.<sup>46</sup> In 1977 Michael Sheppard and colleagues examined 250 patients with

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<sup>44</sup> Card W I, Good, I J, ‘Logical foundations of medicine’, *British Medical Journal*, Mar 21<sup>st</sup> 1971, 718-20

<sup>45</sup> A ‘pathognomonic’ sign is a particular sign or medical finding whose presence means that a particular disease is present beyond any doubt.

<sup>46</sup> Brinton W, *On the Pathology, Symptoms and Treatment of Ulcers of the Stomach*, (London, 1857, John Churchill), pp105-9

peptic ulcers using endoscopy, which today is considered to be the most accurate diagnostic method of diagnosis of gastric and duodenal ulcer. In the summary of their article they stated:

*Clinical features and laboratory data are presented for 100 patients with benign gastric ulceration and 150 patients with duodenal ulceration confirmed endoscopically in a district general hospital unit. Abdominal pain was the commonest indication for endoscopy, but one third of examinations were performed for acute gastrointestinal haemorrhage. Although the patients were selected for referral by endoscopy, their clinical presentation, age and sex distribution were similar to those reported in previous general surveys. There were no clinical features which clearly distinguished between gastric and duodenal ulceration.*<sup>47</sup>

There is no doubt that the clinical manifestations of diseases undergo change with time but it may be that the percentages of those with non-ulcer dyspepsia and those with ulcer dyspepsia, have altered over the years because of improved diagnostic techniques.<sup>48</sup>

One of the main historical databases for the study of the epidemiology of peptic ulcer disease is the death statistics in the Registrar General of Births, Marriages and Deaths Annual Returns. The vast majority of the registered deaths in the nineteenth century were certified on the basis of a doctor's clinical judgement but some deaths were registered without any ante-mortem medical input. Very few of the recorded causes of death were confirmed by autopsy. The history of peptic ulcer today has been heavily influenced by the use of the Registrar General's data by authors such as Jeremy Hugh Baron and Amnon Sonnenberg who appear to have accepted them at face value as 'facts', using them statistically to make assertions about the changing epidemiology of peptic ulcer disease. A discussion of their work appears later in the thesis, most especially in chapter five. One can also look to other sources, such as autopsy records, but these are problematic as sources from which to draw inferences regarding disease prevalence since they represent a selected population. The historian's problem arises from a paucity of statistical information in the past and the necessity to use indirect methods which in themselves may not be appropriate. It is one intention of this thesis to criticise some of the extant history later, keeping in mind

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<sup>47</sup> Sheppard M C, Holmes G K T, Cockel R, 'Clinical picture of peptic ulcer diagnosed endoscopically', *Gut*, Jul 1977, vol. 18, issue 7, 524-30

<sup>48</sup> As diagnostic methods improved and as surgeons increasingly intervened in symptomatic cases, concepts of 'organic' and 'functional' stomach disorders were continually revised.

the difficulties inherent in diagnosis, and to question the received history by re-examining its evidence base.

## 1. 7. 1: Philosophies of health, disease and illness

A recurring issue in the study of peptic ulcer disease is the fact of a patient having an ulcer and being asymptomatic or alternatively of a patient having the symptoms of peptic ulcer and having no ulcer. This raises the medico-philosophical issue of disease and health as concepts, which in turn have practical implications. The concept of lesion-based diagnostic criteria arose in Europe in the late eighteenth and early nineteenth century when diseases themselves began to be believed in early pathological terms to be the consequence of tissue alterations found in the corpse at autopsy. For many centuries before, health had been seen in terms of the Greek notion that disease was a matter of bodily imbalance. Other explanations including supernatural interventions by malign forces were available within the society at this time.<sup>49</sup> Health was considered to be the result of lifestyle choices and good health in particular was what kept a person out of the hands of medical practitioners. René Leriche, the nineteenth-century French physician, said, ‘Health is life lived in the silence of the organs’ and ‘Disease is what irritates men in the normal course of their lives and work, and above all, what makes them suffer.’<sup>50</sup> There are many possible philosophical answers to the question of what health is and two are briefly noted here. Ingmar Pörn writing in Helsinki in 1984 states that: ‘Health is the state of a person which obtains exactly when his repertoire is adequate relative to his profile of goals.’<sup>51</sup> In other words, the person only considers him or herself to be ill if he or she is prevented from living life in the way in which he or she chooses. Another Nordic philosopher, Lennart Nordenfeldt, proposes that, ‘Unhealth or disease should be defined in terms of disability or handicap.’<sup>52</sup>

Christopher Boorse reproduces the medical concept that health is the absence of disease in his paper, ‘Health as a theoretical concept’, which examines many aspects of health to promote his proposition. Its main characteristics are ‘biological functioning and statistical normality’.<sup>53</sup> It is also regarded as ‘scientifically validated’ because it classifies diseases in

<sup>49</sup> Porter R, *The Greatest Benefit to Mankind: A Medical History of Humanity from Antiquity to the Present*, (London, 1997, Fontana Press), p33

<sup>50</sup> Quoted in Canguilhem G, *The Normal and the Pathological*, (New York, 1989, Zone Books), p91

<sup>51</sup> Pörn I, ‘An equilibrium model of health’, in *Health, Disease, and Causal Explanations in Medicine*, eds, Nordenfeldt L, Lindahl B E B, (Dordrecht, 1984, D. Reidel Publishing Company), p5

<sup>52</sup> Nordenfeldt L, ‘On the circle of health’, in *Health, Disease, and Causal Explanations in Medicine*, eds Nordenfeldt L and Lindahl B E B, (Dordrecht, 1984, D. Reidel Publishing Company), p18

<sup>53</sup> Boorse C, ‘Health as a theoretical concept’, *Philosophy of Science*, 1977, vol. 44, 542-73

terms of objective observable concepts such as, say, heart disease or cancer. The issue of latent and asymptomatic disease is covered by his definition since such diseases may be detectable as variants from the normal on biological testing. Boorse's view of health is 'value-free', since he confines his definitions to that which is objectively measurable, discarding the effect of the illness upon the patient. Boorse's view is called the 'naturalist' view of disease and is one disease model currently used by health provision planners in making decisions on how to allocate their resources. It claims a 'value-neutral' perspective, but in an age where healthcare is currently under pressure, rationing is a fact of life and some criteria are required to prioritise those diseases which society sees as being important to treat.

When health is viewed from a value-laden perspective, i.e. taking social aspects of illness into account, this philosophical approach is called 'normativist'. Nordenfelt, quoted above, is a supporter of this position which he calls the 'Holistic Theory of Health' which he contrasts with Boorse's 'Biostatistical Theory of Health'.<sup>54</sup> The normativist approach recognises that there is a social aspect to every illness and the ways in which the illness may socially handicap the person are taken into account.<sup>55 56</sup> Illness is the product of disease and belongs to the 'patient-half' of the health evaluation. Most philosophers believe that it cannot be removed from any discussion about health. A third philosophical point of view, characterised by the term, 'phenomenological', recognises the sufferer's perspective. William Fulford recognised that the traditional divide of naturalist and normative philosophies were weakened by what they both exclude in their terms of reference: naturalist philosophy sees illness solely as the effect of a disease process whereas the normativist philosophy sees illness in terms of its debilitating effects and the impact on society. He proposed a 'bridge theory' to try to bring both sides of the argument together, in order to accurately demonstrate that illness and disease do not operate in a vacuum but their contingencies are worked out in patients' lives.<sup>57</sup> George Kushf has joined the debate asserting that the two positions have more in common than appears to be the case.<sup>58</sup>

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<sup>54</sup> Nordenfeldt I, 'The concepts of health and illness revisited', *Medicine, Health Care and Philosophy*, Mar 2007, vol. 10, 5-10

<sup>55</sup> Carel H, *Illness: the Cry of the Flesh*, (Durham, 2008, Acumen Publishing), p12

<sup>56</sup> Fulford K W M, 'Praxis makes perfect: illness as a bridge between biological concepts of disease and social conceptions of health', *Theoretical Medicine and Bioethics*, Dec 1993, vol. 14, no. 4, 305-20. In this paper, Fulford gives a useful discussion about naturalism and normativism without using these terms.

<sup>57</sup> Fulford K W M, 'Praxis', *ibid*, 305-20

<sup>58</sup> Kushf G, 'An agenda for future debate on concepts of health and disease', *Medicine, Health Care and Philosophy*, Mar 2007, vol. 10, 19-27

The phenomenological approach, which has many of the features of Fulford's 'bridge theory', rejects a definition of disease couched in terms of biological norms and scientific criteria. The sufferer describes the experience of having an illness and how it impacts upon his or her life. Health as defined above becomes a relative matter, and in some senses an irrelevance to the sufferer, who has to get on with the business of living with illness and/or disability. There are elements of similarity of this third approach with that of the aforementioned René Leriche who does not specify illness in diagnostic terms.

The WHO defines health as, 'a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity'.<sup>59</sup> This is indeed a very high standard as a concept of health and, by its definition, there can be few who would be considered 'healthy', when the world's population is viewed from this viewpoint. Perhaps it is best thought of as aspirational rather than practical. In choosing to define health in terms of complete physical, mental and social wellbeing, a normativist perception is noted although a value judgement has been used to exclude other arguably important concepts for the enrichment of health, such as faith/religion or environment to name but two. In its work of trying to deliver health worldwide, the WHO does however resort to naturalistic concepts, as can be seen from its work on disease classification and nomenclature. Phenomenological aspects of health have also been studied as a means of assessing the delivery of healthcare provisions and one example, the Nottingham Health Profile, has been devised to examine patients' subjective comments about their health.<sup>60</sup>

*Comparisons of value in health-related activities must allow the perceptions of the patient an equal, if not greater, place than clinical evaluations. The subjective assessment of the patient may allow more successful interpretations of the impact that disease and treatment have on his or her quality of life, whereas objective indicators may merely be projections of professional mores.*<sup>61</sup>

In her moving monograph, *Illness: The cry of the flesh*, Havi Carel, a senior lecturer in philosophy in the University of the West of England, writes a review of health from a phenomenological perspective using her personal experience of severe ill-health as a framework in her exposition of her theme.<sup>62</sup> In her researches, she met others who were

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<sup>59</sup> World Health Organisation, *The Conceptual Framework for the International Classification for Patient Safety*, 2009, version 1.1, p10

<sup>60</sup> Hunt S M, McEwan J, McKenna S P, 'Measuring health status: a new tool for clinicians and epidemiologists', *Journal of the Royal College of General Practitioners*, Apr 1985, 185-8

<sup>61</sup> Hunt S M, McEwan J, McKenna S P, 'Measuring health', *ibid*, 185

<sup>62</sup> Carel H, *Illness*, op cit

disabled who did not perceive themselves as ‘unhealthy’ and enjoyed the lives they lived, despite the restrictions imposed by their disabilities. Of long-term illness she says,

*Long-term illness or disability redefines the relationship of the person to her world, and moreover transforms this world by altering and limiting it. As embodied persons we experience illness primarily as a disruption of lived body rather than a dysfunction of biological body.*<sup>63</sup>

Returning to the specific example of peptic ulcer disease, a man with a ‘silent’ or asymptomatic stomach or duodenal ulcer may consider himself in good health. He may never know that he has an ulcer and this may be found as a co-incidental finding should he die from another cause, if an autopsy were then performed which revealed the ulcer. When the man attended a medical practitioner with symptoms, however vague, then this might herald the possibility that he had a possible disease which in today’s way of thinking may be due to an underlying pathological condition. It is also possible that a patient who has been diagnosed with a peptic ulcer may become completely asymptomatic despite the fact that, if modern diagnostic means were used to examine his stomach or duodenum, the ulcer was completely unchanged from its symptomatic state when it first presented. In the pre-radiology days, when the only measure of health was based on signs and symptoms of disease, then absence of disease was assumed, in the absence of symptoms. By the definitions of Pörn, Nordenfelt or Leriche then the objectives of medical practitioners could be said to have been fulfilled by them in producing a symptom-free patient who was capable of living a life which, for the patient, seemed to be healthy.

In his book *The Normal and the Pathological*, George Canguilhem asks the question, ‘Do sciences of the normal and the pathological exist?’<sup>64</sup> He addresses the question of what is ‘normal’ by saying, ‘The normal man is not a mean correlative to a social concept, it is not a judgement of reality but rather a judgement of value.’<sup>65</sup> Canguilhem accepts that the goal of therapeutics is to obtain what is called normal, but what matters is the sick man’s desire to return to what he considers normal.<sup>66</sup> He further states, ‘it is life itself and not medical judgement which makes the biological normal a concept of value and not a concept of statistical reality.’<sup>67</sup> Canguilhem addresses the common perception that, in the concept of average, a physiologist may find an objective and scientifically valid equivalent of normal

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<sup>63</sup> Carel H, *Illness*, op cit, p76

<sup>64</sup> Canguilhem G, *The Normal*, op cit, p113

<sup>65</sup> Canguilhem G, *The Normal*, op cit, p119

<sup>66</sup> Canguilhem G, *The Normal*, op cit, p126

<sup>67</sup> Canguilhem G, *The Normal*, op cit, p131

or norm.<sup>68</sup> However he shows that adaptive behaviour produces many different physiologically normal results which are completely appropriate to the life or environment of the individual which might be considered inimical to another of, say, a different race. In concluding, Canguilhem declares, ‘Strictly speaking then there is no biological science of the normal. There is a science of biological situations and conditions called normal. That science is physiology.’ In referring to the role of medicine in the patient/doctor relationship, he says; ‘Thus it is first and foremost because men feel sick that medicine exists. It is only secondarily that men know, because medicine exists, in what way they are sick.’<sup>69</sup>

When a particular illness is recognised, especially if it is chronic, both medical practitioners and their patients can begin to co-operate in its management. A ‘social construction’ then is created which is the product of many elements which are in essence experiential and represent a form of reality not to be found in many purely ‘medical’ texts. It is patients who live with illness, it is doctors who accompany them on their medical journey and it is society which supports both patients and doctors alike by its approval and/or resources. One of the rôles of the doctor is to provide explanations of the patient’s disease and this is used by both parties in the coping mechanism.

Peptic ulcer disease has its own social construction, built up over many generations of suffering. It began to acquire its identity through refinement of diagnosis after 1824, as a consequence of the early researches of such as Abercrombie and Cruveilhier, referred to previously. In the years which followed, the accumulating knowledge of the condition allowed patients and their medical advisors to evolve a common understanding, which allowed individuals for the most part to live with it. Within the UK, especially after the inception of the NHS, peptic ulcer was realised to be an illness which caused debility and mortality and Parliament eventually made allowances for its sufferers and those who also suffered from other serious illnesses, by providing, where necessary, medical support in the surgery, the clinic and in the hospital as well as financially through social security. Now doctors have found the means to cure patients with peptic ulcers who formerly would have experienced long periods off work or dieting or family disruption. Peptic ulcer is no longer regarded as a chronic debilitating illness. The social construction surrounding peptic ulcer disease has thereby changed.

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<sup>68</sup> Canguilhem G, *The Normal*, op cit, pp151-79

<sup>69</sup> Canguilhem G, *The Normal*, op cit, pp228-9

In his paper, ‘Disease in history: frames and framers’, Charles Rosenberg makes the point that, ‘every aspect of an individual’s social identity is constructed – and thus also is disease.’<sup>70</sup> However Rosenberg avoided using the term ‘social construction’ in his writing in an attempt to set disease and illness within an historical and societal context. Instead he chose to use the term ‘framing’ to situate an illness within its society and time.<sup>71 72</sup> Some of his thoughts echo those of others quoted above.

*... disease is an elusive entity. It is not simply a less than optimum physiological state. The reality is obviously a good deal more complex; ... In some way disease does not exist until we have agreed that it does, by perceiving, naming, and responding to it.*<sup>73</sup>

The patient with a symptomatic peptic ulcer is a real person with a real problem and it is a doctor’s responsibility to attempt to alleviate it. In the nineteenth century, the vomiting of blood from what proved in some cases to be peptic ulcers was common and thought lightly-of, despite the known possibility that the bleeding could lead to death.<sup>74</sup> Physicians did employ regimens to deal with it in hospitals, or the same treatments were used in the home, but most patients probably did not seek help unless the bleeding was profuse. However as a consequence of better understanding of vomiting of blood by doctors, a quite different medical response to this life-threatening symptom has occurred and today lives are now not being lost to the same extent as before, possibly because of earlier presentation and effective therapies in hospital. This issue is discussed in chapter 4. In the case of peptic ulcer bleeding, it was the result of a new understanding of what constitutes health and what threatens it, that such change became possible. Philosophical discussions on health become relevant in the face of real illness.

## 1. 7. 2: Authors who have made a significant contribution to the history of peptic ulcer disease in the twentieth century

Denys Jennings, while working as an honorary research clinical assistant in the Radcliffe Infirmary in Oxford, in 1940, published an article in two parts in *The Lancet*.<sup>75</sup> This article has become the basis of the current understanding of the history of peptic ulcer disease by

<sup>70</sup> Rosenberg C E, ‘Disease in history: frames and framers’, *The Milbank Quarterly*, 1989, vol. 67, supp. 1, 1

<sup>71</sup> Rosenberg C E, ‘Illness, society, and history’, in *Framing Disease, Studies in Cultural History*, (New Jersey, 1997, Rutgers University Press), xiii-xxvi

<sup>72</sup> Rosenberg C E, ‘Disease in history’, op cit, 3

<sup>73</sup> Rosenberg C E, ‘Illness, society, and history,’ op cit, pxiii

<sup>74</sup> Budd G, *On the Organic and Functional Disorders of the Stomach*, (London, 1855, John Churchill), p122

<sup>75</sup> Jennings D, ‘Perforated peptic ulcer’, *The Lancet*, Mar 2<sup>nd</sup> 1940, 395-8; Jennings D, ‘Perforated peptic ulcer’, *The Lancet*, Mar 9<sup>th</sup> 1940, 444-7

most authors seeking to write an introduction on different aspects of peptic ulcer research. Jennings concedes early in the paper that there were fallacies in the collection of information from which a history of perforated ulcer can be constructed because published material is of a selected sample. He bases his assumptions of disease prevalence upon hospital statistics at a time when few patients with peptic ulcers were treated in hospital. As a consequence, Jennings accepts that the records of peptic ulcer disease contained in the medical literature of its time may not represent its prevalence in a societal context. This topic is discussed in chapter five of this thesis.

In the last forty years, Jeremy Hugh Baron and Amnon Sonnenberg have written extensively on the subject of peptic ulcer disease both individually and, later, jointly. By any standards, both men have made remarkable contributions to medical knowledge in the field of gastroenterology, especially of the upper gastroenterological tract. In a working lifetime Baron published 298 original articles on mainly stomach-related topics, which concerned contemporaneous aspects of scientific research, including much original research of his own, generating a regular output of papers throughout a large variety of medical publications.<sup>76</sup> A perusal of their titles shows that they covered many current issues in gastroenterology as they were emerging. Dr Baron retired from clinical practice in 1996, having begun to write reflective pieces on aspects of the history of peptic ulcer disease two years earlier, he continued to publish such articles regularly thereafter.<sup>77</sup>

Amnon Sonnenberg has published many articles on gastrointestinal disorders. In 1984, he began to publish papers examining cohort effects in peptic ulcer mortality in different nations using their death certification data. Sonnenberg's statistical researches show a clear 'birth cohort effect' which suggests that there was a communality of experience for persons sharing birth years which made them susceptible to certain illnesses, most notably peptic ulcer, and these illnesses affected different cohorts at different rates. It appears from Sonnenberg's written reflections on his use of this technique that no account is taken of the quality of the data he is inputting especially from the nineteenth century.<sup>78</sup> Several authors have shown how unreliable death certification was in Sweden, Bavaria and Bremen in Germany in the nineteenth century because death certification was undertaken by lay persons for much of the century. This issue is discussed in chapter five. Sonnenberg was

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<sup>76</sup> A *Web of Science* database search using 'Baron J H' with a time limit 1950-2014 and refined to 'gastroenterology, hepatology', yielded 298 articles

<sup>77</sup> Baron J H, 'The history of acid inhibition', *Yale Journal of Biology and Medicine*, May-Aug 1994, vol. 67, 97-106

<sup>78</sup> Sonnenberg A, 'The meaning of the birth-cohort phenomenon', in Marshall B J, *Helicobacter Pioneers*, (Victoria, 2002, Blackwell Science), pp57-61

influenced by the work of Susser and Stein who followed Denys Jennings' historical views regarding the apparent changes in gastric and duodenal ulcer prevalence over the nineteenth and twentieth centuries.<sup>79 80</sup>

Amnon Sonnenberg began a historical writing collaboration with Dr Baron in 2001, contributing ten articles in the first decade of the 21<sup>st</sup> century. In several of these pieces the two men have examined data from a variety of historical sources such as mortality statistics from official national sources and hospital and university records. As a research method, they have developed a technique of counting published accounts of gastric conditions and from the numbers obtained, they have drawn inferences about the prevalence of these conditions in the given time periods they studied. Two of these papers are examined in some detail in chapter five.

Martin Blaser is an American physician and established researcher in the field of microbiology and infectious diseases who has made a major contribution to modern concepts of the topic of *Helicobacter pylori* and its interrelationship with different aspects of peptic ulcer disease. In one of his publications, he relates the history of how duodenal ulcer was an almost unknown disease in the nineteenth century and became the dominant form of peptic ulcer at the beginning of the twentieth century, accepting the accounts proposed by Jennings and Sonnenberg.<sup>81</sup> David Graham is another clinician and writer on the topic of *Helicobacter pylori* and peptic ulcer disease. In his writings he has attempted to explain how the dramatic change occurred between the varying prevalences of gastric and duodenal ulcers in the nineteenth and twentieth centuries, on the basis of changes in diet, food preparation and storage, standards of living, sanitation and hygiene.<sup>82</sup> Both Blaser's and Graham's work is referenced in the writing of other researchers in *Helicobacter pylori* who accept the received historical view of the posited historical changes in peptic ulcer type prevalence.

On May 12<sup>th</sup> 2000, a Witness Seminar symposium was held at the Wellcome Institute for the History of Medicine in London with the title, 'Peptic Ulcer: Rise and Fall'. The programme consisted of four sessions which attempted to set out the history of peptic ulcer

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<sup>79</sup> Susser M, Stein Z, 'Civilisation and peptic ulcer', *The Lancet*, Jan 20<sup>th</sup> 1962, 115-9

<sup>80</sup> Sonnenberg A, 'Geographic and temporal variations in the occurrence of peptic ulcer disease', *Scandinavian Journal of Gastroenterology*, Jan 1<sup>st</sup> 1985, vol. 20, no. 1, 11-24 esp p11

<sup>81</sup> Blaser M J, '*Helicobacters* are indigenous to the human stomach: duodenal ulceration is due to changes in gastric microecology in the modern era', *Gut*, 1998, vol. 43, 721-7

<sup>82</sup> Graham D Y, Correspondence: 'Changing patterns of peptic ulcer, gastro-oesophageal reflux disease and *Helicobacter pylori*: a unifying hypothesis', *European Journal of Gastroenterology and Hepatology*, 2009, vol. 15, 571-2

disease in chronological order using the witness testimonies of senior medical professionals who had spent many years treating and researching peptic ulcer disease. It was a remarkable achievement to successfully gather together in one place such a representative group. It began with the introductory remarks of Sir Christopher Booth who said, ‘Peptic ulcer has unquestionably been a disease of the twentieth century. Rare before the end of the previous century, peptic ulcer became increasingly frequent, reaching a peak during the next 50 years and afflicting as many as 10 per cent of men.’<sup>83</sup> The symposium recorded the memories of the participants backed up by references to substantiate their statements. Noticeably absent were John Warren and Barry Marshall from Australia who first proposed the concept that peptic ulcer disease was caused, in the majority of cases, by a bacterium and could be treated by its eradication by antibiotics. The proceedings were recorded and published as a document which is a rich source of references and anecdotes, covering mainly the period from the inception of the NHS until the present time. It reflects the camaraderie of a cohort of eminent people who strove throughout their careers to help patients who suffered from a disease which has now become uncommon and which was highly resource-dependent during their working lifetimes. There are to be found within the document some residual traces of the controversy which accompanied the germ theory of ulcer genesis but the received history of peptic ulcer disease over two centuries is seen to be accepted without any questioning.

Dr Ian Miller is a contemporary author on the topic of diseases of the stomach and of the rôle they have played in history. His PhD thesis, *A Modern History of the Stomach: Gastric Illness, Medicine and British Society c. 1800-1950*, was accepted in 2009 and he has since embarked on a career as an academic historian.<sup>84</sup> He has published several articles on stomach related topics and much of his thesis has been published as a monograph.<sup>85</sup> Miller’s writing about the stomach is framed thematically within conceptual boundaries of his choice, which he uses to analyse his historical narratives. His themes of ‘The National Stomach’, ‘The Ulcerated Stomach’, ‘The Laboratory Stomach’, ‘The Surgical Stomach’ and ‘The Psychosomatic Stomach’, which are the titles of the five chapters of his PhD thesis and which he uses as the basis of other publications, give a flavour of his approach. Miller’s work complements the narrative contained in this thesis

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<sup>83</sup> Booth Sir C, in *Wellcome Witnesses to Twentieth Century Medicine, volume 14, Peptic Ulcer: Rise and Fall*, edited by D.A. Christie and E.M. Tansey, (London, 2002, The Wellcome Trust), pp i-ii

<sup>84</sup> Miller I R, *A Modern History of the Stomach: Gastric Illness, Medicine and British Society c. 1800-1950*, A thesis submitted to the University of Manchester for the degree of PhD in the Faculty of Life Sciences, 2009, pp143-150

<sup>85</sup> Miller I, *A Modern History of the Stomach: Gastric illness, Medicine and British Society, 1800-1950*, (London, 2011, Pickering & Chatto)

but emphasises different aspects of the history. One minor difference between the two works occurs in chapter four in the section on peptic ulcer disease in soldiers in the Second World War where Miller's analytical content is at variance with the account which I present. However there is agreement concerning the controversy over the 'rise' in the dominance of duodenal ulcer in the twentieth century, which I discuss in more detail in chapter five.

### Conclusion to chapter one

This chapter has set the scene for the thesis which follows, discussing the sources used for its structure and content and examining some of the difficulties faced by an historian in his or her interpretation of past events in terms of the nosology of peptic ulcer disease which changed over the years. Doctors faced problems in agreeing on the terminology to be used to describe peptic ulcer and this is explored also in its modern setting. Philosophical issues have been examined which come into play in matters of health and illness. These are particularly relevant to a disease such as peptic ulcer disease which may or not be symptomatically evident to the sufferer or even to his medical attendant until it is 'looked for' by investigations. The work of authors who have written about peptic ulcer disease is also discussed.

In the next chapter it will be seen how the medical profession as such emerged in the mid eighteenth century and gradually appropriated power to itself by undertaking academic training and later used the medical science of the nineteenth century to begin to displace the irregular healers with whom they were in competition. It will describe how the modern understanding of the pathology and physiology of peptic ulcers had its origins in the practice of autopsy and vivisection and stresses the importance of published research and concepts for the further development of disease concepts and treatments. Societal background and changes over the period will be discussed to show the healthcare options available to peptic ulcers sufferers in the UK in terms of personal treatment in the home and in the hospitals, if such were required.

## Chapter 2. Management and treatment of gastric and duodenal ulcers in Britain in the eighteenth and nineteenth centuries

### Introduction to chapter two

In today's world it is assumed that most health-related matters fall within the responsibility of the medical profession. However, there was no organised medical profession when this history begins, but it was recognised in 1858 by a Parliamentary Act which defined its characteristics. These medical professionals were groups of men who had undergone some kind of medical training and who were increasingly trusted in health matters, displacing relatively less well trained 'alternative practitioners' in medical situations paid for by the public purse. The provision of medical care remained a profitable business which had flourished in the virtually unregulated marketplace of eighteenth and early nineteenth-century Britain.<sup>86</sup> Medical self-help books made a significant contribution to health care at the time. Professional identity did not give registered practitioners an immediate advantage in terms of their marketability over their quack rivals. This still had to be individually and collectively earned by establishing a trusted position within society. Training and access to medical literature made some difference in terms of their standing but made little difference in terms of therapeutic results in any given situation. After 1858, their involvement with situations which only medically registered doctors could legally handle added to their influence which grew throughout the Victorian era.

Peptic ulcer in the eighteenth century was not seen as the sole property of doctors to treat. In an open market, sufferers could attend any healer of their choice, trained or untrained. The condition itself began to be understood as a distinct disease by doctors and surgeons who found recognisable lesions in the bodies of their patients after death in the autopsy rooms of Europe, most especially of Paris, beginning after the Revolution. Later pioneering surgeons saw these lesions in living patients, after the use of anaesthetics allowed painless exploration of the abdomen on the operating table. Throughout the nineteenth century, physiological discoveries made by animal vivisectionists and laboratory experimenters added to understanding of peptic ulceration. William Beaumont's ingenious scientific observations of his patient Alexis St Martin's stomach,

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<sup>86</sup> Porter R, *Bodies Politic: Disease, Death and Doctors in Britain, 1650-1900*, (New York, 2001, Cornell University Press), pp172-3

which became seminal to the understanding of the gastric stage of digestion, is briefly outlined because of its importance. An apparent gender specificity of peptic ulcer which entered the discourse about its cause is also discussed. Finally, it is shown how the hospital changed over the period, eventually becoming the main locus for the care and the treatment of the serious complications of peptic ulcer.

## 2. 1: The Medical profession as it developed from the eighteenth century until 1858

Today's concepts of medical practice, how doctors view illness and treat it, can be traced back before the mid-eighteenth century when a consensus began to grow amongst those who became 'the medical profession' in Europe, as to how doctors should be trained.<sup>87</sup> Throughout Europe, that which distinguished the medical profession from the 'irregular healers' was that intending practitioners underwent accepted forms of professional training. In France, formalised academic medical training, involving regular assessment by written examinations and leading to recognised qualifications which allowed men to practise as doctors, had been in place from 1707 and it survived the disruptions of the 1789 Revolution with some modification.<sup>88</sup> In the UK, 'irregular practitioners' (quacks), who had had no 'formal' medical training were noted for their use of published pamphlets to advertise and sell their wares. Some of them achieved great fame and wealth and were attended by patients from every level of society. They operated in an atmosphere where mystery, exaggeration and often fictitious claims played an important part in their therapeutic regimens. Roy Porter however makes the point that the often-stated view concerning the differences between quacks and regular practitioners were less than is commonly held,

*... in pre-modern medicine, there was far greater convergence between the activities and attitudes of regulars and quacks than either side commonly allowed, or than historians have been primed to perceive.*

*We continue to speak of the history of regular practitioners as the history of a profession, thereby deploying concepts nursed by the profession itself. As a result, the business of medicine remains neglected. When the development of medical entrepreneurship finally receives its due share of attention, it will become clearer*

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<sup>87</sup> Porter R, *The Greatest Benefit to Mankind: A Medical History of Humanity from Antiquity to the Present*, (London, 1997, Fontana Press) pp287-93

<sup>88</sup> Foucault M, *The Birth of the Clinic: An Archaeology of Medical Perception*, (London, 1973, Routledge), p44-5

*how far there truly were distinctions between the ways in which the 'typical' itinerant, and the 'typical' regular practitioner – both mythical beasts – drummed up custom and turned a penny: or whether the differences were as much matters of manner as of substance. Future socio-economic historians of medicine may find it profitable to examine the careers of quacks and regulars in tandem, rather than, as traditional, distinctly in separate genres of study.<sup>89</sup>*

In Britain, medical professional training included ward-round teaching in hospitals, observing autopsies, attending lectures given by the Society of Apothecaries and the colleges of the physicians and surgeons.<sup>90</sup> Medical training valued the wisdom of the past and actively followed the discoveries of the present, and from the early eighteenth century, increasingly aligned itself with dissection of the human corpse and the systematic collection of clinical data. Enlightenment thinking of the mid eighteenth century supported the new approach, with its respect for science and order and the apparent progressive nature of medicine, which was coming to be seen as 'scientific'. Using this particular model as its basis, new concepts of illnesses changed and these could be transmitted to others by publishing discoveries or medico-philosophical ideas in print.

In Edinburgh, a medical school was established at the University in 1726 which taught undergraduates in English.<sup>91</sup> Other aspiring doctors with the ambition, education and money could choose to travel to the Continent where teaching was in Latin in academic centres. From the mid-eighteenth century, in England, apart from the small number of university graduates, medical education was a matter of apprenticeship in which a young man learned from an established practitioner and attended classes located in a voluntary hospital or in a private medical school. The medical education provided by these bodies however was not broad based or academic and largely independent of the universities. The London Incorporation of Surgeons was involved with medical student teaching and awarded licences to practice to those who fulfilled the necessary class attendance and passed its examination which achieved the status equivalent of 'doctor'. The Society of Apothecaries also awarded licences - the Licentiate of the Society of Apothecaries (LSA), a qualification which allowed its possessor to practise medicine.<sup>92</sup> Christopher Lawrence puts it thus:

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<sup>89</sup> Porter R, *Quacks: Fakers and Charlatans in English Medicine*, (Stroud, 2000, Tempus Publishing Ltd), p208

<sup>90</sup> Rosner L, *Medical Education in an Age of Improvement*, (Edinburgh, 1991, Edinburgh University Press) pp1-24

<sup>91</sup> Porter R, *The Greatest Benefit*, op cit, pp290-2

<sup>92</sup> Porter R, *The Greatest Benefit*, op cit, p316

*... the most humble country surgeon and the most exalted hospital physician shared a number of assumptions, notably that attendance at medical classes, hospital experience and a qualification were the prerequisites of proper practice. Although there was division over what particular elements a medical education should contain, the broad outlines were rarely contested.*<sup>93</sup>

Before 1858 there were three disparate groups of practitioners in the UK comprising the mainstream of what became a unified medical profession. These were; the physicians, the surgeons and the surgeon-apothecaries, who were in effect the general practitioners of the time. Although the London medical colleges participated in medical training, one of their main preoccupations was the protection of the incomes of their fellows and members rather than educational improvement. They enjoyed status conferred upon them by Parliamentary statutes which protected their 'modi operandi'. These three groups achieved professional recognition in 1858 when Parliament passed the Medical Act which created a Medical Register that listed the names of all those qualified to practise medicine in the UK and set academic standards to be adhered to by those on it. The General Medical Council was also established to govern the profession on disciplinary matters and would later play a part in determining a necessary programme of medical education.<sup>94</sup> This Act of Parliament excluded irregulars from registration who nevertheless continued to compete with licensed medical practitioners for trade and the reasons for this are many.<sup>95 96</sup>

Patients at the financially higher end of the social ladder were wealthy enough to afford any kind of treatment but at the lowest end, much health care was informal from neighbours or other amateurs, some of whom might have had access to books on health and illness. Medical practice in this competitive market place could bring good rewards to its practitioners and there was much scope for those who could persuade the sick to avail themselves of their skills, but it was by no means a foregone conclusion that the sick would seek the offerings of trained medical men.<sup>97</sup> The paying patient generally dictated his or her treatment by the choice of practitioner, regular or irregular. Many patients could not afford the services of a qualified doctor and, in the eighteenth and nineteenth centuries, a

<sup>93</sup> Lawrence C, *Medicine in the Making of Modern Britain, 1700-1920*, (London, 1994, Routledge), pp7-52 esp p38

<sup>94</sup> Porter R, *The Greatest Benefit*, op cit, pp352-4

<sup>95</sup> Porter D, Porter R, *Patient's Progress: Doctors and Doctoring in Eighteenth-century England*, (Cambridge, 1989, Polity Press), pp16-29

<sup>96</sup> Porter R, 'Profession, fringe and quackery: the nineteenth-century transition', in *Health for Sale: Quackery in England, 1660-1850*. (Manchester, 1989, Manchester University Press), pp222-36

<sup>97</sup> Hamilton D, *The Healers: A History of Medicine in Scotland*, (Edinburgh, 1981, Canongate Publications), pp72-104

scientific view was no more worthy in terms of its beneficial outcomes than that based upon religion, superstition or old long-held ideas of health and illness. An editorial from *The Times* of April 1856, which insulted the medical profession, was reported in the *Association Medical Journal*: ‘There is so much of guesswork in medicine - the President of the College of Physicians is so nearly on a level with the meanest herbalist - the result of the longest, most varied, and most profound medical experience, is so often a discovery of the worthlessness of medicine, that we are not able to attach overwhelming importance to examinations in this department of science.’<sup>98</sup>

The Medical Act of 1858 conferred upon those on the Medical Register a protected status which hitherto they had not enjoyed and excluded the irregular practitioner. This allowed registered doctors only and exclusively to work in the hospitals, the poor law infirmaries and the armed forces, for Britain had a large standing army and navy to protect her interests both at home and abroad.

## 2. 2. 1: Morbid anatomy and the clinico-anatomical method

From the earliest times dissection of the human body after death was performed for either of two purposes: one was to learn about and teach human anatomy and the second, which were called ‘autopsies’, were performed for what would be now called ‘forensic reasons’ by those who wished to exclude foul play and satisfy themselves that death had been a natural occurrence.<sup>99</sup> From the sixteenth century, autopsies began to be performed more commonly and in 1679 Theophilus Bonetus produced a compilation of all the autopsies which he knew of from Galen onwards. In 1700, a second edition was produced in three volumes. Bonetus’ work, known by its shortened title, *The Sepulchretum*, was a major achievement in early autopsy history not bettered until 1761 when Giambattista Morgagni, then professor of anatomy in Padua, published his massive work, *The Seats and Causes of Diseases Investigated by Anatomy*, which made frequent references to *The Sepulchretum* but contained more detailed clinical and pathological descriptions.<sup>100</sup>

These autopsy reports revealed that the previous dissectors were not always able to interpret correctly what they were observing. Indeed when a perforation of the stomach was found at autopsy, it was believed to have been caused by the knife of the operator.<sup>101</sup> This report may have been familiar to Morgagni who was asked to examine a human

<sup>98</sup> Anon, ‘The week’, *Association Medical Journal*, Apr 5<sup>th</sup> 1856, 275

<sup>99</sup> The word ‘autopsy’ is derived from the Greek term, ‘to see for one’s self’.

<sup>100</sup> King L S, Meehan M, ‘A history of the autopsy - a review’, *American Journal of Pathology*, Nov 1973, vol. 73, no. 2, 513-44

<sup>101</sup> Baron J H, ‘Peptic ulcer’, *Mount Sinai Journal of Medicine*, Jan 2000, vol. 67, no. 1, 59

stomach brought to him by a colleague for an opinion as to the nature of the hole in the stomach at the site of a well developed ulcer which penetrated the full thickness of the stomach wall. Morgagni examined the lesion minutely, concluding that a knife wound during dissection could not possibly have caused the perforated ulcer.<sup>102</sup> In proportion to all other causes of death at the time, peptic ulcer was relatively infrequently found by the early researchers.

Morgagni's autopsy technique was thorough, examining all the organs systematically and in volume two of his great work, he has a section on 'diseases of the belly', where he discussed perforations of the stomach.<sup>103</sup> One feature of Morgagni's detailed autopsy records is that many of those bodies which he examined at post-mortem had often several different disease processes in different organs for which no explanation was made, they were simply recorded.<sup>104</sup> Morgagni's autopsy records make no mention of his examining solid organs by slicing the lungs, liver and brain; he simply examined and described their intact appearances. He did however open the heart and the stomach and intestines. With reference to peptic ulcer, Morgagni described the symptoms and the post-mortem appearances of stomach ulcers and other diseases of the stomach and it is evident from his writing that he had a clear concept of which organs and tissues were healthy and those which were the 'seat of disease'. Morgagni was thus an early proponent of a lesion-associated concept of disease linked to symptoms.

In the eighteenth century 'dyspepsia', was a common condition affecting the populations of Europe and the management of the condition was symptom-based and the treatments tailored to the perceived importance of these symptoms and the appearance of the patient when examined. At the end of this century, Matthew Baillie's writings reveal a descriptive pathological approach which included a clinical understanding which was symptom-based but nevertheless he believed that clinicians could learn from post-mortem appearances of the pathological changes associated with diseases. Baillie, nephew of John Hunter, had access to his uncle's collection of pathological and other specimens in London which consisted of a very large number of preparations exhibiting morbid appearances. He was elected physician to St George's hospital in 1787 which allowed him access to 'very frequent opportunities of examining diseases in dead bodies.'<sup>105</sup> In his 1793 book on

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<sup>102</sup> Morgagni G, *The Seats and Causes of Diseases Investigated by Anatomy; in Five Books Containing a Great Variety of Dissections with Remarks*, (London, 1769, Millar and Cadell), vol. 2, p34

<sup>103</sup> Morgagni G, *The Seats*, *ibid*, vol. 2, pp33-5

<sup>104</sup> Morgagni G, *The Seats*, *ibid*, vol. 2, pp46-8

<sup>105</sup> Baillie, M, *The Morbid Anatomy of Some of the Most Important Parts of the Human Body*, (London, 1793, Johnson and Nicol), 1<sup>st</sup> ed., ppvii, viii, ix,

morbid anatomy (pathology), the first to be written in the English language, Baillie recognises both the limitations and the potential of the clinico-anatomical approach.

*There are some diseases which consist only in morbid actions, but which do not produce any change in the structure of parts: These do not admit of anatomical inquiry after death. There are other diseases, however, where alterations in the structure take place, and these become the proper subjects of anatomical examination. ... It is very much to be regretted that the knowledge of morbid structure does not certainly lead to the knowledge of morbid actions, although the one is the effect of the other; yet surely it lays the most solid foundation for prosecuting such inquiries with success.*<sup>106</sup>

Baillie described gastric ulcer and pyloric stenosis in his first edition of 1793 and in a second edition in 1797, provided an excellent illustration of a gastric ulcer, but he offered no explanation of its nature.<sup>107, 108</sup> He also gave a very brief description of the symptoms of gastric ulcer.<sup>109</sup> Baillie was critical of Morgagni and others whom he felt spent too much detail in, ‘smaller collateral circumstances’, by which he meant mainly descriptive issues about illnesses and their impact upon the patient that Baillie considered irrelevant.

An illustration of another eighteenth-century view of autopsy findings is given by Guenther Risse who related an account of Andrew Duncan senior in Edinburgh in 1795 refusing to revise a diagnosis when confronted by the evidence of an autopsy which indicated a quite different cause of death.

*When Edinburgh instructors encountered unexpected post-mortem findings, they simply integrated them into their predetermined view of a given disease. Discussing a case with a long history of stomach complaints believed to be gout, Duncan admitted to his students that the surgeon in charge of the dissection had found a scirrhus growth suggestive of ulcer or cancer. “How far the scirrhus proceeded from the gout we can by no means satisfactorily say”, reasoned Duncan, “we know that the gout will produce tophi, anchyloses etc”. In the end Duncan remained dubious about the results of the autopsy. The possibility that the patient may not have been suffering from the gout or have had two separate diseases was*

<sup>106</sup> Baillie, M, *The Morbid Anatomy* 1<sup>st</sup> ed., *ibid*, preface, ppi-ii

<sup>107</sup> Pyloric stenosis is a complication of peptic ulcer disease where the stomach outlet mechanism called the pylorus becomes scarred and narrowed as a consequence of ulceration. See later for fuller description.

<sup>108</sup> Baillie, M, *The Morbid Anatomy*, 1<sup>st</sup> ed., *op cit*, pp87-8, pp140-1, pp 145-6 and Appendix, Illustration no.

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<sup>109</sup> Baillie, M, *The Morbid Anatomy of Some of the Most Important Parts of the Human Body*, (London, 1797, Johnson and Nicol), 2<sup>nd</sup> ed., pp152-3

*never raised. This approach seems characteristic of all cases copied into the casebooks or discussed in class and probably reflects the secondary importance ascribed to pathological findings, which were sought merely to illustrate preconceived diagnostic notions rather than shape new ones. No serious efforts were made to link the pathology to the patient's clinical manifestations or to use the lesions as criteria for redefining certain diseases.*<sup>110</sup>

## 2. 2. 2: Paris medicine

In the decades leading up to the Revolution in Paris, humoural medicine as practised and taught was little different from elsewhere in Europe and Parisian medicine of the *Ancien Régime* had its noted clinical teachers. One such was Joseph Dessault, a surgeon and anatomist whose pupil Marie François Xavier Bichat was greatly influenced by his friend and mentor. Bichat collected his master's works and three years after his death in 1798, published them. There is an earlier description of Dessault's clinical method recorded by Marc-Antoine Petit and published in 1794;

*Under the eyes of his listeners, he brought in the most seriously sick patients, classified their disease, analysed its features, outlined the action that was to be taken, carried out the necessary operations, gave an account of his methods and the reasons for them, explained each day the changes that had occurred, and then presented the state of the cured patients, or demonstrated on their lifeless body the alterations that had rendered further exercise of his art useless.*<sup>111</sup>

In the nineteenth century the hospitals in Paris became the setting for the new clinico-anatomical approach but before this, hospitals were overcrowded and unhygienic with infectious and infected patients mixed in with surgical patients. Erwin Ackerknecht informs us that in the Hotel Dieu, there could be up to five or six patients in a bed but after the Revolution, surgeons and physicians enjoyed the same rights inside and outside of hospital and in Ackerknecht's opinion their presence and influence was instrumental in improving the patients' lot. In particular they recognised the undesirability of patients with different diseases crowding and mixing in an atmosphere of stagnant air.<sup>112</sup> An autopsy was usually performed on the body of any Parisian patient dying in hospital and, from this

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<sup>110</sup> Risse G B, *Hospital Life in Enlightenment Scotland: Care and Teaching at the Royal Infirmary of Edinburgh*, (Cambridge, 1986, Cambridge University Press), pp265-6

<sup>111</sup> Petit, M A, *Éloge de Pierre Joseph Desault*, (Lyon, 1794, Les Halles), pp38-9 Translated by Sheridan, A. M. in Foucault M, *The Birth of the Clinic: an Archaeology of Medical Perception*, (London, 2003, Routledge), p73

<sup>112</sup> Ackerknecht E H, *Medicine at the Paris Hospital: 1794-1848*, (Baltimore, 1976, Johns Hopkins Press) pp15-22

source, a new understanding of illness emerged, which eventually was adopted by doctors throughout Europe at varying rates. The lesions which had been observed so frequently in association with diseases were now recognised to be the diseases themselves which were causing illnesses. Now that the clinical manifestations of the disease were conceived of as being lesion-based, doctors attempted to explain the effect of the lesion on the functioning of the body.<sup>113</sup>

This new way of understanding began to change medical thinking and eventually opened the way to modern laboratory based medicine. It also changed the relationships within the profession. Malcolm Nicolson puts it thus,

*In France reforms consequent upon the Revolution abolished the professional and educational distinction between surgery and physic and created a unified medical profession. The cognitive consequence of this union of the two disciplines was a body of medical knowledge in which internal disease was newly conceived of from a surgical perspective. That is to say internal disease was reconceptualised in localised structural terms as opposed to whole-body humoural pathology of eighteenth-century physic.*<sup>114</sup>

Pathological anatomy received a new-found impetus from the observations of such French clinicians as Bichat who noted the phenomenon of ‘tissues’. He observed that organs which were surrounded by tissues could look healthy while its covering tissues were diseased. An example is of the heart, enclosed within the pericardial tissues, which could function in the presence of disease of the pericardial tissue. He also taught that all the organs were in fact made up of tissues. Another famous clinician was Jean Nicholas Corvisart who taught internal medicine using the clinico-anatomical method and ‘astounded students with his accuracy in predicting by physical examination in life, the anatomical lesions which would be found at autopsy.’<sup>115</sup> This period of French medical history is replete with the names of men, who by dint of their efforts as physicians, surgeons and teachers deserve mention but space in this dissertation does not permit this. Nevertheless one man was particularly prominent in this time. From 1816, François Joseph Victor Broussais became an eloquent protagonist of his particular view of disease

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<sup>113</sup> See quotation later in this chapter by Dr Clutterbuck which illustrates the former way of understanding disease, in this case TB.

<sup>114</sup> Nicolson M, ‘Gerard Van Swieten and the Innovation of Physical Diagnosis’, in *Medicine and Change: Historical and Sociological Studies of Medical Innovation, Proceedings of the Symposium INSERM Held in Paris, 21-23 April 1992*, (London, 1992, John Libbey, Eurotext), 49-67, esp p57

<sup>115</sup> Gelfand T, *Professionalising Modern Medicine*, (Westport, 1980, Greenwood Press), p187

which reigned for twenty years. Those who write about Broussais say that his main attribute was his forceful personality which effectively swept away old ideas of disease, replacing them with his own. His achievement was to open a new way of thinking about the nature of disease although most of what he taught was later discarded in the light of new discoveries. His view of disease was called ‘localism ... which looked primarily for the tissue lesion instead of the symptom’.<sup>116</sup>

Michel Foucault says of Broussais,

*Everything in Broussais ran counter to his time, but he had fixed for his period the final elements of the way to see. Since 1816 the doctor’s eye has been able to confront a sick organism. The historical and concrete a priori of the modern medical gaze was finally constituted.*<sup>117</sup>

Dezeimeris, wrote of Broussais, saying that: ‘pathological anatomy has renovated medicine through him’.<sup>118</sup> Auguste Comte credited Broussais, rather than Philippe Pinel and Bichat, with having declared that all disturbances, acknowledged as such, are only symptoms and that disturbances of vital functions could not take place without lesions in organs, or rather, tissues.<sup>119</sup> Broussais, however is most remembered for his exanguinatory therapeutic interventions and his peculiar dogma that all illnesses were the consequence of gastroenteritis. The contents of his oratory, which changed the direction of Paris medicine, have largely been forgotten.

At the time, no doubt with Broussais’ assistance, the view of disease was transformed from a symptom-based lesion-associated concept to the belief that disease was manifested in lesions which could be seen at autopsy. The new way of practising and understanding the nature of disease that originated in the teaching hospitals of France which included physical examination in the clinic, the ward and the autopsy room, eventually became the pattern used to study disease in the rest of Europe, the British Empire and the USA from the second half of the nineteenth century. After 1815, foreign students were attracted to Paris to study the clinico-anatomical approach to medicine and the ready availability of corpses for them to observe and dissect was complemented with the excellent teaching of

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<sup>116</sup> Ackerknecht E H, ‘Broussais or a forgotten medical revolution’, *Bulletin of the History of Medicine*, 1953, vol. 27, 337

<sup>117</sup> Foucault M, *The Birth of the Clinic: an Archaeology of Medical Perception*, (London, 1973, Routledge), p192

<sup>118</sup> Dezeimeris J E, *Archives Générales de Médecine*, serie 1, num. 20, p164

<sup>119</sup> Quoted in Canguilhem G, *The Normal and the Pathological*, (New York, 1989, Zone Books), p47

good clinical practice for a part of their training in a manner which had not been done before.<sup>120</sup> According to Jens Lachmund,

*Disease was held to be a local anatomical lesion inside the body and had to be classified according to the visible alterations detected by autopsy. In order to prove the existence of such alterations at the sick-bed, physical diagnosis was considered more reliable than the more capricious symptoms on which the older medical semiotics centred.*<sup>121</sup>

In Vienna in the mid-nineteenth century, Carl Von Rokitansky and Joseph Skoda used pathology in medical education. Rokitansky became the most pre-eminent pathologist of his era by massive activity in the autopsy suite and the publication of his *Handbuch der Pathologische Anatomie*. The decades of unprecedented influence of Paris medicine were replaced by stagnation of ideas after around 1850 because its hospital practitioners and teaching academics refused to adopt the new tools of experimental physiology, chemistry and microscopy which were burgeoning in Germany. Ironically, France at this time had within its medical ranks men of the greatest stature working in these subjects but from a teaching and clinical point of view, they were largely ignored.<sup>122</sup> Ackerknecht sums up the French attitude as follows:

*The superb disdain in which French medicine held medical science was expressed quite simply and strongly by the fact that none of the following was ever a professor in a medical school: Bichat, Lagallois, Magendie, Flourens, C. Bernard, Brown-Sequard, Longet, Poiseuille, Paul Bert, Marey, Chevreuil, Dutrochet, Raspail, Donné, Davaine and Pasteur.*<sup>123</sup>

In 1850, the dominant French approach to the treatment of patients was mainly expectant with little intervention. This contrasted with the interventionalist approach prevailing in Britain as Ackerknecht quotes in the saying, 'The British kill their patients; the French let them die.'<sup>124</sup> Parisian medical education declined and some students migrated elsewhere for part of their education. The majority of UK medical practitioners trained in their home country in a regulated setting but the ideas emanating from Paris reached them through the written medium or from clinical teachers who had experienced them at first hand. Those

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<sup>120</sup> Ackerknecht E H, *Medicine at the Paris Hospital*, op cit, p191

<sup>121</sup> Lachmund J, 'Between scrutiny and treatment: physical diagnosis and the restructuring of 19th century medical practice', *Sociology of Health & Illness*, Nov 1998, vol. 20, no. 6, 779-801

<sup>122</sup> Ackerknecht E H, *Medicine at the Paris Hospital*, op cit, pp121-7

<sup>123</sup> Ackerknecht E H, *Medicine at the Paris Hospital*, op cit, p126

<sup>124</sup> Ackerknecht E H, *Medicine at the Paris Hospital*, op cit, p129

who were taught the Parisian way of practising medicine could not expect similar circumstances upon returning to their own countries but they promoted the practice of autopsy, which was increasingly became more acceptable to the public in the UK as its worth to medicine became recognised.

## 2. 3: The emergence of peptic ulcer as a recognised clinical and pathological entity

In eighteenth-century Edinburgh, William Cullen's writings included lectures giving detailed descriptions of gastritis, pyrosis and dyspepsia, with their symptoms, suggesting that external and internal sources might be their causes.<sup>125</sup> By this he meant things swallowed (external causes) or bodily disorders (internal causes), either of which could cause symptoms. Amongst his many thoughts about dyspepsia is found a comment that 'acidity' played an important part in its symptoms and he recommended alkalis as a treatment. His four volume, *First Lines of the Practice of Physic*, did not include any autopsies. However Cullen's extensive knowledge of Materia Medica is evident from his discussions on the effects of many agents, chemical and botanical, upon the stomach. He viewed the stomach as being sensitive to nervous affection emanating from the body as a whole and included 'dyspepsia' in his section on 'Neuroses'.

Cullen's ideas did not last and his disease classifications were attacked in the pages of *The Lancet* in 1825 by Dr Armstrong<sup>126</sup> and by Dr Nuttall.<sup>127</sup> Nuttall was particularly fierce in his criticism of Cullen's classifications of disease; 'In contemplating Cullen's classes, I never could behold anything like rational conception; I never could comprehend how he could think of pawning on the world, and the world allowing itself to be gulled by such a farrago of dissonant, undigested and bewildering conceptions.'

In 1824, John Abercrombie in Edinburgh was the first clinician to formally publish a comprehensive description of the symptoms of dyspepsia and similar conditions affecting the upper gastro-intestinal tract and identified them as a lesion-based disease, caused by ulcers of the stomach and/or duodenum, which often preceded death from perforation or

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<sup>125</sup> Cullen W, *First Lines of the Practice of Physic - A New Edition Corrected and Enlarged in Four Volumes*, (Edinburgh, 1788, C Elliot), vol. 1, pp416-31, vol. 3, pp217-48, vol. 4, p16. As has been stated in chapter one, nosology in the eighteenth century was mainly symptom-based although pathological diagnoses were to be found also.

<sup>126</sup> Armstrong (Dr), 'From lectures on the principles and practice of physic', *The Lancet*, Aug 27<sup>th</sup> 1825, 225-33

<sup>127</sup> Nuttall (Dr), 'Introductory lecture', *The Lancet*, Oct 15<sup>th</sup> 1825, 119-25

bleeding.<sup>128</sup> He carefully recorded his patients' symptoms and described their clinical progress. If they died, he examined their upper gastrointestinal tract by autopsy. Abercrombie linked the symptoms of indigestion, then called 'dyspepsia', to peptic ulceration, detailing them at length. He noted that many suffered from dyspepsia without fatal outcomes and that the symptoms came and went. He made an early distinction between gastric ulcer pain and duodenal ulcer pain and described the condition called 'gastritis'. He also described a case of perforation of the duodenum.<sup>129</sup> His pathological description of peptic ulcer would be acceptable in a modern textbook.

*The disease which is going on during this course of symptoms, consists of chronic inflammation, which in many cases appears to commence in a circumscribed portion of the mucous membrane of the stomach. The progress of it appears to be extremely slow; and it is probable that it may continue for some time, and then subside, and appear again after a considerable interval, until it at last gradually produces more permanent effects, in thickening of the coats of the stomach, adhesion to the neighbouring parts, and ulceration.*<sup>130</sup>

Few historians beyond Britain have recognised Abercrombie's contribution. In Paris, at the end of the same decade, Jean Cruveilhier published a lavish series of folio illustrations with written descriptions of fatal diseases which included a section on peptic ulcer. He noted a fact about peptic ulcer which has been repeatedly found at autopsy since then, 'It is not very rare to find an ulcer in a body which had had no symptoms'. He also noted the presence of 'ancient scars' in the stomach from old healed ulcers. Cruveilhier's publications eventually brought wide recognition to his work and 'Cruveilhier's disease' became synonymous with gastric ulcer.<sup>131</sup>

As Abercrombie and Cruveilhier were promoting the view that the lesion was in fact the disease, contemporaries continued to express the view that lesions were incidental and that the real cause of disease and death lay elsewhere. This is perfectly illustrated in a lecture by Dr Clutterbuck in 1825 where he makes it clear that pulmonary tuberculosis does not generally lead to death, rather that death is the consequence of illnesses where a continual state of bodily excitement eventually leads to exhaustion which is the actual killer.

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<sup>128</sup> Abercrombie J, 'Contributions to the pathology of the stomach, the pancreas and the spleen', *Edinburgh Medical and Surgical Journal*, Jan 1<sup>st</sup> 1824, 1-14 and Apr 1<sup>st</sup> 1824, 243-9

<sup>129</sup> Abercrombie J, *Pathological and Practical Researches of Diseases of the Stomach, the Intestinal Canal, the Liver and other Viscera of the Abdomen*, (Edinburgh, 1828, Waugh and Innes), pp19, 76, 273

<sup>130</sup> Abercrombie J, 'Contributions', op cit, p2

<sup>131</sup> Cruveilhier J, *Anatomie Pathologique du Corps Humaine*, (Paris, 1829-33, J.B. Bailliere), livraison 10, pp1-3

*Another way a disease may prove fatal is by the general irritation that excited it. Most diseases consist in excessive as well as disordered action of the affected part; and this excess of action by degrees exhausts the vital power. It is in this way that long continued disease of almost all kinds gradually reduce the strength, so as at length to prove fatal. In like manner pulmonary consumption does not generally destroy life, by absolute destruction of the lungs, so as to render them altogether incapable of rendering their functions, (for a small portion of lung is sufficient to support life), but by the continued state of excitement that is taking place throughout the system and the consequent exhaustion of the vital power.<sup>132</sup>*

In 1836, Thomas Hodgkin whilst working as ‘demonstrator of morbid anatomy and curator of the Museum at Guy’s Hospital,’ published his first pathology textbook which comprised the lectures he had given. From the text, it is evident that he was an enthusiastic practitioner of autopsy.

*The practice of examining the dead, for the purpose of ascertaining the seat and effect of disease is absolutely necessary to complete those ideas which is impossible for the best verbal descriptions perfectly to convey: and it is also necessary, as a means of detecting that which yet remains to be either wholly discovered or more fully elucidated.<sup>133</sup>*

Hodgkin’s second volume described duodenal ulcers and pyloric stenosis, as had Abercrombie and Cruvelhier. It was his experience that duodenal ulcers were rarely found in his former patients examined in the autopsy room. In his book, he gives a detailed account of the anatomy of the upper gastro-intestinal tract, and in lecture 20 he mentions the paucity of morbid appearances in the duodenum saying that, ‘It does not appear from the results either of my own inspections or of those of others, that this portion of the alimentary canal is often the seat of morbid appearances’. It is to be wondered how much this statement influenced diagnostic thinking both clinically and in the post-mortem room in the years which followed.

The description of these symptoms and their attribution to what was later called ‘peptic ulcer’ allowed doctors to make a diagnosis clinically. There flowed from this many books on the subject and many case reports appeared in the medical journals of the century describing usually the desperate final illnesses of many people from some or other dire

<sup>132</sup> Clutterbuck (Dr), ‘Lectures on the theory and practice of physic’, *The Lancet*, Jan 7<sup>th</sup> 1826, 502-7

<sup>133</sup> Hodgkin T, *Lectures on the Morbid Anatomy of the Serous and Mucous Membranes*, (London, 1836, Sharwood, Gilbert and Piper) p3 and 1840 edition, vol. 2, pp371-7

complication of usually gastric ulcer. George Budd's textbook is typical of the time. As Professor of Medicine at King's College, London, in 1855 he expanded the state of knowledge of peptic ulcer with such features as the recognition of the separate nature of duodenal ulcer.<sup>134</sup> He commented on William Curling's linkage of acute duodenal ulcer with severe burns in 1842.<sup>135</sup> Curling had noted that several of his seriously burned patients died from perforation and/or haemorrhage from duodenal ulcers while under his care, and published his findings.

In the mid nineteenth century clinical medicine was becoming inextricably joined with pathology which at this time was under the control of clinicians and was seen as the key to the understanding of disease. William Brinton was a physician with a large successful private practice who was attached to the Royal Free Hospital from 1852 until 1860 and who had an interest in upper gastrointestinal disorders, writing papers and books about diseases of the intestines and of the stomach. He became a Fellow of the College of Physicians and was elected a Fellow of the Royal Society in 1864, three years before his death, aged 44 years. His first stomach-related book, published in 1857, *On the Pathology, Symptoms and Treatment of Ulcer of the Stomach: with an Appendix of Cases*, followed the practice of Morgagni and others in reproducing the case histories and findings of many other doctors, mostly from Europe.<sup>136</sup> It was highly praised in its day and there were initially two print runs of it.<sup>137</sup> He published a second book on the subject in 1864, *Lectures on the Diseases of the Stomach with an Introduction on its Anatomy and Physiology*, which *The Lancet* described as; 'An important work, and we augur for it a place in medical literature.'<sup>138</sup> This prediction has come true for Brinton's work is quoted in many historical articles on peptic ulcer written in the years since it was published.

It should be remembered that what any particular physician, surgeon, general practitioner, or even irregular practitioner, believed about the cause or effects of peptic ulcer was largely irrelevant to his patient whose main interest was symptomatic relief. Practitioners of the time could not differentiate between severe dyspeptic symptoms and other possible causes of severe abdominal pain. If the patient survived, the doctor considered that it was due to his therapeutic measures.

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<sup>134</sup> Budd G, *On the Organic and Functional Disorders of the Stomach*, (London, John Churchill, 1855), pp122, 124

<sup>135</sup> Curling T B, 'On the acute ulceration of the duodenum in cases of burn', *Medico Chirurgical Transactions*, 1842, vol. 25, 260-81

<sup>136</sup> Brinton W, *On the Pathology, Symptoms and Treatment of Ulcer of the Stomach: with an Appendix of Cases*, (London, 1857, John Churchill)

<sup>137</sup> Anon, 'Reviews and notices of books', *The Lancet*, May 23<sup>rd</sup> 1857, 532

<sup>138</sup> Anon, 'Reviews and notices of books', *The Lancet*, Dec 3<sup>rd</sup> 1864, 635-7

## 2. 4: Self-help remedies

Nicholas Culpeper published a famous book of herbal remedies in 1652, which still remains in print, containing remedies composed of common English herbs for many stomach complaints. These include wood betany for ‘the rising of the stomach’, bilberry ‘to cool the liver and the stomach’, calamint ‘for pains in the belly and stomach’, and caraway was said to be ‘pleasant and comfortable to the stomach and helpeth digestion’.<sup>139</sup>

William Buchan’s *Domestic Medicine* of 1772 was also typical. His frontispiece describes it as, ‘an attempt to render the Medical Art more generally useful, by shewing [sic] people what is in their own power both with respect to the prevention and cure of diseases’.<sup>140</sup>

Buchan had advice for the treatment of ‘vomiting of blood’, ‘heartburn’ and ‘pain of the stomach’ which included dietary advice and the use of chalk. Bowel regulation also featured.<sup>141 142</sup>

In 1776, the English preacher and founder of Methodism, John Wesley, produced his book, *Primitive Physick*, which could be bought at Methodist preaching houses. Wesley was answering a real need in the society of the day to enable poor people to obtain medical advice without involving the expense of a doctor or other practitioner. His book was reprinted many times and in 1858, William Cornell published his book, *The Ship and Shore Surgeon* bound together with John Wesley’s *Primitive Physick* in the same volume. Cornell says of his publication, ‘It is designed for that numerous class of person who follows the seas, or who are pioneers in the settlement of new lands in the vast west, and who cannot obtain properly qualified, nor indeed, any, physicians.’ Cornell gives a description of most of the common disorders of health as does Wesley’s book which had its origins in an earlier century. The remedies however vary little, which may in part be due to the fact that Wesley’s book was repeatedly updated over the period and this conjoined version was the 24<sup>th</sup> ‘revised and enlarged’ edition.<sup>143</sup> Both books recognise what is now called haematemesis, inflammation of the stomach and sour stomach or heartburn. The emphasis of all the treatments was to try to calm the stomach by

<sup>139</sup> Culpeper N, *The English Physician Enlarged with Three Hundred and Sixty-nine Medicines Made of English Herbs, that were not in any Impression until this*. (London, 1799, W Baynes) pp36, 38, 62, 68

<sup>140</sup> Buchan W, *Domestic Medicine or the Family Physician*, (London, 1772, John Dunlap), frontispiece

<sup>141</sup> Buchan, *Domestic Medicine*, *ibid*, pp241-2 and 254-7

<sup>142</sup> Such books enjoyed considerable popularity well into the nineteenth century and one particularly celebrated owner was Fletcher Christian of the Mutiny on the *Bounty*. The National Maritime Museum holds his copy which is a sixth edition, which he took to Pitcairn Island. Archive Item no. PBD6069, nmm.ac.uk

<sup>143</sup> Cornell W M, ed, *Primitive Physick: or an Easy and Natural Method of Curing most Disease, by John Wesley*, jointly published with Cornell W M, *The Ship and Shore Physician and Surgeon*, (Boston, 1858, Cyrus Stone)

medicaments or diet. Cornell recommended light diet for haematemesis and small doses of ‘fluid extract of matico’, which was an astringent herb. Wesley’s book offers several other choices in the form of nettle juice or a small amount of saltpetre taken regularly. Creosote or alternatively turpentine both in small quantities and with other ingredients were also suggested.<sup>144</sup> While these books were widely used, especially in the ‘New World’, and would be referred to for many years after their purchase, publications directed at medical practitioners eventually promoted diet, alkalis and bed rest as the mainstays of peptic ulcer treatment, although other remedies continued in use.

## 2. 5: Gender Issues

From the middle of the nineteenth century, it was firmly believed that the particular dyspeptic disease that doctors were treating was gastric ulcer or ulcer of the stomach. While the better-read of them knew of the existence of duodenal ulcer, most preferred the diagnosis of gastric ulcer in their writings, believing that it had a predilection for young women of the servant class. This view appeared in the writings of a number of authors of the time, many of whom held hospital appointments as physicians. They believed that menstrual functions were in some way implicated in the patients’ final illnesses. In 1843, Edward Crisp published a paper in *The Lancet* concerning a putative link between young women of the ‘servant class’ and gastric ulcer.<sup>145</sup> A contemporary, John Prichard, in correspondence with Edward Crisp in the same journal, stated his belief that gastric perforations in male and female patients were different and distinct types and situated in the stomach predictably with the female type being closer to the proximal (or upper) end of the stomach and the male type around the pylorus.<sup>146</sup> He also believed that menstruation played a part in the pathological process which led to the perforation.<sup>147</sup> According to these authors, gastric ulcer was largely a fatal affliction of young servant girls who in all probability had been lifted out of relative poverty to serve in the houses of the wealthy where they enjoyed a diet of a reasonable quality in an uncrowded healthy environment, possibly for the first time in their lives. Disordered menstrual function was blamed and the term ‘menstrual ulcer’ was created to explain the timing of perforation.

I suggest that Crisp and Prichard’s class/gender linkage was a reflection of their particular experiences of the patient group they served and that their gender and occupations were

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<sup>144</sup> Wesley, *Primitive Physick*, *ibid*, pp32-3, or Cornell, *The Ship*, *ibid*, pp11-3

<sup>145</sup> Crisp E, ‘Cases of perforation of the stomach with deductions therefrom relative to the character and treatment of the lesion’, *The Lancet*, August 5<sup>th</sup> 1843, 639-48

<sup>146</sup> The pylorus is the part of the stomach situated at its outlet which controls the emptying of its content.

<sup>147</sup> Prichard J, ‘Perforating ulcers of the stomach in the male and female’, *The Lancet*, Sept 9<sup>th</sup> 1843, 837-8

coincidental. These papers anticipated many of the journal articles published on the subject of gastric ulcer in women in the next half century including Sir Astley Cooper's treatment of 'menstrual ulcer' which is mentioned by Crisp.<sup>148</sup> *The Lancet* reported the deaths of three further female patients from gastric ulcer between 1849 and 1862, all of whom were described as 'servants'.<sup>149</sup> <sup>150</sup> In another case involving a young woman, the deceased was not described as 'a servant' but as 'a delicate girl'.<sup>151</sup> Cases of death from perforation in males also appear in the journals at the same time and Prichard writes of them in the letter quoted above.

In the nineteenth century, admission to a voluntary hospital required a letter from a subscriber who usually came from the upper and middle social classes and employed servants. Servants who became seriously ill were likely to be admitted to a voluntary hospital if only to avoid the inconvenience of having someone who was not a relative dying in the home of her employer. The option of hospitalisation was usually available to only those who could find a sponsor. This is discussed later in this chapter. Gender specificity in gastric ulcer is not obvious in the earliest publicised work on the subject by Abercrombie and Cruveilhier who made no such comment. However it is difficult for any student of nineteenth-century medical literature to avoid the view that gastric ulcer seemed to have a degree of predilection for women on the basis of reports of deaths from perforation in journals such as *The Lancet* and the *British Medical Journal*.

Edward Crisp's 1843 article describes his management of a woman dying from a perforation of a gastric ulcer. Although he was a surgeon, he never contemplated surgical intervention, preferring conventional measures to relieve his patient's distress. These included leeches, hot fomentations to the abdomen, magnesium sulphate given repeatedly as an aperient and ipecacuana which would induce vomiting. In the terminal stages of this 20 year old woman's illness, Crisp gave her a grain and half (90 milligrams) of opium repeated four hourly.<sup>152</sup> His paper included the clinical details of other unpublished cases known to him with the addition of all the published cases he could find in the English language, describing 51 deaths from perforation, 39 of which were in women and 12 males. All perforations were found in the stomach and in the case of the women, they

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<sup>148</sup> Crisp E, 'Cases of perforation', op cit, p648

<sup>149</sup> Broxholm F G, 'On a case of perforated ulcer of the stomach', *The Lancet*, Sept 15<sup>th</sup> 1849, 294-5

<sup>150</sup> Waterland H J, 'Perforating ulcer of the stomach', *The Lancet*, Oct 22<sup>nd</sup> 1853, 391

<sup>151</sup> Hinds W, 'Cases of perforating ulcer of stomach and of intestines', *British Medical Journal*, Feb 1<sup>st</sup> 1862, 114-5

<sup>152</sup> Crisp E, 'Cases of perforation', op cit, 639-48

were mainly located near the cardia of the stomach and in the men, more likely to be found towards the pylorus.<sup>153</sup>

Gender predilection of illnesses which affect both sexes is not an unusual phenomenon in medicine. For example, it is accepted that women are five times more susceptible than men to hyperthyroidism and six times more to hypothyroidism.<sup>154</sup> Under the age of 40, three times more women have gallstones than men.<sup>155</sup> Historically this is the commonest age group of women dying from perforated gastric ulcers in the nineteenth century. Rheumatoid arthritis is three times more common in women under 40 than men and they are the largest group of sufferers from osteoarthritis in middle and old age.<sup>156</sup> It is evident that men are more likely to get duodenal ulcers than women with an average ratio of 6:1. With ageing, disease patterns change and the ratios change, but women retain their higher prevalence of gastric ulcer into old age. There are many other examples of illness/gender predilection to be found in medicine, too numerous to include here.

## 2. 6. 1: Elective abdominal surgery

The nineteenth century was a time of considerable expansion of medical understanding as new procedures, concepts and technology were changing medical practices. In 1809, in Danville, Kentucky, a former army surgeon, Ephraim McDowell, successfully surgically removed an enormous ovarian cyst from the abdomen of a Mrs Crawford without an anaesthetic and she lived for 34 years afterwards.<sup>157</sup> McDowell later successfully removed 11 more ovarian tumours with only three deaths in this pre-anaesthesia and pre-antiseptic era.<sup>158</sup> Other surgeons ventured into the abdomen often in the most extreme of circumstances, but their patients usually died.<sup>159</sup> Augustin Prichard, a Bristol surgeon, in the ten years to 1860, did not open any abdomens.<sup>160</sup>

Surgeons were increasingly inclined to try to help their patients with upper gastrointestinal obstruction, but without success. The operation of gastrostomy was attempted by Charles-Emmanuel Sedillot in 1849 where a fistula was surgically fashioned to allow feeding

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<sup>153</sup> The cardia is at the top end of the stomach near the gullet entrance

<sup>154</sup> Edwards C R W, Bouchier I A D, eds, *Davidson's Principles and Practice of Medicine*, (Edinburgh, 1991, Churchill Livingstone) pp622, 629

<sup>155</sup> Edwards, Bouchier, *Davidson's Principles*, ibid, p539

<sup>156</sup> Kumar P, Clark M, eds, *Clinical Medicine*, (Edinburgh, 1998, WB Saunders), pp466, 470

<sup>157</sup> McDowell E, 'Three cases of extirpation of diseased ovaria', *The Eclectic Repertory and Analytical Review*, 1817, 242-4

<sup>158</sup> Ellis H, *The Cambridge Illustrated History of Surgery*, (Cambridge, 2009, Cambridge University Press), pp63-66

<sup>159</sup> Astley Cooper operated upon a man in 1817 to tie off a leaking abdominal aneurysm using a surgical access through the abdomen but the patient died forty hours later.

<sup>160</sup> Prichard A, 'Ten years of operative surgery in the provinces', *British Medical Journal*, Oct 27<sup>th</sup> 1860, 833-6

directly into the stomach below an obstruction which was caused by a cancer.<sup>161</sup> Others followed with little success.<sup>162</sup> Later, in a period of three years from 1879 until 1881, three surgeons removed parts of the stomach for the first time with varying successes. They were Jules Emile Péan in Paris, Ludwig Rydygier in Culm, Poland and Theodor Billroth in Vienna.<sup>163</sup> <sup>164</sup> Péan's patient died five days later and Rydygier's only lasted for twelve hours post-operatively. Billroth's patient lived for four months before succumbing to her cancer which had spread elsewhere. His approach had been much more deliberate and studied, for he had experimented on dogs by removing parts of their stomachs, and he knew beforehand that the stomach which had been cut and surgically rejoined, would heal, something which had been doubted until that time.<sup>165</sup> In 1881, Ludwig Rydygier in Poland, performed a partial gastrectomy on a woman for gastric ulcer and 25 years later, he paraded her before a surgical congress in Berlin in good digestive health.<sup>166</sup> Arthur William Mayo Robson records that the first gastroenterostomy was fashioned by Anton Wölfer in 1881 for cancer of the pylorus.<sup>167</sup> Three years later, Rydygier is credited as using gastroenterostomy for the treatment of peptic ulcer.<sup>168</sup>

By the eighteen-eighties, patients had anaesthesia but the use of Lister's antiseptics had not yet been universally accepted. Initially few partial gastrectomy operations were performed but there was a high mortality.<sup>169</sup> *The Lancet* comments that the operation was performed in Vienna repeatedly without enough success to make it practicable.<sup>170</sup> Those partial gastrectomies, mostly performed to remove cancers of the stomach, were of the types devised by Billroth but in the years which followed over forty modifications of them were devised by other surgeons. Another surgeon Eugene Polya of Budapest devised other ways of doing partial gastrectomies and his name is associated with these.<sup>171</sup>

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<sup>161</sup> A fistula is an abnormal communication between the lumen (inside space of a tubular organ) of one viscus (internal organ) and the lumen of another, or the body surface as in this case. It is lined with the epithelium of the lining from which it communicates.

<sup>162</sup> Lowe J. 'On gastrostomy: with case', *The Lancet*, Jul 22<sup>nd</sup> 1871, 119-21

<sup>163</sup> 'Paris correspondence', *The Lancet*, June 7<sup>th</sup> 1879, 826

<sup>164</sup> Finney J M T, 'The development of surgery of the stomach', *Annals of Surgery*, Nov 1929, vol. 90, no. 5, 829-46

<sup>165</sup> Gordon-Taylor G, Hudson R V, Dodds E C, et al, 'The remote results of gastrectomy', *British Journal of Surgery*, 1929, vol. 16, 641-67

<sup>166</sup> Kinsella V J, 'Bad gastrectomies', *British Medical Journal*, Dec 1<sup>st</sup> 1956, 1277-81

<sup>167</sup> Robson A W M, 'Three lectures on surgery of the stomach', *The Lancet*, Mar 24<sup>th</sup> 1900, Lecture iii, 830-43

<sup>168</sup> Ivy A C, Grossman M I, Bacharach W H, *Peptic Ulcer*, (Philadelphia and Toronto, 1950, The Blaikiston Company), p968

<sup>169</sup> Editorial, 'The surgery of the stomach', *The Lancet*, Mar 24<sup>th</sup> 1883, 505-6

<sup>170</sup> Editorial, 'The Annus Medicus 1883', *The Lancet*, Dec 29<sup>th</sup> 1883, 1135

<sup>171</sup> Rains A J H, Capper W M, *Bailey & Love's Short Practice of Surgery*, (London, 1965, H K Lewis & Co Ltd), pp769-773

Elective or planned non-emergency surgery within the abdominal cavity was an unusual procedure when seen in a national context.<sup>172</sup> The major problem of ‘hospitalism’ or secondary post-operative sepsis existed for the surgical patient which was potentially fatal and had a mortality rate of 38% in four London hospitals for those having limb amputations from 1866-71.<sup>173</sup> Abdominal surgery tended to be a measure resorted to when all other measures had failed, because it carried very high mortality. The exception to this was the operation of ovariectomy, which was performed more often, but surgery generally was confined to the surfaces of the body and the limbs.<sup>174</sup>

## 2. 6. 2: Emergency abdominal surgery for peritonitis

Peritonitis, which can be caused by any internal cause of spillage of intestinal contents into the sterile peritoneal cavity, was easy to diagnose and generally fatal.<sup>175</sup> Medical attendants facing such a case would attempt to make their patient comfortable with large doses of morphine until they died, usually within hours. When intestinal ulcers perforated, as they tended to do in the case of typhoid fever, it was expected that the patient would die. However surgical intervention by suturing the perforation and washing out the contamination of the peritoneal cavity first saw success in 1884 in a case of Mikulicz’s described by Finney in 1897.<sup>176</sup> Then in 1888 in England, John Taylor successfully repaired a hole in the small intestine caused by a perforation of small bowel in a case of typhoid enteritis.<sup>177</sup> This was a most remarkable achievement because of the considerable contamination of the peritoneal cavity from the spilled bowel contents. Even today this would present a major threat to life despite modern surgical methods and antibiotics which were unavailable at that time. It should be noted that surgeons had been treating stab wounds of the abdomen for most of the nineteenth century especially those acquired in war. In 1851 George James Guthrie published an article on the treatment of wounds and injuries of the abdomen which indicated that stab wounds could be successfully dealt with surgically by the methods he suggested.<sup>178</sup> Guthrie gained much of his surgical experience

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<sup>172</sup> Robson A W M, ‘An introductory address on the advances of surgery during 30 yrs’, *The Lancet*, Oct 4<sup>th</sup> 1902, 912-6

<sup>173</sup> Erichsen J E, ‘Lectures on hospitalism and the causes of death after operations’, *British Medical Journal*, Jan 17<sup>th</sup> 1874, 65-7

<sup>174</sup> Porter, *The Greatest Benefit*, op cit, pp363-5

<sup>175</sup> Peritonitis is that condition of inflammation of the lining of the abdomen and its contents. Inflammation occurs within the peritoneal cavity because it is contaminated by the contents of the particular organ which has spilled into it. Untreated it is almost always fatal although exceptions did occur.

<sup>176</sup> Finney J M T, ‘The surgical treatment of perforating typhoid ulcer’, *Annals of surgery*, Mar 1897, vol. 25, issue 3, 233-69

<sup>177</sup> Taylor J, ‘Typhoid fever; perforation; local peritonitis; operation; recovery’, *The Lancet*, May 3<sup>rd</sup> 1890, 961

<sup>178</sup> Guthrie G J, ‘Lectures on some of the more important points in surgery’, *The Lancet*, Apr 12<sup>th</sup> 1851, 387-8

as a young army surgeon on the battlefields of the Iberian peninsula during the Napoleonic wars.<sup>179</sup>

Despite these few successes, gastric perforations continued to be managed conservatively without surgery with the expectation that patients with peritonitis caused by gastric (or duodenal) perforations would die. Some surgeons did operate but with universal failure until 1892 when the first patient with a perforated gastric ulcer survived his operation.<sup>180</sup> This achievement was exceptional and most surgery for the effects of peritonitis remained unsuccessful in saving lives for the rest of the century. Nevertheless more surgeons became willing to operate whereas before they considered these cases hopeless.

In reading the clinical details of cases described by surgeons from around 1890 it is evident that there was a growing belief that surgery could offer salvation for the patient who had peritonitis following gastric ulcer perforation. The few therapeutic successes described above offered surgeons the hope at least that surgical intervention might be successful. This was very much the mind-set of Gilbert Barling who wrote in 1893:

*The mortality after perforation is probably at least 95 per cent., so that each case recovering after operation may be looked upon as saved from almost certain death. Although the third case proved the most successful, it is clear that resort to operation, at the earliest moment after perforation, is recognised as most likely to prove serviceable in the large majority of cases. The diagnosis of perforation is as a rule not difficult, but in some cases there may be no evidence pointing to the stomach as the organ at fault.*<sup>181</sup>

The turning point in the understanding of the best management of perforation came with the aforementioned successful repair of the gastric ulcer by Ludwig Heusner in what is now Wuppertal in Germany in 1892.<sup>182</sup> Shortly afterwards, Hastings Gilford operated on a young woman at home in Reading in England, with her general practitioner giving the

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<sup>179</sup> Guthrie G J, 'Biographical sketch of G J Guthrie', *The Lancet*, Jun 15<sup>th</sup> 1850, 726-36

<sup>180</sup> Anon, 'Perforation of the stomach by a gastric ulcer, which was subsequently closed by adhesions: circumscribed peritonitis, and large collection of pus', *The Lancet*, Jul 15<sup>th</sup> 1865, 65-6

<sup>181</sup> Barling G, 'The treatment of perforated gastric ulcer, with report of successful drainage in a case', *British Medical Journal*, Jun 21<sup>st</sup> 1893, 1258-9; Simon R M, Barling G, 'Perforation of a gastric ulcer and its treatment by abdominal section and suture', *British Medical Journal*, Jan 9<sup>th</sup> 1892, 63-4

<sup>182</sup> Ellis H, *A History of Surgery*, (London, 2001, Greenwich Medical Media Ltd), p114

anaesthetic. Two years later a duodenal ulcer was successfully repaired by Percy Dean in England.<sup>183</sup>

In his book *A History of Surgery*, Harold Ellis says, ‘An important factor that facilitated surgical progress at this time was the rapid dissemination of the news of important discoveries and major advances in the well-established medical press in Europe and America.’<sup>184</sup> When surgeons increasingly intervened in what had been regarded as hopeless cases of peritonitis, they were surprised to discover that what they presumed would be perforated gastric ulcers were found instead to be perforated duodenal ulcers, which hitherto were considered to be rare. There was also a dominance of male patients with perforated duodenal ulcers. This was not immediately evident since the experience of the first ten or more years was relatively limited and it took surgical successes in the hospitals for doctors in the community to start sending their patients with peritonitis into hospital.<sup>185</sup>

There was not an initial rush of enthusiastic referrals from general practitioners to submit their patients to surgery for perforation, which was far from certain in its outcomes in the majority of cases. In 1899 Arthur Barker, at a meeting of the Clinical Society of London, opened a discussion on cases of perforated gastric ulcer treated by operation. He and his colleagues discussed the issue of the very high mortality rates following surgery, which then was greater than 50%.<sup>186</sup> Berkeley Moynihan in 1901 searched all the medical journals then available to him on the topic of operations for perforated duodenal ulcer and was able to discover only 51 cases. Only eight of these had survived their surgery.<sup>187</sup> He later discovered when talking to the eminent European surgeon Jan Mikulicz in 1903, that, of the first 35 cases of perforated ulcer he had operated on, 34 had died.<sup>188</sup> In a paper Moynihan published in 1903 on perforations of both gastric and duodenal ulcers, survival rates were 35-40%.<sup>189</sup> This was far from untypical however and success in rescuing these patients grew in the following two decades.

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<sup>183</sup> Dean H P, ‘A case of perforation of a chronic ulcer of the duodenum successfully treated by excision’, *British Medical Journal*, May 12<sup>th</sup> 1894, 1014-5

<sup>184</sup> Ellis H, *A History*, op cit, p70

<sup>185</sup> Robson A W M, ‘Observations on the evolution of abdominal surgery from personal reminiscences extending over a third of a century and the performance of 2000 operations’, *The Lancet*, Aug 1<sup>st</sup> 1903, 292-7

<sup>186</sup> Barker A, ‘Cases of perforated gastric ulcer treated by operation’, *The Lancet*, Dec 16<sup>th</sup> 1899, 1668-70

<sup>187</sup> Moynihan B G A, ‘On Duodenal Ulcer and its surgical treatment’, *The Lancet*, Dec 14<sup>th</sup> 1901, 1656-63

<sup>188</sup> Moynihan B G A, ‘The surgery of yesterday and tomorrow’, *The Lancet*, Jun 9<sup>th</sup> 1928, 1208

<sup>189</sup> Moynihan B G A, ‘The surgical treatment of gastric and duodenal ulcers’, *The Lancet*, Jan 31<sup>st</sup> 1903, 294-8

Physicians and general practitioners were well used to dealing with dying patients and they recognised fatal conditions. In particular, peritonitis was relatively easy to diagnose from the history and physical findings.<sup>190</sup> They knew how to relieve their patients' pain and distress until death occurred at home. Surgical intervention for duodenal perforation only began in 1896 in Edinburgh<sup>191</sup> and in 1897 in Belfast.<sup>192</sup> The number of patients referred for surgery was small in the early days of surgical intervention. The choice for patients was stark. There was only a rudimentary ambulance service in most cities, those who could afford it would use a cab and those who could not probably would be conveyed on a cart or hand-barrow over cobbled streets.<sup>193</sup> In Edinburgh, the Royal Infirmary provided a sedan chair arrangement which of necessity could only travel short distances.<sup>194</sup> Long distance transport of a patient with peritonitis would have been out of the question. It took time, improved transport and increasing surgical success to change longstanding habits of treating patients with peritonitis as terminally ill. Surgical success did come but it took at least three decades for survival rates to rise above 50% for the repair of perforation of gastric and duodenal ulcer.

In contrast, by 1900, elective surgery on the stomach carried risks of mortality rates of approximately 10%. Ernest Maylard's series of 22 operations with two deaths is typical of the time.<sup>195</sup> In the USA, William Mayo's published series of 303 operations on the stomach and duodenum included 31 deaths post-operatively.<sup>196</sup>

## 2. 6. 3: Anaesthesia and antiseptics

None of the later surgery would have been possible without the benefit of anaesthesia and antisepsis which revolutionised the practice of surgeons. Until the development of anaesthesia, the only analgesia available to people undergoing surgery was the dangerous practice of swallowing cocktails of opiates and alcohol. In 1844 nitrous oxide was used to remove a tooth painlessly by Horace Wells, a dentist of Connecticut. This gas was first

<sup>190</sup> Crisp E, 'Cases of perforation', op cit, 640

<sup>191</sup> Caird F M, Cotterill J M, Cathcart C W, et al, 'Perforated Duodenal Ulcer', *Edinburgh Medical Journal*, Nov 1913, vol. 11, 405-18

<sup>192</sup> McConville S R, Crookes P F, 'The history of gastric surgery: the contribution of the Belfast school', *Ulster Medical Journal*, vol. 76, no.1, Jan 2007, 31-36

<sup>193</sup> Pollock A C, 'Ambulance services in London and Great Britain from 1860 until today: a glimpse of history gleaned mainly from the pages of contemporary journals', *Emergency Medical Journal*, Mar 2013, vol. 30, issue 3, 218-22

<sup>194</sup> Editorial Article, 'A history geared for excellence', *Response, The newsletter of the Scottish Ambulance Service*, Summer 2008, vol. 16, no. 4, p6

<sup>195</sup> Maylard A E, 'An address on the surgery of the stomach with illustrative cases', *The Lancet*, Nov 3<sup>rd</sup> 1900, 1253-8

<sup>196</sup> Mayo W J, 'A review of three hundred and three operations on the stomach and first portion of the duodenum', *Annals of Surgery*, Jul 1903, vol. 38, no. 1, 30-46

prepared by Joseph Priestley in 1772, one of the discoverers of oxygen, but it was Humphry Davy who initially suggested that it might be of use ‘for surgical use as it was capable of destroying physical pain’.<sup>197</sup> In 1846 William Morton used ether as an anaesthetic for the first time in an operating theatre as John Warren removed a tumour from a patient’s face.<sup>198</sup> The account of the operation was reported by H J Bigelow who was present at the demonstration and reported it in the *Boston Medical and Surgical Journal*. Ether was discovered in 1540 by the German botanist Valerius Cordis. Wells and Morton have contested the claim to first use of ether as an anaesthetic and the dispute is recorded.<sup>199</sup> Justus von Liebig synthesised chloroform in 1831<sup>200</sup> and James Young Simpson’s introduction of it into Britain in 1847 for intra-partum pain relief and for gynaecological operations, is well known as is its use surgically.<sup>201</sup> Anaesthesia was not immediately universally accepted as being in the patient’s best interests since there were fatalities apparently as a consequence of its use.<sup>202 203 204</sup>

Despite the risks, many patients chose to undergo surgery under anaesthesia rather than face the pain and terror of an operation wide-awake. Possibly because of anaesthesia, patients died in large numbers post-operatively due to ‘the curse of hospitalism’ or what is now called ‘hospital acquired infection’. The increased time spent by the surgeon whilst operating had the effect of increasing the exposure time of the open wound of the patient to unsterile conditions and instruments. Surgeons became more ambitious in the techniques they undertook and this increased exposure times. Hospitalism remained ill-understood as can be seen in Professor Erichsen’s lecture series published in the *British Medical Journal* in 1874.<sup>205</sup>

*To the surgeon, the importance of septic disease in hospitals cannot be overestimated. As matters now stand, the most consummate skill and the most*

<sup>197</sup> Bynum W F, *Science and the Practice of Medicine in the Nineteenth Century*, (Cambridge, 1994, Cambridge University Press), p121

<sup>198</sup> Bigelow H J, ‘Insensibility during surgical operations produced by inhalation’, *Boston Medical and Surgical Journal*, 1846, vol. 35, 309-17

<sup>199</sup> Correspondence, ‘The original discoverer of the application of ether to surgical operations’, *The Lancet*, Mar 6<sup>th</sup> 1847, 265-7

<sup>200</sup> Porter R, *The Greatest Benefit*, op cit, pp365-8

<sup>201</sup> McCrae M, *Simpson: The Turbulent Life of a Medical Pioneer*, (Edinburgh, 2011, Birlinn Ltd), pp117-137

<sup>202</sup> A review of this topic may be found in, Burney I, ‘Anaesthesia and the evaluation of surgical risk in mid-nineteenth-century Britain’, in *The Risks of Medical Innovation: Risk Perception and Assessment in Historical Context*, eds Schlich T, Trohler U, (London and New York, 2006, Routledge), pp38-52

<sup>203</sup> 42 deaths are recorded in Crisp E, ‘On the recorded deaths from chloroform’, *The Lancet*, Jun 4<sup>th</sup> 1853, 523-4

<sup>204</sup> Editorial, ‘The use and abuse of chloroform’, *The Lancet*, Dec 16<sup>th</sup> 1854, 513

<sup>205</sup> Erichsen J E, ‘Lectures on hospitalism and the causes of death after operations’, *British Medical Journal*, Feb 14<sup>th</sup> 1874, 65-7

*devoted attention are often alike rendered unavailing by the influences of septic diseases generated within the hospitals themselves by the operation of causes entirely beyond the surgeon's control - diseases which neutralise the best directed efforts of his art, and which, in no small degree, increase the pressure of the heavy responsibility and deep anxiety which under the most favourable circumstances, attend its exercise.*<sup>206</sup>

Aware of the work of Pasteur, Joseph Lister changed his surgical practice to adopt an antiseptic technique publishing his results in *The Lancet* in 1867.<sup>207</sup> Lister's advance was slow to be adopted in the UK, taking almost two decades to be universally accepted, but surgeons who visited from Europe adopted the concept and post-operative sepsis diminished in their practices.<sup>208</sup> Later, aseptic techniques were developed which led to the abandonment of the carbolic spray which caused many health problems for those working in an operating theatre in which it was being employed.<sup>209</sup>

## 2. 7. 1: Animal vivisection and physiological experimentation

For centuries animal dissection has been used to further knowledge and understanding of the internal workings and structure of the human body. This was based upon the assumptions that comparative anatomy could yield understanding of human anatomy and that human physiology could be inferred from that of other mammals. Galen was an early practitioner of animal dissection for this purpose. During the nineteenth century, there was a large increase in animal experimentation which was accompanied by a growing public unease about the conditions under which such work took place. Surgeons designed operations, practising on animals before using the procedures on live human patients. Earlier in this chapter it was described how Theodor Billroth used animal vivisection in preparation for his first gastrectomy operation.<sup>210</sup>

The Anti-Vivisection Society was formed in England in 1875 to oppose and publicise all animal experimentation, which was believed to be cruel and not justified in terms of

<sup>206</sup> Erichsen J E, 'Lectures on hospitalism', op cit, 193-6, esp p196

<sup>207</sup> Lister J, 'On a new method of treating compound fracture, abscess, etc: with observation on the conditions of suppuration', *The Lancet*, Mar 16<sup>th</sup> 1867, 326-9; Lister J, 'On a new method of treating compound fracture, abscess, etc: with observation on the conditions of suppuration', *The Lancet*, Mar 23<sup>rd</sup> 1867, 357-9; Lister J, 'On a new method of treating compound fracture, abscess, etc: with observation on the conditions of suppuration', Mar 30<sup>th</sup> 1867, 387-9; Lister J, 'On a new method of treating compound fracture, abscess, etc: with observation on the conditions of suppuration', Apr 27<sup>th</sup> 1867, 507-9

<sup>208</sup> Ellis H, *The Cambridge Illustrated History*, op cit, pp88-9

<sup>209</sup> Porter R, *The Greatest Benefit*, op cit, pp371-374

<sup>210</sup> De Moulin D, *A History of Surgery*, (Dordrecht, 1988, Martinus Nijhoff Publishers), p308

knowledge gained in relation to suffering caused.<sup>211</sup> In 1902, a live demonstration of the dissection of a dog's parotid gland was performed for medical students by Dr William Bayliss, which was followed by a surgical exploration of the dog's pancreatic duct that had previously been operated upon by his superior, Professor Ernest Starling. Two Swedish students were present at the demonstration and recounted their experiences to the Anti-Vivisection Society. This was reported three months later at their annual meeting at which the press were present and their reports stirred up anti-vivisection feelings and led to Dr Bayliss suing the Anti-Vivisection Society. There were strong feelings expressed on both sides of the argument but Dr Bayliss was exonerated in court.<sup>212</sup> All such experiments were supposed to be performed under the terms of Cruelty to Animals Act of 1876 which stood unaltered for 110 years. Today vivisection continues to be seen as a valuable means of investigating human physiology and pharmaceutical testing.

Many of the clinical techniques currently in use today in clinical practice were devised in the early part of the nineteenth century by animal experimentation. Blood transfusions were attempted in animal experiments and on patients themselves.<sup>213 214</sup> Early surgical and physiological experiments were performed on small mammals, usually dogs. By chemical analysis, William Prout demonstrated in 1824 that the acid in the stomach was mainly 'muriatic acid' or hydrochloric acid and that this was the chemical agent upon which gastric digestion was dependent in a variety of animals, including the hare, the calf, the horse and the dog.<sup>215</sup> His discovery was contested by other chemists of the time but later research justified his conclusion.<sup>216 217</sup>

## 2. 7. 2: William Beaumont and Alexis St Martin

Modern human gastric physiology owes much to the studies of William Beaumont, a USA army surgeon who published his work in 1833.<sup>218</sup> Beaumont described a patient, Alexis St Martin, the skin and muscles of whose anterior abdominal wall had been damaged by an accidental gun discharge in 1822. He repaired this wound surgically leaving a fistula.

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<sup>211</sup> The history of the National Anti-vivisection Society can be found on their website; [www.navs.org](http://www.navs.org).

<sup>212</sup> Pollock A, 'Vivisection and the Experiments of the Physiologist', *Vesalius*, Summer 2012, vol. xvii, no. 1, 36-8

<sup>213</sup> Editorial, *The Lancet*, Oct 8<sup>th</sup> 1825, 111-2

<sup>214</sup> Editorial, *The Lancet*, Feb 29<sup>th</sup> 1824, 295

<sup>215</sup> Prout W. 'On the nature of the acid and saline matters usually existing in the stomachs of animals', *Philosophical Transactions of the Royal Society of London*, 1824, vol. 114, 45-49

<sup>216</sup> Editorial, 'Physiology: On the digestive process', *The Lancet*, Sep 3<sup>rd</sup> 1825, 279

<sup>217</sup> Thomson R D, 'On the proofs of the presence of free muriatic acid', *The Lancet*, Apr 11<sup>th</sup> 1840, 93

<sup>218</sup> Beaumont W, *Experiments and Observations on the Gastric Juice and the Physiology of Digestion: Reprinted from the Plattsburgh Edition*, (Edinburgh, 1838, Maclachlan and Stewart) pp 298-302, 100-107

This allowed Beaumont to study the workings of St Martin's stomach under experimental conditions for several periods between 1825 and 1831. As a consequence Beaumont was able to observe how a stomach turned foodstuffs into a material ('chyme') which could pass into the upper intestine to undergo further digestion. Beaumont discovered that gastric juice was the main agent for 'chymification', or of chemical break-down, of food in the stomach, which only occurred in the stomach after eating had begun. He showed that the main constituent of gastric juice was muriatic acid or hydrochloric acid, observing that, 'Gastric juice is never found free in the gastric cavity, but is always excited to discharge itself by the introduction of food or other irritants'. He saw that acid acted as a solvent of food whose physical properties it changed and described the churning action and other movements of the stomach. After the chyme had passed through the stomach into the duodenum in an acidic form, bile and pancreatic juice were secreted by the liver and pancreas into the gut lumen converting it into 'chyle'.<sup>219</sup>

### 2. 7. 3: Ivan Pavlov and the vagus nerve

Physiologists performed experiments to further their understanding of gastric function mainly by creating fistulae in dogs. Initially these were technically unsatisfactory for the collection of gastric juice because the fistula was usually too small and the food consumed and duodenal secretions contaminated their samples. In 1879 Ivan Pawlaw (or Pavlov) a Russian physiologist invented a means to observe the workings of a dog's stomach by surgically isolating part of it in what became known as a Pavlov Pouch. This allowed Pavlov to collect uncontaminated gastric juice under controlled circumstances. At the same time, Rudolf Heidenhain, a German physiologist, invented a slightly different pouch to allow for the extraction of gastric juice. Pavlov's pouch retained a vagus nerve connection while Heidenhain severed the vagus connection. Pavlov worked in Heidenhain's laboratory in 1877 and saw his pouch in action, but Pavlov's own book makes no mention of this, saying that Heidenhain described his pouch in 1880, one year after Pavlov had published his own work.<sup>220 221</sup>

We owe the understanding of what is called the 'cephalic phase of digestion' to Pavlov. His experiments showed that dogs produce gastric juices in anticipation of feeding and in response to mastication and swallowing and that the vagus nerve was the key to this and when it was experimentally severed, the secretion of gastric juice ceased. Pavlov also

<sup>219</sup> Beaumont W, *Experiments and Observations*, op cit, pp100-07, 298-302

<sup>220</sup> Quoted in *The Physiology and Treatment of Peptic Ulcer*, Allan J G, ed, (Chicago, 1959, University of Chicago Press) p17

<sup>221</sup> Pawlow J P, *The Work of the Digestive Glands*, (London, 1902, Charles Griffin & Company), p5

found that gastric juice was not entirely dependent upon vagal excitation and that there was a factor in the stomach itself which stimulated gastric juice production.<sup>222</sup> It was for this work that Pavlov received the Nobel Prize in 1904.

In the presentation oration, Pavlov's discoveries were briefly summarised as follows,

*Before Pavlov's work it was the general opinion that the gastric secretion was not influenced via the nerves connecting the stomach and the central nervous system. This conception has, however, been shown to be incorrect. Pavlov has demonstrated that the vagus nerve linking the brain with various thoracic and abdominal organs contains fibres which during their activity stimulate gastric secretion and others which have an exactly opposite effect. In this way the secretion of gastric juice is controlled by the central nervous system and can be influenced from different parts of the body. It has also been found that by this means the gastric secretion is influenced by psychic impressions and impulses.*<sup>223</sup>

## 2. 7. 4: Gastrin

John Sydney Edkins, an English physiologist working on gastric function in 1906 and following upon the studies of William Bayliss and Ernest Starling, found an explanation for Pavlov's and others' observations of the secondary phase of digestion, later called the 'gastric or chemical phase', which occurred after food had entered the stomach. Bayliss and Starling had discovered in 1902 that the pancreas could be stimulated to secrete its digestive juices in the absence of nerve stimulation by a substance which they called 'secretin' which entered the circulation in response to the entry of food or other substances into the duodenum. Starling's discovery of what he called 'hormones' in 1905 led to the beginnings of endocrinology.<sup>224</sup> Questioning whether the stomach also had such a substance which stimulated gastric juice secretion, Edkins extracted a substance from part of a pig's stomach and injected it intravenously into another pig and this induced gastric secretion. This substance had a much weaker effect in producing gastric secretion when injected into a cat.<sup>225</sup> The substance was later called 'gastrin', but other physiologists had

<sup>222</sup> Pawlow J P, *The Work of the Digestive Glands*, ibid, pp1-19, 45-61

<sup>223</sup> Mörner K A H, Count, Rector of the Royal Caroline Institute, see Nobel Lectures, Presentation speech, Dec 10<sup>th</sup> 1904, *Physiology or Medicine 1901-1921*, (Amsterdam, 1967 Elsevier Publishing Company)

<sup>224</sup> Bayliss W M, Starling E H, 'The mechanism of pancreatic secretion', *Journal of Physiology*, Sep 12<sup>th</sup> 1902, vol. 28, 325-55

<sup>225</sup> Edkins J S, 'The chemical mechanism of gastric secretion', *Journal of Physiology*, Mar 13<sup>th</sup> 1906, vol. 34, 133-144

great difficulty in replicating Edkins' work.<sup>226</sup> Nevertheless, they persisted but their early samples were contaminated with histamine which was known to be a major gastric juice stimulant so that many physiologists believed that gastrin was in fact histamine.<sup>227</sup> In 1961 gastrin in its pure chemical form was finally obtained by Roderic Gregory and Hilda Tracy, after many experiments which can be followed in the *Journal of Physiology*.<sup>228 229 230 231</sup>

## 2. 8. 1: Changes in hospital care over the period of the nineteenth century

Between 1760 and 1840, Britain underwent huge societal changes at the time of the Industrial Revolution. Its industries served the needs of a home market and an empire. The 1851 census showed that by then a majority of the population had become urban dwellers, as increasing numbers of people deserted the countryside for the towns and industrial cities where the poorest set up home in the slums. A potato famine in Ireland caused the mass immigration of thousands of poor Irish people to the large cities and towns on Britain's western seaboard from 1846-51. In the following years many of their successors remained in the poorest of circumstances and suffered ill-health and reduced life expectancy. The Industrial Revolution did confer improvement upon the lives of those whose health and circumstances allowed them to work in the industries of the time but injury and ill health were always spectres which haunted the streets of working-class people.

Health-care provisions for the majority of the British population in the nineteenth century began and usually ended with self-help from relatives or other non-medical sources in their own homes. The well-off could consult a doctor and might undergo surgery at home. The voluntary hospitals provided in-patient services for those who were in employment and who could find a subscriber to recommend them.<sup>232 233 234</sup> They mainly took patients with

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<sup>226</sup> Gastrin stimulates the parietal cell in the stomach to secrete hydrochloric acid.

<sup>227</sup> Smith A N, 'Gastrin and histamine release', *Proceedings of the Physiological Society*, Feb 12<sup>th</sup>-13<sup>th</sup> 1954, 71-2

<sup>228</sup> Gregory R A, Tracy H J, 'The preparation and properties of gastrin', *Journal of Physiology supp.*, 1959, vol. 149, 70-1

<sup>229</sup> Gregory R A, Tracy H J, 'The further purification of gastrin-secretory responses in a human subject', *Journal of Physiology-London supp.*, 1960, vol. 154, 52-3

<sup>230</sup> Gregory R A, Tracy H J, 'Preparation and properties of gastrin', *Journal of Physiology-London*, 1961, vol. 156, 523-43

<sup>231</sup> Gastrin stimulates hydrochloric acid secretion by the parietal cell which is located in the part of the stomach called 'the body'.

<sup>232</sup> Granshaw L, 'The Rise of the Modern Hospital in Britain', in Wear A, ed., *Medicine in Society: Historical Essays*, (Cambridge, 1992, Cambridge University Press), pp200-08

<sup>233</sup> Rivett G, *The Development of the London Hospital System 1832-1982*, (London, 1986, King's Fund Publishing Office), pp29-30

longstanding symptoms who were relatively stable and while emergencies were not refused, there is evidence that they would not readily admit dying patients.<sup>235</sup> Voluntary hospitals also set up outpatient dispensaries.<sup>236</sup> Comparatively few of those who required hospital attention could find a place in them.<sup>237</sup> Scottish voluntary hospitals were possibly less strict in their admission criteria than London hospitals which admitted patients only on specified days and would turn away all except those who had been involved in serious accidents.<sup>238</sup>

## 2. 8. 2: Voluntary hospitals and the Poor Law

In the nineteenth century, sick poor people needing care outside the home were admitted to the Poor Law Institutions which provided little more than meagre feeding and shelter. Incurables or paupers who had found their ways into the voluntary hospitals were discharged into the Poor Law Hospitals.<sup>239</sup> Many poor people died at home without ever seeing a doctor in the course of their final illness. In the strict application of Poor Law regulations, barriers were placed in the way of those seeking admission to its hospitals and ‘moral issues’ played a part in decision making. A distinction was made between the ‘deserving poor’, those who had fallen on hard times on account of injury or disease, and, the ‘undeserving poor’, those who had no recent record of self-sufficiency. Sick paupers who were admitted to the part of the Poor Law workhouses called ‘infirmaries’, were exempted from physical labour.<sup>240</sup> In effect the Poor Laws did little to provide medical care for most of the nineteenth century and no major surgery was performed in their infirmaries until the last decades when investment in staffing and improvement of facilities and conditions occurred.<sup>241 242</sup> The numbers of destitute poor varied from five to ten per cent of the population over the century.

The appendix of the third report of the Registrar General states that in 1841, 5.5 % of deaths in the metropolis of London occurred in hospital.<sup>243</sup> There were 11,848 voluntary hospital beds in 1861, in England, for a population of 20 million persons. This equates to a

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<sup>234</sup> Woodward J, *To Do the Sick No Harm*, (London, 1974, Routledge & Keegan Paul), p39

<sup>235</sup> Woodward J, *To Do the Sick No Harm*, *ibid*, p135

<sup>236</sup> Granshaw L, Porter R, eds, *The Hospital in History*, (London, 1989, Routledge), pp4-8

<sup>237</sup> Rivett G, *The Development*, *op cit*, p49

<sup>238</sup> Rivett G, *The Development*, *op cit*, p29

<sup>239</sup> Toogood F S, ‘The genesis of the modern infirmary’, *The Lancet*, Aug 14<sup>th</sup> 1909, pp446-9

<sup>240</sup> Lawrence C, *Medicine in the Making*, *op cit*, pp42-3

<sup>241</sup> Rivett G, *The Development*, *op cit*, p69; Clark-Kennedy A E, *The London, a Study in the Voluntary Hospital System*, vol. 2, (London, 1963, Pitman Medical), pp64, 201

<sup>242</sup> Toogood F S, ‘The genesis’, *op cit*, 447

<sup>243</sup> Farr W, *Appendix to the Third Annual Report of the Registrar General of Births, Deaths and Marriages in England*, (London, 1841, H.M.S.O), p19

bed availability of 0.59 beds per thousand of population. The average in-patient stay was between 30-40 days and the conditions of admission meant that the hospitals were generally full of ‘curables’.<sup>244 245</sup> In Glasgow Royal Infirmary in 1810, approximately 3% of in-patients had a diagnosis of ‘dyspepsia.’ The annual mortality for the hospital was 5% and no deaths were recorded from dyspepsia. In the city as a whole, that year, a quarter of deaths were from consumption.<sup>246</sup> In 1857, St George’s Hospital in London admitted 63 patients with a diagnosis of ‘dyspepsia’ which represented 2.6% of all admissions and only two of these died. Over a seven year period from 1851-7, 434 patients were admitted with dyspepsia.<sup>247</sup>

Between 1860 and 1890 Britain experienced a prolonged economic depression. Since increasing numbers were becoming affected by unemployment and illness, the poor law establishments took rudimentary steps toward providing medical care within their doors and began separating the insane, the elderly and the paupers from the chronic sick. However, little was available to the sick poor for health amelioration or treatment in the nineteenth century. In an attempt to reduce in-patient numbers, ‘out-door relief’ was provided, but this was not generous and in reality few if any ever wished to enter the poorhouse, for such was its reputation as an evil parsimonious place for its inmates.<sup>248</sup> Gradually in the second half of the nineteenth century, schemes were devised to allow increased access to medical help for the working classes in the voluntary hospitals.

Increasing public sector finance of the Poor Law improved the scope of medical provision which nevertheless varied greatly between local authorities. For most of the century, nursing was basic and inadequate, with only one nurse at best per ward, and much of the caring of patients was done by fitter inmates, a practice which, though time-honoured, was eventually banned. In the last decades of the nineteenth century nursing schools were opened in the Poor Law Infirmarys and a supply of newly qualified young doctors working in them raised the overall standards and the range of treatments available, including surgery which increased so that in the following century some of the Poor Law Infirmarys rivalled some of the voluntary hospitals in terms of clinical facilities.<sup>249</sup> With all the major advances in surgical techniques and care, hospitals improved to such an

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<sup>244</sup> Woodward, *To Do the Sick*, op cit, pp36-45

<sup>245</sup> Rivett G, *The Development*, op cit, p30

<sup>246</sup> Anon, ‘Medical report of Glasgow Infirmary for 1810’, *Edinburgh Medical Journal*, Apr 1811, 246-9

<sup>247</sup> Rogers G G, ‘Annual report of cases admitted into the medical wards of St George’s Hospital 1857’, *The Lancet*, Oct 23<sup>rd</sup> 1858, 418-21

<sup>248</sup> Crowther M A, *The Workhouse System, 1834-1929*, (London, 1981, Batsford Academic and Educational Ltd)

<sup>249</sup> Toogood F S, ‘The genesis’, op cit, 447

extent over the first twenty years of the twentieth century, that they became a preferable site for the care of those with the most serious complications of peptic ulcer.

## Conclusion to chapter two

This chapter has examined how the medical profession became established in the early part of the nineteenth century and was recognised by an Act of Parliament in 1858. The importance of autopsy as a means of understanding disease as being lesion-based was then seen as was the part played by the Paris hospitals in promoting this novel concept of disease which became accepted in Europe and the English-speaking world. Arising out of this approach, the emergence of peptic ulcer as a recognised clinical and pathological entity was examined from the earliest clinical accounts of it. The chapter then dealt with a number of issues including self-help books for use by patients and apparent gender predilection in peptic ulcer before examining how knowledge grew as a consequence of the work of surgeons in emergency and elective situations due to the developments in anaesthesia and antiseptic techniques. Human and animal physiological experimentation increased allowing the physiology and pathology of gastric digestion to become more clearly understood. Throughout the time period, major changes were taking place in society and in medical and surgical care in hospitals.

In the next chapter it will be seen how medical practitioners tried to 'see inside the body' to assist diagnosis of peptic ulcer diseases and understand the working of the stomach using chemistry. They also used the new discovery of X-rays and endoscopies which began to be developed as diagnostic aids without surgery. Aetiological concepts which achieved prominence for a time but later were discarded under the medical gaze of later generations whose research pointed to an understanding of the issues in different terms will be discussed.

## Chapter 3. How medical practitioners investigated cases of peptic ulcer disease and theories of its causation

### Introduction to chapter three

In this chapter it is seen how understanding of peptic ulcer disease changed as clinical investigators in the nineteenth and twentieth centuries used the technology of the day as they tried to envisage the body's internal working and diagnose its diseases by means of test meals, X-rays and endoscopy. Over the period different theories of what caused peptic ulcers emerged from the work of researchers and eight of these are discussed in this chapter examining them in their clinical settings.

### 3. 1. 1: 'Looking inside the body' 1: the test meal and gastric analysis

In order to better understand the nature of peptic ulcer disease in the nineteenth century, medical practitioners looked to chemistry to find ways of 'seeing inside the body', by analysing its physiological workings.

*During the first half of the 19th century, clinical chemistry emerged from applications of chemistry to medical diagnosis. The discoveries of new substances in the healthy and diseased body that accompanied the beginning of scientific medical research, and the development of organic and physiological chemistry, spawned a wave of interest in clinical chemistry as a recognizable identity in the late 1830s and 1840s. There followed a systematic search for pathologic changes in the chemical composition of body fluids to guide medical diagnosis, follow the course of the disease, and control therapy. A search for chemical explanations for physiologic phenomena became a major preoccupation of leading scientists during the 19th century.<sup>250</sup>*

As stated in the previous chapter, William Prout discovered hydrochloric acid in the stomach and approximately one month after he published his findings in 1824, they were confirmed by Friedrich Tiedemann and Leopold Gmelin using a different method.<sup>251</sup> However this did not settle the matter and physiologists, including François Magendie, believed that the acid was lactic acid and taught that hydrochloric acid was a by-product of

<sup>250</sup> Rosenfield I, 'William Prout: Early Nineteenth Century Physician-Chemist', *Clinical Chemistry*, 2003, vol. 49, no.4, 699-705

<sup>251</sup> Prout W. 'On the nature of the acid and saline matters usually existing in the stomachs of animals', *Philosophical Transactions of the Royal Society of London*, 1824, vol. 114, 45-9

a secondary chemical reaction. Then in 1852, Carl Schmidt of the University of Dorpat conclusively demonstrated that the acid in stomach juice was hydrochloric acid by sampling and analysing the gastric juices of different species of live animals from fistulae.<sup>252</sup> William Beaumont's contribution led to much research built upon his observations and experiments. Clinicians came to perceive that in different illnesses affecting the stomach, the gastric juices could vary in constitution and amount and if that variation could be detected then this might be the basis of a diagnostic test.

The 'test meal' was invented to allow experimenters to assess stomach gastric juice output. The technique evolved by trial and error until clinicians eventually agreed a regime of giving a patient a standardised meal after which they sampled the gastric juices using a stomach tube. The gastric juice thus obtained was analysed and hopefully yielded useful information. William Osler's 1892 textbook of medicine detailed the method of gastric analysis which he considered was necessary in investigation of a stomach complaint. He used the 'Ewald test' which comprised a 30 gram white bread roll and a cup of plain tea or water given to a patient by mouth. An hour later, he aspirated the stomach's contents and measured the quantity of gastric juice present. A normal stomach yielded between 20 and 40 cc of clear yellow or yellow-brown fluid which tested positive for acid on litmus paper. He was then able to measure the quantities of those acids known to be present in the stomach, viz. hydrochloric, lactic and butyric acids. He also measured pepsin and pepsinogen as well as 'curdling ferment' and zymogen. Osler makes no comment on normal values, except to say that if more than 40cc of fluid were present then he would suspect the stomach to have 'diminished motor power'.<sup>253</sup>

Martin Rehfuss in 1916 established that there was a variable pattern of gastric secretion, both in terms of rate of secretion and gastric emptying, and the quantity of gastric juice secreted in response to a test meal.<sup>254</sup> Rehfuss used the same 'Ewald meal', this time comprising tea and toast. He found that,

*After studying the average collective response of all normal individuals it becomes apparent that while the motor function in perfect health varies within very narrow limits, the quantity and quality of the secretion has considerable variations. There is a group by no means small in which the secretion is very abundant, the acid figure high, and there is often present a post-digestive or continued secretion.*

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<sup>252</sup> Rosenfield I, 'William Prout', op cit, 703-4

<sup>253</sup> Osler W, *The Principles and Practice of Medicine*, (Edinburgh and London, 1892, Young J Pentland), pp344-8

<sup>254</sup> Geraghty E M, 'Test Meals', *The American Journal of Nursing*, Mar 1932, 291-300

*These people always react in this way while there is a group diametrically opposed who show a rather tardive secretory response. Both are normal: both without symptoms: both must be considered in the analysis of any pathological case.*<sup>255</sup>

Such conclusions illustrate the new-found difficulty of interpreting any biological test which is rarely, 'positive or negative', but often, 'within normal limits' or 'not within normal limits'. John Ryle in 1920 undertook a study of gastric acid secretions in different medical conditions and found that certain conditions seemed to be associated with high, low or normal acid levels. He found that duodenal ulcer was associated with high acidity and gastric neoplasm with low levels.<sup>256</sup> The following year, John Ryffell produced results he had found in patients with gastric ulcer.<sup>257</sup> Neither Ryle nor Ryffell suggested that their technique would be a diagnostic test for peptic ulcer but the Medical Research Council (MRC) thought it might have had merit and a standardised method of working was published in 1921.<sup>258</sup> Five years later careful analysis of results in a larger series demonstrated that test meals as diagnostic aids were of little use. This was the finding of Lucy Wills, a chemical pathologist who stated in 1926:

*It cannot be too emphatically stated that, with the exception of new growth of the stomach (neoplasm), the test meal examination gives very little help in diagnosis. In medical conditions such as pernicious anaemic, the diagnosis rests upon other examinations. In the surgical conditions other than new growth, a good X-ray plate gives far more valuable information. In confirmed cases of gastric and duodenal ulcer the chances are practically equal that the test meal findings will be the so called typical ones or normal (or subnormal), so that the fact that the gastric curve is normal will not rule out these conditions. Further, a hyperchlorhydric curve without symptoms in no way suggests a lesion.*<sup>259</sup>

Gastric test meals were not killed off as a technique for diagnosing peptic ulcers by this damning assessment and they appear to have continued to be used for this purpose as can be seen in a leading article in *The Lancet* in 1951 where it was stated, 'The full value of

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<sup>255</sup> Rehffuss M E, 'The Normal Gastric Secretion', *Proceedings of the American Philosophical Society*, 1916, vol. 55, no. 6, 461-70

<sup>256</sup> Ryle J A, 'The fractional test meal', *The Lancet*, Sep 4<sup>th</sup> 1920, 490-2

<sup>257</sup> Ryffell J H, 'Chemical estimation of gastric function by the test meals of Ewald and Boas', *The Lancet*, Mar 19<sup>th</sup> 1921, 586-8

<sup>258</sup> Cole S W, Adie W J, 'Analysis of the gastric contents obtained by the fractional method: a report to the Medical Research Council', *The Lancet*, Feb 26<sup>th</sup> 1921, 423-6

<sup>259</sup> Wills L, 'Fractional test meals: analysis of results obtained in one hundred and sixty consecutive cases', *The Lancet*, Apr 25<sup>th</sup> 1928, 825-8.

Hyperchlorhydria is the condition when the stomach secretes an excess of acid.

the fractional test meal is of little value in the diagnosis of gastric or duodenal ulcer, and its significance in prognosis has never been convincingly determined.<sup>260</sup>

Test meals are now used in testing for intestinal malabsorption conditions and diseases. Although test meals were unhelpful diagnostically to clinicians trying to find peptic ulcers in their patients, nevertheless where blood was found in the gastric contents along with achlorhydria, this suggested the possibility of gastric cancer.<sup>261</sup>

### 3. 1. 2: 'Looking inside the body' 2: the development of X-rays

On December 28<sup>th</sup> 1895 Wilhelm Röntgen sent a scientific paper describing his new discovery of X-rays as a 'preliminary communication' to the Wurtzburg Physical Medical Society which was published in the journal, *Nature* on the 23<sup>rd</sup> January 1896 under the title, 'On a New Kind of Rays'.<sup>262</sup> In its attempts to 'see inside the body', doctors quickly realised the potential of X-rays in making diagnoses. In the months after Röntgen gave his first lecture, medical journals contained many articles proclaiming the usefulness of X-rays for diagnostic purposes. One major reason for this was that the equipment which Röntgen had used to produce X-rays was in regular use in the physics laboratories of the universities for other experimental purposes and anyone with access to the equipment could replicate the results. Electrical manufacturers were able to produce new modified vacuum tubes and other suitable apparatus easily. Public interest was stimulated by demonstrations where admission was gained upon payment of a fee.<sup>263</sup>

From an upper gastro-intestinal point of view, plain x-ray examination does not allow a clinician to see the structure of the oesophagus, stomach or duodenum. As a consequence routine radiographs of the abdomen were unhelpful in the diagnosis of peptic ulcer except in the case of ulcer perforation when air which had been in the stomach escapes into the peritoneal cavity giving the classical appearance of 'gas under the diaphragm' on an X-ray taken with the patient standing. However in 1898 Walter Cannon demonstrated that if he fed a goose with meal containing bismuth this would outline its upper gastro-intestinal tract if X-rayed.<sup>264</sup> In 1899, Francis Williams used a bismuth-containing meal to allow the human stomach to be studied using X-rays via fluoroscopy and film.<sup>265</sup> Walter Cannon

<sup>260</sup> Leading article, 'Fractional test meals', *The Lancet*, Jul 11<sup>th</sup> 1953, 3-4

<sup>261</sup> Achlorhydria is the condition when the stomach secretes no acid.

<sup>262</sup> Röntgen W C, 'On a new kind of rays', *Nature*, Jan 23<sup>rd</sup> 1896, 274-6

<sup>263</sup> Burrows E H, *Pioneers and Early Years; a History of British Radiography*, (Alderney, 1986, Colophon), pp20-23

<sup>264</sup> Cannon W B, Moser A, 'The movements of the food in the oesophagus', *American Journal of Physiology*, Jul 1<sup>st</sup> 1898, vol. 1, 435-44

<sup>265</sup> Williams F, 'X-ray examinations of the abdomen', *Boston Medical and Surgical Journal*, 1900, vol. 142, 23

and his associates continued their X-ray researches on stomach physiology using bismuth subnitrate meals fed to cats.<sup>266</sup> Francis Scrimger in 1911 described his experiences of the use of bismuth carbonate to be used in the radiological diagnosis of stomach diseases. His article makes mention of the work of pioneers of the technique, Reider in Germany and Holzkecht in Austria.<sup>267</sup> Two years later, Berkeley Moynihan wrote enthusiastically of his experience of the use of bismuth meal as a diagnostic aid in ulcers of stomach and duodenum.<sup>268</sup> Very gradually thereafter, opaque meals, as they were known to radiologists, were used in the diagnosis of diseases of the upper gastrointestinal tract as experience in this area of radiology grew.<sup>269</sup> Barium sulphate was substituted for bismuth carbonate later in the 1920s being cheaper and non-toxic. Barium meals eventually became one of the commonest radiological procedures performed in hospitals as will be seen in chapter eight of this thesis as will be their refinements which followed.

### 3. 1. 3: 'Looking' inside the body 3: the development of endoscopy

From the earliest times, it was only possible to see deep inside the human body after death. A doctor's examination techniques were limited in life to visually examining the surface of the body and using the indirect methods of palpation, percussion, auscultation to interpret normality or not within it. The body's orifices offered an opportunity to further the scope of examination but they presented formidable access problems without causing pain or damage to the patient. In the second half of the nineteenth century, much ingenuity was employed to sample the contents of the stomach in an attempt to add to diagnostic accuracy. One answer lay in endoscopes which allowed visual inspection of accessible hollow organs which could not be seen by normal examination. Specialists working in ear, nose and throat disorders produced the first such instruments for routine use but getting adequate illumination was a problem. After initially using different flame based light sources, safe electrically operated lights were produced towards the end of the nineteenth century.

The oesophagus was the first area of the upper gastrointestinal tract to be reached by an instrument which was mainly used to remove impacted food. Adolf Kussmaul was one early user of the rigid gastroscope but difficulties in illumination and visualisation hindered

<sup>266</sup> Cannon W B, Murphy F T, 'The movements of the stomach and intestines in some surgical conditions', *Annals of Surgery*, Apr 1906, vol. 43 no. 4, 512-36

<sup>267</sup> Scrimger F A C, 'X-rays with Bismuth test meals in diagnosis of gastric conditions', *Canadian Medical Journal*, Jan 1<sup>st</sup> 1911, vol. 1, issue 1, 53-8

<sup>268</sup> Moynihan B G A, 'Some points in the diagnosis and treatment of chronic duodenal ulcer', *The Lancet*, Jan 6<sup>th</sup> 1912, 9-13

<sup>269</sup> Horder Sir T, 'The value of the opaque meal in the diagnosis of diseases of the intestinal tract', *The British Journal of Radiology*, Mar 29<sup>th</sup> 1929, vol. 2, no. 15, 97-135, esp 128-31

acceptance of the technique for most of the nineteenth century.<sup>270</sup> John Bevan, writing about his version of the oesophagoscope, stated that ‘it is possible to visualise the oesophagus but the stomach may be demonstrated, should this answer any useful purpose’.<sup>271</sup> Johannes von Mikulicz invented an oesophagoscope with an angled end which allowed some visualisation of the stomach but Georg Kelling in London made the first flexible instrument which allowed a greater field of vision.<sup>272</sup> The next major improvement of a semi-flexible gastroscope was co-invented in Berlin by Rudolf Schindler and Georg Wolf appearing in 1932. Schindler came to the USA as a refugee from Hitler’s Germany bringing his instrument with him and he introduced many gastroenterologists to endoscopy.<sup>273 274</sup> The limitations of the Wolf-Schindler gastroscope were known for it did not allow some parts of the inside of the stomach to be visualised because of its design. A British alternative invented by Hermon Taylor was introduced in 1941. Its tip could be moved more to allow an increased field of vision compared with the Wolf-Schindler gastroscope and it was used in the UK.<sup>275</sup> In 1957 the first flexible endoscopes were introduced thanks to fiberoptic technology used by Basil Hirschowitz.<sup>276 277</sup> The original models were relatively bulky and less flexible than could be desired but multiple improved variations from the Japanese and American optical industries quickly followed.

For most of its history, endoscopy was performed by gastroenterologists but nurse specialists are now trained to perform the task.<sup>278</sup> Endoscopy now stands as the ‘gold standard’ for internal diagnosis in peptic ulcer disease and has virtually replaced barium meals for most situations. Video and still cameras attached to the endoscope produce permanent records of the examination. Endoscopes are now used for directly visualising biopsies and for therapeutic intervention in the case of acute gastric haemorrhage where

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<sup>270</sup> The early history of endoscopy is well covered in Edmondson J M, ‘History of the instruments for gastrointestinal endoscopy’, *Gastrointestinal Endoscopy*, 1991, vol. 37, no. 2, 27-56 and Marsh B R, ‘Historic development of bronchoesophagology’, *Otolaryngology-Head and Neck Surgery*, Jun 1996, 699-16.

<sup>271</sup> Bevan J A, ‘Oesophagoscope’, *The Lancet*, Apr 11<sup>th</sup> 1868, 470-1

<sup>272</sup> Kelling G, ‘Endoscopy of the oesophagus and stomach’, *The Lancet*, Apr 28<sup>th</sup> 1900, 1074-8

<sup>273</sup> Schindler R, ‘Gastrosocopy with a flexible gastroscope’, *American Journal of Digestive Diseases and Nutrition*, Nov 1935, vol. 2, issue 11, 656-63

<sup>274</sup> Benedict E B, ‘Examination of the stomach by means of a flexible gastroscope: a preliminary report’, *The New England Journal of Medicine*, Mar 29<sup>th</sup> 1934, vol. 210, 669-74

<sup>275</sup> Taylor H, ‘A new gastroscope with controllable flexibility’, *The Lancet*, Sep 6<sup>th</sup> 1941, 276-7

<sup>276</sup> Hirschowitz B I, Curtis L E, Pollard H M, ‘Demonstration of the new gastroscope, the “fibrescope”’, *Gastroenterology*, Jul 1958, vol. 35, 50-3

<sup>277</sup> Hirschowitz B I, ‘Endoscopic examination of the stomach and duodenal cap with the fiberscope’, *The Lancet*, May 20<sup>th</sup> 1961, 1189-98

<sup>278</sup> Williams J, Russell I, Durai D, et al, ‘Effectiveness of nurse delivered endoscopy: findings of multi-institution endoscopy trial’, *British Medical Journal*, Feb 10<sup>th</sup> 2009, vol. 338, 519-21

peri-lesion injection and heat coagulation are now established treatments and recently cryotherapy has been used with good results in some cases.<sup>279 280</sup>

### 3. 2: Factors believed to be important in the genesis of peptic ulcers

#### 3. 2. 1: Bacteriological theories

By the end of the nineteenth century a powerful new theory of disease aetiology was establishing itself. The ‘germ theory’ would ultimately abolish older concepts of miasma and contagion as the causes of infectious diseases as a result of the work of bacteriologists demonstrating the actual agents responsible for many of the infectious diseases then prevailing.<sup>281</sup> However one barrier to its acceptance was their inability to demonstrate any micro-organisms in the cases of smallpox and measles, which were highly infectious and contagious diseases in the nineteenth century which killed many people.<sup>282</sup> Bacteria isolated from stomach ulcer margins were seen microscopically in 1875 but their significance was not appreciated.<sup>283 284</sup>

The discoveries in bacteriology promised much in the realms of scientific understanding of diseases caused by infecting agents, however the ‘bacterial hypothesis’ of peptic ulcer causation fell into disuse within a short period of its introduction.<sup>285</sup> Whilst it was accepted that bacteria might play a part in the genesis of ulcers, no specific organism was isolated as a definite cause for them although Giulio Bizzozero demonstrated what are now recognised to be helicobacters in the stomachs of dogs.<sup>286</sup> In the years which followed, researchers continued to see bacteria in the stomach. These included Bertrand Dawson, who in 1911, wrote about the varieties of bacteria which could be found in the stomach, both in health and ill-health despite the powerful antibacterial action of hydrochloric acid.<sup>287</sup> Edward Rosenow, an American bacteriologist working in the Mayo Institute, had

<sup>279</sup> Barkun A, Bardou M, Marshall J K, et al, ‘Consensus recommendations for managing patients with nonvariceal upper gastrointestinal bleeding’, *Annals of Internal Medicine*, Nov 18<sup>th</sup> 2003, vol. 139, no. 10, 843-59

<sup>280</sup> Kantsevov S V, Cruz-Correa M R, Vaughn C A, et al, ‘Endoscopic cryotherapy for the treatment of bleeding mucosal vascular lesions of the G I tract: a pilot study’, *Gastrointestinal Endoscopy*, 2003, vol. 57, no. 3, 403-6

<sup>281</sup> Miasma was a foul smelling vapour which was caused by decomposed material which was considered poisonous and could cause illnesses. Contagion caused illnesses by either direct or indirect contact.

<sup>282</sup> Reiser S J, *Medicine and the Reign of Technology*, (Cambridge, 1978, Cambridge University Press), p82

<sup>283</sup> Kidd M, Modlin I M, ‘A century of *Helicobacter pylori*; paradigms lost-paradigms regained’, *Digestion*, vol. 59, 1998, 1-15

<sup>284</sup> Editorial, ‘Diseases of the stomach’, *The Lancet*, Apr 13<sup>th</sup> 1878, 539

<sup>285</sup> Kidd M, Modlin I M, ‘A century of *Helicobacter pylori*’, op cit, 4

<sup>286</sup> Figura N, Bianciardi L, ‘Helicobacters were discovered in Italy in 1892’, in Marshall B.J, ed, *Helicobacter Pioneers*, (Victoria, Blackwell Science, 2002), pp1-11

<sup>287</sup> Dawson B, ‘Microbic factor in gastro-intestinal disease’, *The Lancet*, Apr 29<sup>th</sup> 1911, 1124-9

a major interest in bacterial colonisation of the upper gastro-intestinal tract. He experimented with laboratory animals injecting them with Streptococci to observe the effects on the stomach.<sup>288</sup> He summarised his findings in this very long sentence at the end of one of his publications,

*The apparently almost constant occurrence of streptococci in the depths of human ulcers, commonly the more numerous the younger the ulcer, and the more marked cellular infiltration, to the total or almost total exclusion of other bacteria, and the fact that when injected into animals, such streptococci show a marked tendency to localise in the stomach and duodenum, a property which other bacteria isolated do not possess, taken in conjunction with clinical facts, constitute good evidence that streptococci are not merely accidental invaders of the tissues, but are commonly the original cause, as well as the important factor in preventing the healing of the ulcer.[sic]<sup>289</sup>*

In an earlier experiment in 1913 to prove that bacteria could cause gastric ulcers, Rosenow injected bacteria into the sub-mucous layer of a dog's stomach and succeeded in producing ulcers.<sup>290</sup> His papers were influential and subsequent researchers accepted his findings. However the authors of the 1950 textbook, *Peptic Ulcer*, stated that they had tried and failed to replicate Rosenow's experimental results using his technique.<sup>291</sup>

### 3. 2. 2: Visceroptosis

Franz Glénard was a French surgeon who introduced the concept of 'enteroptosis' whereby abdominal organs may cause symptoms or even pathological conditions by their being 'prolapsed' or 'downwardly displaced'.<sup>292</sup> He asserted that this downward displacement caused symptoms of poor health. Glénard wrote a book to support his theory, *Les Ptoses Viscérales*, describing in great detail, the technique and diagnostic findings of manual examination of the abdomen.<sup>293</sup> Despite opposition to his views by Carl Ewald in Germany, the concept became established as a dyspeptic syndrome in its own right and by

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<sup>288</sup> Streptococci are a type of bacteria which may or not be pathological but the pathological varieties tended to cause very severe and often fatal infections in the pre-antibiotic era.

<sup>289</sup> Rosenow E C, Sanford A H, 'The bacteriology of the stomach and duodenum in man', *Journal of Infectious diseases*, 1915, vol. 17, 219-26

<sup>290</sup> Rosenow E C, 'The production of ulcer of the stomach by injection of streptococci', *Journal of the American Medical Association*, Nov 29<sup>th</sup> 1913, vol. 61, 1947-50

<sup>291</sup> Ivy A C, Grossman M I, Bachrach W H, *Peptic Ulcer*, (Philadelphia and Toronto, 1950, The Blakiston Company), p271

<sup>292</sup> Glénard F, *A Propos d'un Cas de Neurasthénie Gastrique*, (Paris, 1887, Librairie de l'Académie de Médecine), Chapitre iv, Diagnostic, pp58-63

<sup>293</sup> Glénard F, *Les Ptoses Viscérales*, (Paris, 1899, Ancienne Librairie Germer Baillière et Cie)

1917 ‘Glénard’s Disease’ or ‘gastroptosis’ became an accepted diagnosis.<sup>294 295</sup> ‘Glénard’s Disease’ was also associated with displacement of the liver and one or both kidneys, and disturbances of the gastrointestinal tract and other pelvic organs were attributed to it. While there was no pathological association of gastroptosis with peptic ulcers, the symptoms attributed to both conditions could be confused clinically.

When bismuth meals became available to make a diagnosis of gastroptosis, radiologists distended the stomach with the patient standing up by using carbon dioxide gas produced from the interaction of swallowed tartaric acid and sodium bicarbonate or else they distended it with air via a stomach tube prior to taking their X-ray pictures.<sup>296</sup> It rapidly became evident that the position of the stomach and other organs, using this technique, was not where they appeared to be on the dissecting table as taught by anatomists. The bismuth meal (which dragged down the stomach and distorted its shape) was taken as proof of the existence of visceroptosis. Visceroptosis now had a ‘scientific’ basis for it, for X-rays demonstrated clearly the downwardly displaced stomach and intestines. Its popularity as a diagnosis did not last and by the nineteen-thirties it had virtually fallen out of use.<sup>297</sup>

### 3. 2. 3: Ulcer diathesis

In the nineteenth century the concept of ‘diathesis’ was part of a theory of health whereby individuals could have an hereditary predisposition to a number of illnesses which included arthritis, insanity, tuberculosis and syphilis to name a few. Sir Dyce Duckworth’s paper questioned this concept in 1908 as becoming increasingly irrelevant with the advent of more ‘scientific’ or laboratory based diagnoses.<sup>298</sup> Nevertheless the belief that an ‘ulcer diathesis’ existed, manifested by physical characteristics which contributed to the likelihood of developing an ulcer. Anthropomorphic data was gathered to ascertain whether or not particular bodily measurements made individuals more or less susceptible to particular diseases but Jacob Feigenbaum and David Howat’s detailed study of a large range of measurements of the parts of the human body was unable to justify this

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<sup>294</sup> Riegel F, *Diseases of the Stomach*, (Philadelphia, New York, London, 1904, WB Saunders & Company), pp440-1

<sup>295</sup> Kemp R C, *Diseases of the Stomach, Intestines and Pancreas*, (Philadelphia and London, 1917, W B Saunders Company), pp442-68

<sup>296</sup> McCallum H A, ‘A clinical lecture on visceroptosis: its symptoms and treatment’, *British Medical Journal*, Feb 18<sup>th</sup> 1905, 345-7

<sup>297</sup> Baron J H, Sonnenberg A, ‘The wax and wane of intestinal autointoxication and visceroptosis – historical trends of real versus apparent new digestive diagnoses,’ *The American Journal of Gastroenterology*, Nov 2002, vol. 97, issue 11, 2695-9

<sup>298</sup> Duckworth Sir D, ‘An address on the diathesis: the personal factor in disease’, *The Lancet*, Mar 7<sup>th</sup> 1908, 699-02

assertion.<sup>299</sup> The disease groups examined by this study included peptic ulcer, cholecystitis and diabetes mellitus. In the 1920s this concept was linked to a particular bodily habitus or build and with the advent of contrast X-rays of the stomach, the appearance of the stomach was considered almost diagnostic.<sup>300</sup> Arthur Hurst considered the concept to be relevant as a major aetiological factor in peptic ulcer disease.<sup>301</sup> Like ‘dyspepsia’, the term ‘ulcer diathesis’ stuck in the thinking of doctors and it continued to be used as late as 1985 without any real understanding of its nature.<sup>302</sup>

### 3. 2. 4: Vascular hypotheses

In 1853 Rudolph Virchow suggested that blockage of small blood vessels in the stomach wall may have created the conditions which allowed ulcer formation.<sup>303 304 305</sup> Robert Saundby in 1892 stated, that it was generally believed, that ulcer was due to thrombosis of ‘a limited vascular area with secondary necrosis and digestion of the dead part by the action of the gastric juice’.<sup>306</sup> Otfried Müller believed that ulcer sufferers had abnormal blood capillary arrangements in their stomachs and duodenums.<sup>307</sup> This theory continued into the 1950s by which time the nature of vasculature in the sub-mucosal layer of the stomach was better understood. It was shown experimentally that there was an arterio-venous arrangement which allowed blood flow in the layer under the mucosa (absorptive lining tissue) to vary according to the digestive processes. Spasm of the stomach muscle apparently could damage these delicate blood vessels and cause areas of anoxia.<sup>308</sup> This was suggested as the mechanism whereby the digestive effect of acid-pepsin in the stomach began and continued to damage the stomach lining (mucosa) which then developed an ulcer. Eddy Palmer described the process in two papers changing his pathological description from ‘anoxia and ischaemia’ in the first to that of ‘relative hypoxia’ which would start the ulcer to form by causing ‘sufficient depression of mucosal

<sup>299</sup> Feigenbaum J, Howat D, ‘The relationship between physical constitution and the incidence of disease’, *Journal of Clinical Investigation*, Jan 1934, vol.13, issue 1, 121-138

<sup>300</sup> Hurst A F, ‘An address on the hypersthenic gastric diathesis’, *The Lancet*, Dec 30<sup>th</sup> 1922, 1369-73

<sup>301</sup> Hurst A F, ‘An address on recent advances in the treatment of gastric diseases’, *British Medical Journal*, Nov 3<sup>rd</sup> 1928, 779-83

<sup>302</sup> Taylor T V, ‘Deaths from peptic ulceration’, *British Medical Journal*, Sep 7<sup>th</sup> 1985, 653-4

<sup>303</sup> Berg B N, ‘Gastric ulcers produced experimentally by vascular ligation’, *Archives of Surgery*, Jan 1947, vol. 51, no. 1, 58-66

<sup>304</sup> Osler W, ‘Diseases of the digestive system’, in *The Principles and Practice of Medicine*, (Edinburgh and London, 1892, Young J Pentland), p370

<sup>305</sup> Sun D, ‘Etiology and pathology of peptic ulcer’, in *Gastroenterology*, 3<sup>rd</sup> edition, ed Bockus H L, (Philadelphia and London, 1974, Saunders), p583

<sup>306</sup> Saundby R, ‘Clinical lecture on chronic ulcer of the stomach,’ *The Lancet*, Feb 14<sup>th</sup> 1891, 353-5

<sup>307</sup> Hurst A F, Stewart M J, *Gastric and Duodenal Ulcer*, (London, 1929, Oxford Medical Publications), pp58-9

<sup>308</sup> Hypoxia, anoxia and ischaemia are all pathological words which describe the reduction or loss of oxygen to tissues. Hypoxia means reduction of oxygen flow to tissue. Anoxia is absence of oxygen flow to tissue and finally the resultant tissue damage by total loss of oxygen is called ischaemia.

vitality to allow the acid-pepsin mechanism to cause ulcer'.<sup>309</sup> This theory did not advance the therapeutics of peptic ulcer disease for there was no known operation or drug which could influence the gastric vasculature at the time.

### 3. 2. 5: Mechanical and nerve theories

In 1915 William Mayo offered two more theories; 'the mechanical theory' and the 'nerve theory' as playing a part in the aetiology of both gastric and duodenal ulcer.<sup>310</sup> It was believed that a blow to the abdomen it could be responsible for initiating the process leading to gastric ulcers.<sup>311 312</sup> Trauma to the stomach lining caused by swallowing excessively hot liquids or by coarse food inadequately masticated was also implicated as a physical cause for peptic ulcer formation.<sup>313 314</sup> However the mechanical theory was challenged since it was known that the stomach could receive swallowed sharp objects with little sign of damage.<sup>315 316</sup>

The 'nerve' theory blamed 'a diseased innervation of the stomach, owing to a morbid condition of the vagus and to extreme acidification of the gastric juice' as a possible initiator of gastric ulceration. Mayo was quoting Carl Rokitansky who had a theory that ulcer patients had diseased stomach nerves.<sup>317</sup> The rôle of the vagus in production of gastric acid production was inadequately understood in Mayo's day and only began to be fully elucidated after vagotomy became a surgical procedure and is discussed later.<sup>318</sup>

### 3. 2. 6: Focal infection

As we have seen earlier in this chapter, micro-organisms had been observed in the stomach by scientists and clinicians in the nineteenth century but their significance was not appreciated and they were not precisely identified. A theory of 'focal infection' grew out of bacteriological discoveries which proposed that there were pockets of infections in the body, mostly in the teeth or tonsils or adenoids or nasal sinuses which were capable of

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<sup>309</sup> Palmer E D, Buchanan D P, 'On the ischaemic basis of peptic ulcer', *Annals of Internal Medicine*, Jun 1<sup>st</sup> 1953, vol. 38, no. 6, 1187-05; Palmer E D, Sherman Jr. J L, 'Hypoxia of abnormal physiologic origin as the final common pathway in gastroduodenal ulcer genesis', *Archives of Internal Medicine*, Jun 1958, vol. 101, no. 6, 1106-17

<sup>310</sup> Mayo W J, 'Chronic duodenal ulcer', *Journal of the American Medical Association*, Jun 19<sup>th</sup> 1915, vol. 64, 2036-40

<sup>311</sup> Editorial, 'Traumatic ulcer of the stomach', *The Lancet*, Dec 16<sup>th</sup> 1905, 1788-9

<sup>312</sup> Kemp R C, 'Diseases of the stomach', op cit, 278

<sup>313</sup> Mayo W J, 'Chronic duodenal ulcer', op cit, 2038

<sup>314</sup> Stewart M, 'On the pathology of gastric ulcer', *British Medical Journal*, Nov 24<sup>th</sup> 1923, 955-7

<sup>315</sup> Stewart M, 'On the pathology', ibid, p955

<sup>316</sup> Kemp R C, 'Diseases of the stomach', op cit, p278

<sup>317</sup> Rokitansky C, *A Manual of Pathological Anatomy*, (London, 1849, Sydenham Society), p36; also quoted in Avery Jones F, *Modern Trends in Gastroenterology*, (London, 1952. Butterworth & Co), pp383-4

<sup>318</sup> Vagotomy is the operation to cut the vagus nerve. It is discussed at length in chapter 4.

causing local and systemic illness by blood-borne spread, (metastatic spread), of the bacteria themselves or immune complexes of bacteria or of toxins produced by them.<sup>319</sup> In the early twentieth century, there arose a body of opinion that they were implicated in gastric ulceration by swallowing of the pus or bacteria from these sites.<sup>320</sup> Edward Rosenow's 1913 experimental production of gastric ulcers in dogs by injecting them with Streptococci led to the conclusion that infective agents could be a cause of gastric ulcers.<sup>321</sup> It was believed that septic foci could cause other major health problems. Frank Billings in 1914 wrote, 'In my opinion focal infection is frequently related to local and general disease.'<sup>322</sup>

In a paper presented at a symposium on mouth infection in 1914, Charles Mayo said,

*We have long looked upon the acids in the stomach as destructive to such bacteria (ingested with food), but Smithies in a microscopic examination of gastric extracts from 2,406 different individuals with 'stomach complaints' (dyspepsia, indigestion and the like), showed that irrespective of the degree of acidity of such extracts, bacteria were found in 87 per cent.*

*... in 54 cultural studies of saliva from 'dyspeptic patients', Streptococci and Staphylococci were demonstrated in over 80 per cent and bacilli in 66 per cent.'*<sup>323</sup>

Rosenow, at the same symposium, stated that 'These other foci are so common in patients suffering from arthritis, neuritis, appendicitis, ulcer of the stomach, cholecystitis, goitre, etc. and are so rare in individuals who have had superb health for years, that their direct etiologic role can scarcely be queried.'<sup>324</sup> Removal of focal infection was regarded as a necessary precursor of treatment in the Sippy regimen of which more in a later chapter.<sup>325</sup>

As a consequence, the belief grew that 'focal infection' or 'focal sepsis', caused by tooth disease, gum disease, infected tonsils and infected sinuses had causal links with peptic ulcers.<sup>326</sup> Cases continued to be presented of focal infection associated with peptic ulcer

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<sup>319</sup> van Veltzen S K T, Abraham-Inpijn L, Moorer W J, 'Plaque and systemic disease: a reappraisal of the focal infection concept', *Journal of Clinical Periodontology*, 1984, vol. 11, 209-20

<sup>320</sup> Kidd M, Modlin I M, 'A century of *Helicobacter pylori*', p7

<sup>321</sup> Rosenow E C, 'The production of ulcer of the stomach', op cit, 1947-50

<sup>322</sup> Billings F, 'Focal infection – its broad application in the etiology of general disease', *Journal of the American Medical Association*, Sep 12<sup>th</sup> 1914, 899-03

<sup>323</sup> Mayo C H, 'Mouth infection as a source of systemic disease', *Journal of the American Medical Association*, Dec 5<sup>th</sup> 1914, vol. 63, 2025-6

<sup>324</sup> Rosenow E C, 'Mouth infection as a source of systemic disease', *Journal of the American Medical Association*, Dec 5<sup>th</sup> 1914, vol. 63, 2026-7

<sup>325</sup> Anon, 'The Sippy treatment for gastric ulcer: (Compiled from directions of the Sippy Clinic)', *Journal of the National Medical Association*, Apr 1924, vol. 16, issue 2, 105-7

<sup>326</sup> Hurst A F, Stewart M J, *Gastric and Duodenal Ulcer*, pp46-52

which was cured by the removal of these foci. One particular experimental study supported the theory when bacteria from these foci were injected into laboratory animals which then died of duodenal haemorrhage.<sup>327</sup> It was believed that there was a predilection for bacteria in blood to have ‘selective preference for certain sites’.<sup>328</sup>

Focal sepsis provided physicians with a working hypothesis for the treatment of peptic ulcer disease which was surgical but remote from the abdomen. Vaccine therapy was also used. Henry Cotton, a New York psychiatrist, took an special interest in focal infection, believing it to be the cause of most mental illness.<sup>329</sup> He also believed that the stomach could also be a focus of infection and he produced autogenous vaccines using the bacteria extracted from the stomachs of his patients to treat ‘chronic gastric infection’.<sup>330 331</sup> Martin Rehfuss, a professor of medicine in Philadelphia and prolific medical author, also supported the view that vaccines should be used in the treatment of peptic ulcer disease. He used ‘stock vaccines’ by which he meant commercially available vaccines and also ‘autologous’ vaccines which were prepared from the bacteria obtained from the patients’ own bacteria in their infective foci (usually the tooth roots or the tonsils).<sup>332</sup> The latter vaccines were used when an infection was severe and or when stock vaccines had failed to work.<sup>333</sup> Dr William Hinton in New York’s Bellvue Hospital included vaccine therapy in his armamentarium for the treatment of gastric and duodenal ulcer in 1931 along with diet and the use of surgery when diet and other medical treatments had failed.<sup>334</sup>

Arthur Hurst also advocated the use of vaccines to treat peptic ulcers.<sup>335</sup> Vaccine use continued into the 1930s and in the UK, the pharmaceutical company of Parke Davis manufactured an anti-Streptococcal vaccine for the treatment of gastric and duodenal ulcer patients. Their handbook of vaccine therapy stated that; ‘long-chained non-haemolytic Streptococci are always present in cases of gastric and duodenal ulcer.’<sup>336</sup>

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<sup>327</sup> Haden R L, Bohan P T, ‘Focal infection in peptic ulcer’, *Journal of the American Medical Association*, Feb 7<sup>th</sup> 1925, vol. 84, 409-13

<sup>328</sup> Smith L, ‘Focal Infection’, *British Medical Journal*, Nov 14<sup>th</sup> 1925, 915

<sup>329</sup> Cotton H A, ‘Infection of the gastrointestinal tract in relation to systemic disorders’, *American Journal of the Medical Sciences*, 1922, vol. 164, 328-38

<sup>330</sup> Cotton H A, ‘Infection of the gastrointestinal’, *ibid*, 336

<sup>331</sup> Kopeloff N, ‘Is the stomach a focus of infection?’, *American Journal of the Medical Sciences*, 1923, vol. 165, 120-9

<sup>332</sup> Autologous and autogenous vaccines were essentially produced in the same way.

<sup>333</sup> Rehfuss M E, *Diagnosis and Treatment of Diseases of the Stomach*, (Philadelphia and London, 1927, W B Saunders Company), pp412-4

<sup>334</sup> Hinton W J, ‘The management of patients with gastric and duodenal ulcers’, *Annals of Surgery*, May 1931, vol. 93, issue 5, 1082-5

<sup>335</sup> Hurst A F, Stewart M J, *Gastric and Duodenal*, *op cit*, pp388-9

<sup>336</sup> Gale J N, ‘Vaccines in peptic ulcer’, *The Lancet*, Sep 8<sup>th</sup> 1934, 572

There were dissenting voices with reference to focal infection for it was evident to many doctors that it was possible to live a completely healthy life and have focal sepsis in the teeth or elsewhere. One such dissident, Campbell Stark, wrote in a letter to the *British Medical Journal* in 1925, ‘At present all we know is that, if we look for a focus of infection, in many diseases we will find it. If this was shown to be present in the majority of presumably healthy persons, what becomes of its importance in aetiology?’<sup>337</sup> There was an additional problem in the concept for those who advocated surgical removal of foci of infection which was that it was not technically possible in a large percentage of cases. Paul Rhoads showed that in 1928, pieces of tonsillar tissue ‘of appreciable size’ were to be found in the throats of over 70% of persons who had undergone tonsillectomy.<sup>338</sup> In 1934 Myers Solis-Cohen when writing of the efficacy of tonsillectomy, adenoidectomy, sinus surgery and tooth extraction in the pursuit of removal of foci of infection said, ‘It is insufficient to remove surgically infective tissue because it does not remove all of the focus of infection’. He suggested that it was necessary to supplement the surgery with specific antibody treatment made from the specific antigens from removed infected tissue. (autologous vaccine).<sup>339</sup> The eradication of focal infection carried with it appreciable mortality. In the case of Cotton’s referrals for abdominal surgery for focal sepsis, around 30% of his patients died from peritonitis in attempts to cure their psychoses.<sup>340</sup> Lesser procedures carried lesser mortalities.

The surgical risks of elimination of focal infection were known to be considerable at this time but the procedures were performed in the hope that they would relieve longstanding illnesses for which there was no other apparent solution. Simon Wessely’s paper makes this point that even after Margaret Fisher, a young woman who suffered from a severe intractable psychosis, died from septicaemia, having had her cervix removed, no blame was attached to Cotton who had recommended the procedure. Another factor lies with fear of the organism itself. The *Streptococcus* was greatly feared for it was known to be capable of causing many other serious infections, all of which could be rapidly fatal.<sup>341</sup>

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<sup>337</sup> Stark A C, ‘Focal infection’, *British Medical Journal*, Mar 13<sup>th</sup>, 1925, 979

<sup>338</sup> Rhoads P S, Dick G F, ‘Efficacy of tonsillectomy for the removal of focal infection’, *Journal of the American Medical Association*, 1928, vol. 91, 1149-54

<sup>339</sup> Solis-Cohen M, ‘Necessity for revising the common conception of focal infection’, *Journal of the American Medical Association*, 1934, vol. 102, 1128-31

<sup>340</sup> Wessely S, ‘Surgery for the treatment of psychiatric illness: The need to test untested theories’, *Journal of the Royal Society of Medicine*, Oct 1<sup>st</sup> 2009, vol. 102, no. 10, 445-51 esp 447

<sup>341</sup> Crowley M C, ‘Focal infection: a review of the current literature’, *American Journal of Orthodontics and Oral Surgery*, Feb 1946, vol. 32, issue 2, A126-A130

As the science of bacteriology progressed, it was realised that some subtypes of *Streptococci* could be identified which were more pathogenic than others whilst others were harmless to healthy humans. As always, the pathogenic potential of any organism depended upon the immunological fitness of any potential host it might encounter. As will be seen later in the thesis, in the first half of the twentieth century, a large proportion of the British population was relatively malnourished and many were suffering from chronic infections such as tuberculosis, both conditions being reckoned to reduce natural immunity to some extent. However two developments occurred in the second half of the twentieth century which eventually made the *Streptococcus* less feared. The first was the discovery of penicillin as a bactericidal treatment for Streptococcal and other infections and the second was the natural decline of the organism itself as a pathogen. By 1950, surgical treatment of focal infection appeared to be well on the wane as a therapy for peptic ulcers if relative lack of its mention in articles and books is a guide to the amount of surgery done for its eradication. However there remained an interest in dental hygiene in this context.<sup>342</sup>

### 3. 2. 7: Gastric acid

In terms of therapeutic advancement of peptic ulcer disease, the vascular, mechanical and focal infection theories eventually did not improve its management for it seemed to be growing as a problem as decade succeeded decade from the beginning of the twentieth century. After years of argument, it was eventually agreed that gastric acid played a most important rôle in peptic ulcer formation. It was described as the ‘sine qua non’ in peptic ulcer genesis and the circumstances under which peptic ulceration occurred were known, although not understood.<sup>343</sup> Acid had been consistently alluded to in the written record from its discovery in 1824. The evidence became compelling that this acidic gastric juice, which could tarnish metals and rot fibres, in the right circumstances caused ulcers.<sup>344</sup> Alexis Thomson wrote in 1909, ‘I believe that hyperacidity is one of the essential factors in the production of an ulcer.’<sup>345</sup> However it was not believed that acid itself caused the ulcer and that there had to be a lesion present for the acid to act upon. Others disagreed. In 1923, Frank Mann and Carl Williamson wrote,

*Many attempts have been made to evaluate acid as a primary or secondary factor in the cause of peptic ulcer. The results of such attempts have led to diametrically*

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<sup>342</sup> Ivy A C, Grossman M I, Bacharach W H, *Peptic Ulcer*, op cit, pp633-4

<sup>343</sup> Sun D, ‘Etiology and pathology’, pp579-80

<sup>344</sup> Illingworth C F W, *Peptic Ulcer*, (Edinburgh and London, 1953, E.& S. Livingstone), p6

<sup>345</sup> Thomson A, ‘The diagnosis and treatment of chronic ulcer of the stomach and duodenum’, *British Medical Journal*, Mar 13<sup>th</sup> 1909, 648-51

*opposite conclusions. Certain observers believe the acid to be directly responsible for the ulcer, while others believe that there is no causal relationship. Of those holding the former view, some believe that the ulcer develops in association with an overproduction of acid, or an increase in the degree of acidity, and others, that it develops when there is a decrease in the amount or degree of acidity. Neither of these points have been proven, but there is evidence to substantiate both.*<sup>346</sup>

In their paper they describe a series of animal experiments where they changed the normal anatomy of the upper gastrointestinal tract and rerouted the neutralising secretions of bile and pancreatic juices. Their experiment demonstrated that peptic ulcers could form on intestinal mucosa when the normal anatomy is changed surgically to allow the acidic stomach contents to come in contact with a section of small intestine not normally so exposed. This explained in part why ulcers form where surgeons produce new stomach openings into portions of the small intestine.<sup>347</sup> The role of gastric juices in the production of ulcers continued to be held to be important in peptic ulceration but in 1926, still not causal, when John Finney wrote,

*It is now generally thought that gastric juice has little or no part in the initiation of ulceration, but that its digestive action, after injury to the mucosa, is an important contribution towards the chronicity of the ulcer. It is even probable that these two factors - initial injury and subsequent digestion - if unaccompanied by a continuance of the underlying cause, are insufficient to prevent healing. Without previous injury, the gastric mucosa resists digestion. With ordinary injuries, gastric digestion alone is insufficient to prevent healing.*<sup>348</sup>

In 1936, Lester Dragstedt presented a paper in which he had come to the contrary conclusion that gastric acid alone was capable of causing peptic ulcers.<sup>349</sup> More research substantiated the link between acid hypersecretion and ulcer formation but this was not universally accepted.<sup>350</sup> Nevertheless research into gastric acid continued for most of the twentieth century and a vast volume of literature was created.<sup>351</sup> This will be further discussed later in the thesis. By 1970, it was possible to accurately measure acid output

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<sup>346</sup> Mann F C, Williamson C S, 'The experimental production of peptic ulcer', *Annals of Surgery*, Apr 1923, vol. 77, no. 4, 409-22

<sup>347</sup> This is discussed in chapter 7 in a section dealing with operations on the stomach

<sup>348</sup> Finney J M T, 'The surgery of gastric and duodenal ulcer', *The American Journal of Surgery*, Dec 1926, vol. 1, no. 6, 330-1

<sup>349</sup> Dragstedt L R, 'Some physiologic principles involved in the surgical treatment of gastric and duodenal ulcers', *Annals of Surgery*, Oct 1935, vol. 102, 563-80

<sup>350</sup> Editorial, 'Aetiology of peptic ulcer', *The Lancet*, Nov 26<sup>th</sup> 1949, 997-8

<sup>351</sup> Spiro H M, 'Peptic ulcer: Moynihan's or Marshall's disease?', *The Lancet*, Aug 22<sup>nd</sup> 1998, 645-6

from the stomach and it was apparent that the risk for ulcer for a given individual depended upon the stomach output of acid.<sup>352</sup> This confirmed what had been the basis of therapy. It is summed up in the aphorism, ‘no acid - no ulcer’ and set the problem for the clinician as to how to approach treatment.<sup>353 354</sup>

### 3. 2. 8: Psychological factors

Edwin Ackerknecht’s paper, ‘The history of psychosomatic medicine’, traces the apparent effect of the mind upon the functioning of the body as far back as Galen who spoke of ‘passions’ as being an important component in illness.<sup>355</sup> The suggested linkage of the mind to illnesses and diagnoses throughout the ages is described in Ackerknecht’s study which asserts that Galen’s ‘passions’ continued to influence medical thinking as far as the nineteenth century. ‘Passions’ were the sixth of Galen’s ‘six things non-natural’ which were aspects of a person’s life over which a person had some control and which had the power to affect health.<sup>356</sup> It was recognised that the mind played an important part in many illnesses with doctors using the word ‘moral’ when today the term would be ‘emotional’ or in other situations, ‘psychological’. The effect of the mind in some illnesses is recognised in the work of Armand Trousseau who identified psychological factors in such conditions and diseases as hyperthyroidism, diarrhoea, dyspepsia, angina pectoris and asthma.<sup>357</sup>

William Cullen was also an advocate of the rôle of the mind in illness. In his book of 1788 the terms ‘neuroses’ or ‘nervous diseases’ were defined by him as ‘the interruption and debility of the powers of sense and motion, or in the irregularity with which these powers are exercised’.<sup>358</sup> Cullen linked three mental states, which he classified as melancholia, hysteria and ‘the vapours’ (low mood), with dyspepsia saying that, ‘The combination of dyspepsia with the vapours is very frequent and in seemingly very different circumstances.’<sup>359</sup>

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<sup>352</sup> Hobsley M, in *Wellcome Witnesses to Twentieth Century Medicine, vol. 14, Peptic Ulcer: Rise and Fall*, Christie D A, Tansey E M, eds, (London, 2002, The Wellcome Trust), pp27-9

<sup>353</sup> Taylor T V, ‘Parietal cell vagotomy: long-term follow-up studies,’ *British Journal of Surgery*, Nov 1987, vol. 74, 971-2

<sup>354</sup> Logan R F A, Gillon J, Logan E C M, ‘Benign gastric ulceration with pernicious anaemia,’ *British Medical Journal*, Feb 3<sup>rd</sup> 1979, 308

<sup>355</sup> Ackerknecht E H, ‘The history of psychosomatic medicine,’ *Psychological Medicine*, 1982, vol. 12, issue 1, 17-24

<sup>356</sup> Berrymann J W, ‘The art of medicine: motion and rest, Galen on exercise and health,’ *The Lancet*, July 21<sup>st</sup> 2012, vol. 380, 210-1

<sup>357</sup> Ackerknecht E H, ‘The history,’ op cit, 20

<sup>358</sup> Cullen W, *First Lines of the Practice of Physic: A New Edition Corrected and Enlarged in Four Volumes*, (Edinburgh, 1788, C Elliot), vol. 3, p123

<sup>359</sup> Cullen W, *First Lines*, ibid, p262

The concept of ‘sympathy’ in the context of stomach disorders was current at the end of the eighteenth century and was promoted as an explanation of how a disorder of the stomach causes remote effects in other organs or parts of the body. These effects may be due to a nervous connection of remote organs with the stomach or by other means are consequent upon it but not fully understood and has been briefly alluded to in chapter one. John Abernethy, professor of anatomy and surgery to the Royal College of Surgeons in London in 1814 was a particular advocate of the theory of sympathy with reference to the stomach as being its centre in the body.

*Many of the symptoms recorded in the description of the state of health of those persons who are affected by a disorder of the digestive organs, denote a disturbance of the nervous and muscular forms... Whether this disorder of the digestive organs be primary or secondary, it generally produces irritation in the brain; and thus it may cause in many instances actual diseases in that organ.*<sup>360</sup>

In a lecture given in 1815, Abernethy reproduced the opinions of John Hunter whom he claimed was a supporter of theories about sympathy:

*This subject had indeed particularly attracted the attention of Mr Hunter who believed that the stomach had a remote sympathy with remote organs and parts of the body: whilst he equally observed, how it might reciprocally affect and be affected by the head. It was on this account, probably, that he was led to call the stomach the center [sic] of sympathies, a term, which such observations, if correct, would render particularly apt and expressive.*<sup>361</sup>

A reference to the mental states of patients which played a part in causing dyspepsia, ‘cerebral dyspepsia’, is recorded in 1841 by W D Husband,

*The influence of the mind over the body is especially marked in the sympathy which exists between the brain and the stomach. Disease of the brain very rarely exists without producing a disorder of the apparatus of digestion. ... Dyspepsia originates as often in the brain as in the stomach – possibly oftener. ... The secondary disease of the stomach may be alleviated by medicine but the primary disordered disease of the mind can only be removed by moral treatment. The*

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<sup>360</sup> Abernethy J, *Surgical Observations on the Constitutional Origin and Treatment of Local Diseases and Aneurysms*, (London, 1814, Longman, Hurst, Rees, Orme and Brown), 3<sup>rd</sup> Ed., p54

<sup>361</sup> Abernethy J, *Part of the introductory Lecture for the year 1815 Exhibiting some of Mr Hunter’s opinions respecting diseases*, (London, 1815, Longman, Hurst, Rees, Orme and Brown), p 103

*patient's confidence must be gained, his feelings understood, his general tone of mind comprehended, and his circumstances in life considered.*<sup>362</sup>

The perception that the brain played a part in peptic disease was assumed to be an insensible or subconscious one. William Fox in 1872 writes of, 'disturbances of the stomach resulting from perverted innervations' in his chapter on 'neuroses of the stomach'.<sup>363</sup> He links these disturbances indirectly to life events, gender issues including menstruation, anxieties and 'severer intellectual efforts'. He continues, 'There is, however, little doubt that, in whatever manner originating, the peculiar mental state accompanying this condition serves in no small measure to intensify the gastric disturbance already existing'. However at the end of the nineteenth century and the beginning of the twentieth century, major textbooks by Pepper,<sup>364</sup> Osler<sup>365</sup>, Reigel,<sup>366</sup> and Kemp<sup>367</sup> classify 'nervous dyspepsia' as a physical disorder arising in a disordered nervous system with no apparent psychological input.

Hurst and Stewart's textbook, *Gastric and Duodenal Ulcer*, published in 1929, stated that the first appearance of duodenal ulcer (in patients) often followed a period of combined physical and mental overwork, especially if it was accompanied by worry.<sup>368</sup> A later chapter, written by Hurst, discussed 'functional' gastric disorders by which was meant that sufferers had chronic symptoms suggestive of gastric or duodenal ulcer which could be not demonstrated by X-rays but required thorough investigation to exclude organic disease. He also described 'hysterical pain and vomiting and aerophagy', (air swallowing), as on-going problems which might occur in patients who had had an ulcer which had been successfully treated. Hurst recognised the powerful effect of the mind on the symptoms of gastric and duodenal ulcer patients.<sup>369</sup> Arthur Hurst was later to write about psychosomatic disorders which had the presenting symptoms of gastric and duodenal ulcers which

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<sup>362</sup> Husband W D, 'On dyspepsia resulting from disordered states of the mind', *Provincial Medical and Surgical Journal*, Dec 11<sup>th</sup> 1841, vol. 3, 205-8

<sup>363</sup> Fox W, *Diseases of the Stomach*, (London, 1872, Macmillan & Co). pp78-9

<sup>364</sup> Armour S G, 'Functional and inflammatory diseases of the stomach', in *A System of Practical Medicine by American Authors*, ed Pepper W, vol. 2, (London, 1885, Sampson Lowe, Marston, Searle and Rivington), pp436-79

<sup>365</sup> Osler W, *The Principles and Practice of Medicine*, (Edinburgh and London, 1892, Young J Pentland) pp368

<sup>366</sup> Reigel F, 'Nervous affections of the stomach', in *Diseases of the Stomach*, (Philadelphia, New York, London, 1904, W B Saunders & Company), pp748-812

<sup>367</sup> Kemp R C, 'Nervous affections in the stomach', in *Diseases of the Stomach, Intestines and Pancreas*, (Philadelphia and London, 1917, W B Saunders Company), pp469-98

<sup>368</sup> Hurst A F, Stewart M J, *Gastric and Duodenal Ulcer*, op cit, p70

<sup>369</sup> Hurst A F, Stewart M J, *Gastric and Duodenal Ulcer*, op cit, pp238-231

affected soldiers in wartime. His writing suggests that he was not enthusiastic about formal psychotherapy in such cases.<sup>370</sup>

In 1932, Harvey Cushing published a paper, 'Peptic ulcers and the interbrain', where he begins with the statement that,

*It is only in man that ulcers occur spontaneously with any considerable frequency, and it is not at all improbable that the prevalence, particularly of duodenal ulcers, has something to do with the strain and stress of modern life; for people today rarely find it possible to lead the comparatively placid existence enjoyed by their forebears.*<sup>371</sup>

He adds to his proposition by describing the 'highly strung' person prone to 'nervous indigestion' and ulcer and points to the value of rest for recovery and the propensity for recurrence in such people when re-stressed. The remainder of his 34 page paper describes nine cases under his care who had died from upper gastrointestinal bleeding or perforation following attempted curative surgical removal of their brain tumours, including one case in a six year old child. His literature search confirmed that others had found a similar link between brain pathology and peptic ulcer. He concluded,

*Those favourably disposed towards the neurogenic conception of ulcer have in the process of time gradually shifted the burden of responsibility from the peripheral vagus to its center in the medulla, to the midbrain, and now to the interbrain, now newly recognised as a highly important, long overlooked station for vegetative impulses easily affected by psychic influences.*<sup>372 373</sup>

Cushing was thereby offering a mechanism which linked worry and anxiety with peptic ulceration and because of his high standing in the profession, his proposition stood unchallenged for many years and added gravitas to theories which linked temperament with peptic ulcer. A database search reveals that this paper was cited 533 times by other medical authors.<sup>374</sup>

The rôle of the mind as it interacts with the body in diseases began to be explored after 1918 but it was after 1933, that the concept flourished largely due to the influx of refugee

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<sup>370</sup> Hurst Sir A, *Medical Diseases of War*, (London, 1943, Edward Arnold & Co), pp184-192

<sup>371</sup> Cushing H, 'Peptic ulcer and the interbrain', *Surgery, Gynaecology and Obstetrics*, Jul 1932, vol. 55, no. 1, 1-34

<sup>372</sup> Cushing H, 'Peptic ulcer', *ibid*, 33

<sup>373</sup> The medulla, midbrain and interbrain are parts of the brain situated deep in its structure.

<sup>374</sup> A *Web of Science* database search on 29.03.12, using 'Cushing H' with a time limit '1932', showed that this paper had been cited 533 times in other articles

German Jewish psychoanalysts to the USA.<sup>375</sup> In England in 1937, the effects of ‘life events’ on dyspeptic patients were studied in a paper published in *The Lancet* by Daniel Davies and Macbeth Wilson. They showed that in a series of 205 cases of peptic ulcer patients, 85% had relapses attributed to some kind of serious life event, often related to family tragedy or ill-health or financial hardship, often a combination of some or all of these.<sup>376</sup> They also demonstrated statistically that a ‘significant excess’ out of 100 peptic ulcer patients, when compared with a matched group of 100 hernia patients, suffered ‘undue tension long antedating their ulcer symptoms’. Their paper also discussed ‘the ulcer type’ of patient ‘whose outstanding characteristics are to be found in their facial expression, their intense mental and physical activity, and their reaction to illness. ... A serene contented facies is never seen.’<sup>377</sup>

The concept of ‘psychological stress’ slowly gained acceptance in the minds of many doctors and patients in the 1930s, there having been no mention of it in the writings of physicians and surgeons in the first three decades of the century. In the fourth decade of the century, it was beginning to be seen that the mind could exert a powerful influence over the body. Largely due to Sigmund Freud and the next generation of psychoanalytical colleagues’ influence, ‘neurosis’ had entered the regular vocabulary of both the medical profession and the public by the 1950s.<sup>378</sup>

In 1947, Burrill Crohn published a paper called ‘Peptic ulcer as a psychosomatic disease’ which reinforced the view that mental state could influence gastric secretion via the vagus and thereby facilitate ulcer formation.<sup>379</sup> He stated that, ‘The personal lives of most adolescents and adults today are likely to be a succession of tensions, frustrations, emotional struggles, domestic and family troubles.’ He believed he had shown in five of the cases he described, that psychic trauma had been the cause of peptic ulcer complications especially where there had been pre-existent peptic ulcer disease. He further supported Dragstedt’s new operation of vagotomy saying, ‘By eliminating the psychic phase of gastric secretion by inducing a relative anacidity, certainly in the earlier periods of the post-digestive secretory activity, cure is motivated.’<sup>380</sup>

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<sup>375</sup> Ackerknecht E H ‘The history’, op cit, 22-3

<sup>376</sup> Davies D T, Wilson A T M, ‘Observations on the life-history of chronic peptic ulcer’, *The Lancet*, Dec 11<sup>th</sup> 1937, 1353-60

<sup>377</sup> Davies, Wilson, ‘Observations’, ibid, 1358

<sup>378</sup> Porter R, *The Greatest Benefit To Mankind: A Medical History of Humanity from Antiquity to the Present*, (London, 1997, Fontana Press), p519

<sup>379</sup> Crohn B B, ‘Peptic ulcer as a psychosomatic disease’, *Surgical Clinics of North America*, 1947, vol.27, issue 2, 309-14

<sup>380</sup> Absence of acidity

By 1950, Ivy, Grossman and Bacharach's encyclopaedic 1144 page textbook, *Peptic Ulcer*, had one chapter of 26 pages discussing the 'Psychosomatic Etiology of Peptic ulcer'. In it they said,

*Much circumstantial evidence indicates that psychic factors play a rôle in initiating the onset or recurrence of peptic ulcer. We believe that there is ample evidence to show that perforations and haemorrhages from peptic ulcer are increased in number when a population is exposed to an environmental situation of which sustained anxiety is an outstanding component.*<sup>381</sup>

In 1952, Charles Illingworth suggested that 'formal psychotherapy has no place in the treatment of established ulcer but the informal psychotherapy which every practitioner employs is undoubtedly valuable'.<sup>382</sup> 'Stress' as a factor in the aetiology of peptic ulcer disease had become established and would be rarely absent from the advice given by doctors dealing with peptic ulcer patients in the following forty years.

### Conclusion to chapter three

This chapter has discussed the attempts of doctors to 'see inside the body' using test meals, X-rays and endoscopy from their initial developments to their use in present times. The remainder of the chapter is devoted to an examination of eight possible aetiological factors in the formation of peptic ulcers. Bacteriology and the development of the germ theory played a part in establishing the concept of focal infection which for a time was believed to be important as a cause of peptic ulcers. Of the remaining seven putative causes of peptic ulcers discussed, only gastric acid survived as a basis for the explanation of ulcer formation in the upper gastrointestinal tract despite its exact rôle not being fully discovered until the second half of the twentieth century. Psychological factors as a cause of peptic ulcer never fully waned but doctors treating ulcers could not apply theory to practice to successfully utilise their implications therapeutically.

In the next chapter the three most serious complications of peptic ulcer will be examined and it will be seen how doctors and surgeons dealt with them and how increasing numbers of lives began to be saved. The first successful emergency operative intervention by surgeons led to a new confidence among them to intervene both in emergency situations and later to attempt to treat patients' peptic ulcers by devising new surgical procedures to attempt to heal them. It will be seen how physicians and general practitioners also enjoyed

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<sup>381</sup> Ivy A C, Grossman M I, Bacharach W H, *Peptic Ulcer*, op cit, pp658-84

<sup>382</sup> Illingworth C F W, 'Refresher course for general practitioners: peptic ulcer', *British Medical Journal*, Jul 26<sup>th</sup> 1952, 206-7

success treating patients with peptic ulcers using a combination of old 'recognised' treatments and newer physiologically based regimens. The unexpectedly high proportion of soldiers in the Second World War found to have peptic ulcers will be discussed also.

## Chapter 4. Increasing success in the treatment and management of the complications of peptic ulceration from 1900 until the beginning of the National Health Service

### Introduction to chapter four

This chapter discusses three serious clinical complications of peptic ulcer disease which may become life-threatening or cause death. These complications which are described in turn are; sudden gastric or duodenal perforations, catastrophic bleeding from ulcers or severe biochemical imbalance from severe vomiting due to pyloric stenosis. The medical and surgical responses to them are examined in detail as blood transfusion and different surgical operations were introduced in an attempt to save lives. Surgeons were involved in treating patients with intractable symptoms and physicians used many regimens to help to heal ulcers without recourse to surgery. Professional soldiers at the start of World War II unexpectedly began to have to be withdrawn from active service on account of their development of peptic ulcers and this is also discussed in this chapter.

### 4. 1. The complications of peptic ulcer disease

#### 4. 1. 1: Perforation of peptic ulcers in the first third of the twentieth century

The early history of elective and emergency surgery for abdominal conditions was discussed in chapter two. By the end of the nineteenth century surgeons were increasingly intervening in hitherto hopeless clinical cases with growing success, albeit with high mortality rates. In 1900 Robert Weir in the USA showed that mortality rates for surgical operations for gastric and duodenal perforations were 42% and 33% respectively.<sup>383</sup> Prior to the days of surgical intervention, mortality from all forms of perforation was of the order of 95% or more. In 1903, Berkeley Moynihan's surgical mortality rate was 60% in his ten recorded cases.<sup>384</sup> Weir showed that early operative intervention was of great importance in influencing outcomes for delay led to higher mortality. Early clinical diagnosis was not accurate for cases of peritonitis, for up to one third of patients were initially diagnosed as appendicitis pre-operatively when they had in fact had gastric or duodenal perforations.

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<sup>383</sup> Weir R F, 'Perforating ulcer of the duodenum', *Boston Medical and Surgical Journal*, May 3<sup>rd</sup> 1900, vol. 142, 453-463

<sup>384</sup> Moynihan B G A, 'The surgical treatment of gastric and duodenal ulcers', *The Lancet*, Jan 31<sup>st</sup> 1903, 294

Moynihan himself had opened 18 cases of suspected appendicitis out of a series of 49 cases where perforation of the duodenum or stomach proved to be the correct diagnosis.<sup>385</sup> Delay in diagnosis could be due to slowness by patients in seeking medical help because of the cost of a doctor's visit especially at an early stage of the illness. Distance and transport to hospital were considerations also for the general practitioner who was treating a patient with the severe pain of peritonitis. General practitioners needed to see evidence that his patients had a chance of successful recovery for this hitherto uniformly fatal condition before they would subject them to more suffering.

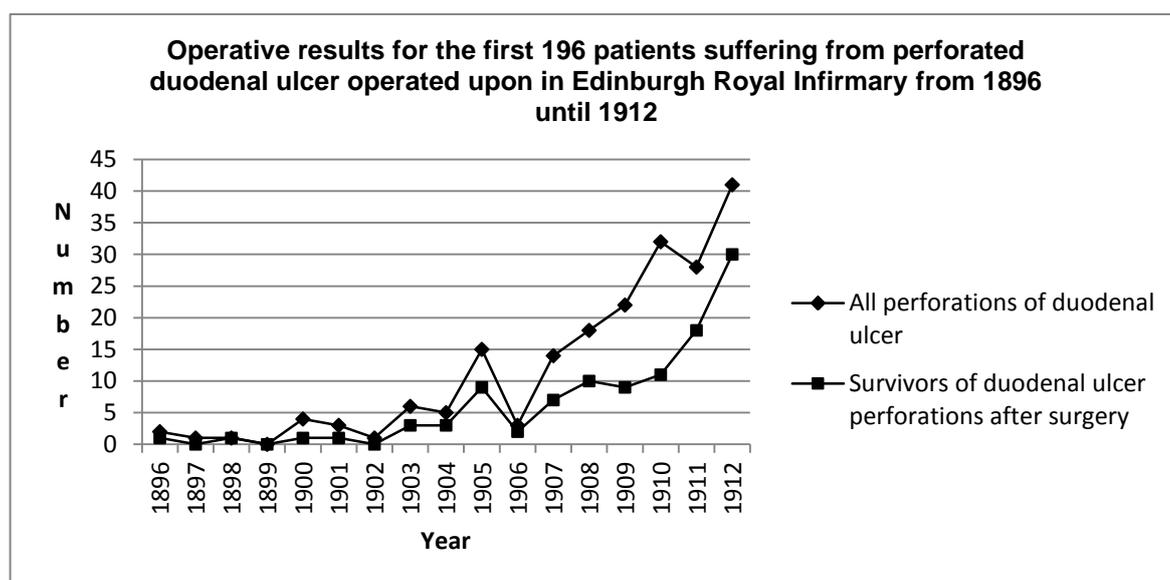


Figure 1

Data extracted from article by Caird FM, Cotterill JM, Cathcart C W, et al, 'Perforated Duodenal Ulcer,' *Edinburgh Medical Journal*, Nov 1913, vol.11, 405-18.

By the early decades of the twentieth century, the numbers of patients being operated upon for what was increasingly found to be duodenal ulcer perforation was rising sharply. In Edinburgh, general practitioners increasingly began to send their perforation cases into its Royal Infirmary as can be seen in the graph above constructed from the data in Francis Caird's paper in the period 1896-1912.<sup>386</sup> By 1912 Caird's patients had a 75% chance of recovery following duodenal perforation which was a vast improvement on the survival ratio for 1900 of 25%. In a series of one hundred cases of perforation of peptic ulcer operated upon and reported in Pennsylvania in 1929, there was a mortality rate of 33% and in a similar German series published in 1933 by Amos Graves, mortality rates had

<sup>385</sup> Moynihan B G A, 'On duodenal ulcer and its surgical treatment', *The Lancet*, Dec 14<sup>th</sup> 1901, 1658

<sup>386</sup> Caird F M, Cotterill J M, Cathcart C W, et al, 'Perforated Duodenal Ulcer', *Edinburgh Medical Journal*, Nov 1913, vol. 11, 405-18. NB the title of paper states that the series was of 200 patients when in fact there were only 196 in the data

decreased from 68% in 1897 to 17% by 1931.<sup>387</sup> The most obvious factor which appeared to determine satisfactory outcomes was delay in coming to surgery.<sup>388</sup> A smaller British series by John Gilmour and James Saint in 1932 showed mortality figure of 0.5% in patients operated on in less than 12 hours and 15% mortality in those after 12 hours had elapsed.<sup>389</sup> Perforation of duodenal ulcer clearly was a condition with a high mortality.

#### 4. 1. 2: Loss of blood from bleeding ulcers

By the twentieth century, haematemesis or the vomiting of blood was beginning to be treated more seriously than in the previous century, thanks to the leadership of surgeons such as Mayo Robson of Leeds who said at a meeting in 1902,

*The very fact of this discussion at this society [Medical Society of London] shows that the treatment of haematemesis by purely medical means is not altogether satisfactory. Not only the statistics from which I quoted in my address before the Edinburgh Medico-Chirurgical Society, but the more recent statistics from the London Hospital also, show that we are dealing with a very serious and common accident, and I feel that the opinion held by many practitioners of medicine that bleeding from the stomach rarely proves fatal requires carefully revising, as does the question of its treatment.*<sup>390</sup>

Despite the fact that haematemesis generally did not cause death, it could be catastrophic as stated by John Lindsay Steven, a physician and lecturer on clinical medicine in Glasgow Royal Infirmary, who wrote in 1904 in *The Lancet*: ‘There is perhaps no affection of the stomach, the treatment of which causes the physician more anxiety than that which is accompanied by copious vomiting of blood.’<sup>391</sup>

The successes of surgeons such as Caird and Moynihan heralded a period of new learning for general practitioners, physicians and surgeons as they acquired a new confidence in their ability to successfully manage previously hopeless conditions. Most cases of haematemesis were still managed at home by general practitioners but now they were being referred to hospital specialists if the patient’s condition began to cause alarm.

<sup>387</sup> Brown H P, ‘Perforation of peptic ulcer – observation of one hundred cases at the Pennsylvania and Presbyterian hospitals’, *Annals of Surgery*, Feb 1929, vol. 89, no. 2, 209-17

<sup>388</sup> Graves A M, ‘Perforated peptic ulcer in German clinics – an analysis of 4,402 cases’, *Annals of Surgery*, Aug 1933, vol. 98, no. 2, 197-09

<sup>389</sup> Gilmour J, Saint J H, ‘Acute perforated peptic ulcer. A review of 64 cases’, *The British Journal of Surgery*, Jul 1932, vol. 20, issue 77, 78-90

<sup>390</sup> Robson A W M, ‘Discussion on the surgical treatment of haematemesis,’ *The Lancet*, Dec 13<sup>th</sup> 1902, 1626-1630

<sup>391</sup> Steven J L, ‘On the surgical treatment of the diseases of the stomach from the physicians point of view’, Lecture iii, *The Lancet*, May 28<sup>th</sup> 1904, 1487-93

Haematemesis could also occur in patients with other severe chronic illnesses such as renal failure, heart disease and cirrhosis of the liver. Haematemesis was one of the diagnostic symptoms of ulcer of the stomach and duodenum but in mild forms it was not regarded as a life-threatening condition and did not cause alarm until it was severe.<sup>392</sup>

Melaena, the passing of altered blood products per rectum, was also known to be due to upper gastrointestinal bleeding but again was thought to be something which would pass without serious consequence. When it was suspected that bleeding from the stomach was occurring but not seen in sufficient quantities to produce the typical black tarry appearance of the stools which was recognisable as melaena, blood in the stool could be detected by a chemical test called the faecal occult blood test (FOB test). The test was first invented by a Dutch physiologist called Izaak A Van Deen in 1864.<sup>393</sup>

George Budd, writing about haematemesis in 1855, suggested that it could be a recurring problem, but added, ‘notwithstanding that haemorrhage is generally abundant, it seldom proves fatal’.<sup>394</sup> His treatment regime included bland diet and the use of ‘trisnitrate of bismuth’ [sic] and magnesia as medication. He also makes the suggestion of the use of cold in the form of swallowed ice to control haemorrhage.<sup>395</sup> William Brinton’s views on the management and treatment of haematemesis were published in 1856 and were subsequently widely followed.<sup>396</sup> He recommended, ‘perfect rest in the recumbent position, a minimum of the blandest food, and the application of cold, both externally and internally, to the bleeding organ ...’ Brinton also suggested, ‘the use of transfusion being useful, deserves also to be borne in mind.’<sup>397</sup> There is no evidence that transfusion of blood or of any other substance was used for treating haematemesis patients in the nineteenth century. In 1870, George Johnston, published a lecture on the subject whilst Professor of Medicine in Kings College Hospital.<sup>398</sup> He reaffirmed that absolute bed rest and no feeding by mouth were essential whilst the bleeding continued. He added astringent medications in the forms of tannic acid or perchloride of iron or oil of

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<sup>392</sup> Morton T, ‘Haematemesis as a symptom of peptic ulcer’, *The Lancet*, Jan 31<sup>st</sup> 1931, 268-9  
Haematemesis was one of the trio of symptoms which allowed for a diagnosis of gastric ulcer, the other two being pain of a gnawing type in the epigastrium and vomiting.

<sup>393</sup> Kiefer E D, ‘Detection of occult blood in feces’, *American Journal of Surgery*, Sep 1934, vol. 24, no.3, 530

<sup>394</sup> Budd G, *On the Organic and Functional Disorders of the Stomach*, (London, 1855, John Churchill), pp122, 124

<sup>395</sup> Budd G, *On the Organic*, *ibid*, pp140-2

<sup>396</sup> Brinton W, ‘Haematemesis from ulcer of the stomach: illustrated by three cases’, *Association Medical Journal*, Jun 28<sup>th</sup> 1856, 534-7

<sup>397</sup> Brinton W, ‘Haematemesis’, *ibid*, p536. Brinton was referring to blood transfusion here.

<sup>398</sup> Johnson G, ‘Clinical lecture on haematemesis and perforating ulcer of the stomach’, *British Medical Journal*, Mar 26<sup>th</sup> 1870, 305

turpentine, taken orally, and the patient was fed by nutritive enemata. Astringents as treatment are also to be found in the writings of John Wesley and other writers.<sup>399</sup> The important issue in treatment was to avoid exciting the patient which might set off catastrophic arterial bleeding from an ulcer.

Samuel Fenwick and W Soltau Fenwick's book *Ulcer of the Stomach and Duodenum and its Consequences*, published in 1900, reasserted that, 'The haemorrhage which occurs from acute primary ulcer of the stomach is hardly ever fatal.'<sup>400</sup> They suggested that haematemesis sufferers should be confined to bed for three weeks or a month and food denied them for up to forty-eight hours. When feeding began they suggested that, 'All that is necessary is to provide a form of nourishment which does not irritate the surface of the ulcer nor unduly excite the secretory and motor functions of the stomach.'<sup>401</sup> They suggested that the ulcer took about a month to heal and that solid food be avoided until then. They challenged the usefulness of any available drugs to exercise a curative effect upon the ulcer but offered bismuth or bicarbonate if epigastric pain were a problem. The Fenwicks criticised the practice of giving rectal feeding by enemata for prolonged periods of up to ten days which they said could not possibly sustain life and that young people dying after haematemesis, succumbed 'for want of nourishment'.

Surgeons who operated to save the lives of patients with copious gastric haemorrhage discovered that the bleeding could occur from acute ulcers or chronic ulcers or diffusely from the stomach lining without a defined bleeding point. Diffuse gastric bleeding was called 'gastrorrhagia' or 'gastrotaxis' and was recognised as a condition in its own right which commonly affected young women but could affect men too.<sup>402 403</sup> Clinically in many of these cases, gastric ulcer was suspected but rarely found at autopsy. Acute ulcer bleeding in men was also reported but it tended to be in an older age group.<sup>404</sup> In the majority of these cases bleeding stopped spontaneously and required no further treatment and some physicians suggested that all that was required was medical management.

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<sup>399</sup> Cornell W M, ed, *Primitive Physic: or an Easy and Natural Method of Curing Most Disease*, by John Wesley, jointly published with Cornell W M, *The Ship and Shore Physician and Surgeon*, (Boston, 1858, Cyrus Stone), Wesley, *Primitive Physick*, pp32-3, or Cornell, *The Ship*, pp11-3

<sup>400</sup> Fenwick S, Fenwick WS, *Ulcer of the Stomach and Duodenum and its Consequences*, (London, 1900, J&A Churchill), p165

<sup>401</sup> Fenwick, Fenwick, *Ulcer of the Stomach*, *ibid*, pp167-8

<sup>402</sup> White W H, 'An address on gastrotaxis or oozing of the blood from the mucous membrane of the stomach', *The Lancet*, Nov 3<sup>rd</sup> 1906, 1189-95

<sup>403</sup> White W H, 'Are not some patients said to be afflicted with gastric ulcer really suffering from a different disease?', *The Lancet*, Jun 29<sup>th</sup> 1901, 1819

<sup>404</sup> White W H, 'An address on gastrotaxis', *op cit*, 1189-0

According to Berkeley Moynihan, acute ulcers were sudden in onset with no previous symptoms of indigestion and bleeding was usually very copious.<sup>405</sup> Sometimes 'gastric erosions' or small superficial ulcers, were seen on the mucosal surface of the stomach at operation, often in groups. Surgeons could do little to stop bleeding except to apply astringents or cautery to the surface although some tried to undersew the layer under the mucosa. Moynihan in common with other surgeons of the time also advocated performing a gastroenterostomy at the same time which was believed to promote healing in these cases.<sup>406</sup>

Chronic ulcers presented differently with a history of vague and minimally troublesome indigestion. The bleeding was often less but tended to be repetitive and when surgical intervention was required, the ulcer was usually found to be solitary, with a thickened base. In such cases, Moynihan excised the ulcer and performed a gastroenterostomy. Mayo Robson also used this technique to good effect in the two cases he reported on in his presentation at a meeting of the Medical Society of London in 1902 and this view was endorsed by numerous other surgeons present.<sup>407</sup> Robson advocated that medical management should be tried in the first instance in most cases and his view was unopposed.<sup>408</sup> However an editorial in *The Lancet* in 1903 suggested that there was no agreed view on the best surgical treatment for acute upper gastrointestinal ulcer haematemesis.<sup>409</sup>

#### 4. 2. 1: Blood transfusion: a brief history of its clinical application

Blood transfusion has been mentioned as a treatment for haematemesis but this was not what it was initially used for.<sup>410</sup> An account of its use in 1492 is recorded and in the following centuries, attempts to relieve illnesses by blood transfusions saw little success.<sup>411</sup> After 1675 the Pope and the Parisian authorities banned its use and no further research appears to have been done for another 150 years.<sup>412 413</sup> Throughout the nineteenth century

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<sup>405</sup> Moynihan B G A, 'On the surgical treatment of gastric and duodenal ulcers', *British Medical Journal*, Jan 31<sup>st</sup> 1903, 294-8

<sup>406</sup> A gastroenterostomy is an operation which creates a new outlet from the stomach joining it to a piece of intestine which is also opened, effectively short circuiting the duodenum. The nearest piece of intestine to the stomach which allows its emptying is the proximal part of the small bowel called the jejunum. The term 'gastro-jejunosomy' commonly is used as an alternative to gastroenterostomy. The procedure could be done either from the front or from the back of the stomach as seen from the opened abdomen.

<sup>407</sup> Robson A W M, 'Discussion on the surgical treatment', op cit, 1627

<sup>408</sup> Robson A W M, 'Discussion on the surgical treatment,' op cit, 1630

<sup>409</sup> Editorial, 'Gastric erosions', *The Lancet*, Oct 17<sup>th</sup> 1903, 1109

<sup>410</sup> This is briefly summarised in Weiner A S, *Blood Groups and Blood Transfusion*, (London,1935, Baillière, Tindal & Cox), pp36-43

<sup>411</sup> Wilks S, 'Correspondence', *British Medical Journal*, Sept 12<sup>th</sup> 1863, 307-8

<sup>412</sup> 'Early history of blood transfusion', *The Lancet*, Oct 7<sup>th</sup> 1939, 792

there are many recorded instances in the medical literature of transfusion performed for the benefit of patients. Indications included unspecified anaemia, pernicious anaemia, cachexia from serious illness and anaemia from blood loss. In 1824, Dr James Blundell used blood transfusion experimentally on a dog and the following year he transfused a woman in a state of collapse from postpartum haemorrhage using her husband as a donor.<sup>414 415</sup> In 1832 a case was described where transfusion of large volumes of saline was used to save the life of a patient with cholera.<sup>416</sup> Puerperal haemorrhage presented a particular danger to life which could be saved by transfusion of blood.<sup>417</sup> Donor substances included milk, sheep's blood, saline, gum, and human blood and its products – plasma and red cells.<sup>418 419 420 421 422</sup> There were no agreed indications for transfusion and in the cases of milk and sheep's blood, they were given in desperation by their medical attendants but often their recipients suffered severe reactions.

Karl Landsteiner, a pathologist working in Vienna began researching agglutination reactions in red cells in 1900 and out of his researches emerged the concept of blood groups whereby human could tolerate the reception of transfused blood from some human individuals but not from all.<sup>423</sup> In 1911, Landsteiner's system was refined to become the basis for the A B O blood grouping system in use today.<sup>424</sup> In Czechoslovakia in 1907 and in Baltimore in 1910, two other different blood grouping system using numerals were developed.<sup>425</sup> In 1928 the ABO blood group nomenclature was adopted by the League of Nations and gradually most Western nations complied.<sup>426</sup>

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<sup>413</sup> Harding A J, 'A brief history of blood transfusion', *The Biomedical Scientist*, Nov 2005, p1147

<sup>414</sup> Linton R J, 'Letters to the editor', *The Lancet*, Feb 29<sup>th</sup> 1824, 295

<sup>415</sup> Editorial, 'Transfusion', *The Lancet*, Sept 17<sup>th</sup> 1825, 342-3

<sup>416</sup> Lewins R, 'Injections of saline in extraordinary quantities into veins in cases of malignant cholera', *The Lancet*, May 26<sup>th</sup> 1832, 243-4

<sup>417</sup> Boulton P, 'Treatment of puerperal haemorrhage: Lecture to Harvean Society of London', *British Medical Journal*, Mar 10<sup>th</sup> 1883, 460

<sup>418</sup> Pepper W, 'Transfusion of Milk', *British Medical Journal*, Apr 12<sup>th</sup> 1879, 557-8; Jennings C E, 'The intravenous injection of milk', *British Medical Journal*, Jun 6<sup>th</sup> 1885, 1147-9

<sup>419</sup> Bateman W A F, 'The use of defibrinated sheep's blood for transfusion', *British Medical Journal*, Jan 4<sup>th</sup> 1896, 17

<sup>420</sup> Jennings C E, 'Transfusion', in 'Obstetrical society of London', *British Medical Journal*, Jan 27<sup>th</sup> 1883, 158-9

<sup>421</sup> Bayliss W M, 'The use of gum solutions for intravenous injections', in 'Correspondence', *British Medical Journal*, Apr 28<sup>th</sup> 1917, 564; editorial, 'Surgical shock', *British Medical Journal*, Feb 23<sup>rd</sup> 1918, 238

<sup>422</sup> Jennings C E, 'The treatment of excessive haemorrhage', *British Medical Journal*, Feb 8<sup>th</sup> 1896, 331-2

<sup>423</sup> Durand J K, Willis M S, 'Karl Landsteiner MD: Transfusion Medicine', *Labmedicine*, Jan 2010, vol. 41, no 1, 53-5

<sup>424</sup> Durand J K, Willis M S, 'Karl Landsteiner', *ibid*, 54

<sup>425</sup> Harding A J, 'A brief history', *op cit*, 1148; Durant J K, Willis M S, 'Karl Landsteiner', *op cit*, 54

<sup>426</sup> Editorial, 'Topics of interest: Standardisation of therapeutic preparations', *Canadian Medical Association Journal*, Nov 1928, vol. 19, no. 5, 618. This is a summary extracted from Publications of the League of Nations, *Annual Report for 1928*, III, Health, 1928, vol. iii, p6

Initially, blood transfusion was done either directly from donor to patient using a syringe or by arterio-venous surgical connection or by the indirect use of a receptacle using anticoagulated blood.<sup>427 428</sup> During World War I, it became possible to store blood for transfusion, preventing it from clotting by adding sodium citrate to it.<sup>429</sup> Blood could be collected in an open receptacle or into a closed bottle.<sup>430</sup> Storage conditions for the blood at around 4-6°C were recognised as being important and freezing was to be avoided.<sup>431</sup> Increased understanding of the many risks, benefits and suitable use of blood transfusion grew but there were problems with deaths attributed to its use and the issue of transfer of infection from donor to recipient was also recognised.<sup>432 433</sup> In Russia they had experience of using auto-transfusion in women with intra-abdominal haemorrhage from ectopic pregnancy or in persons with traumatic ruptured spleen.<sup>434</sup> In 1937 the provision of live volunteer donor blood was a cultural problem in Russia and the collecting of blood from corpses, of which they had a large supply, was a lesser issue for them.<sup>435</sup>

For military casualties, blood transfusion offered immense potential for benefit and this was demonstrated in the Spanish Civil War, where in 1938, the Republican forces had a well organised blood transfusion service which could treat the wounded on the battlefield.<sup>436</sup> This was a foretaste of what was to follow in the UK. By the summer of 1939, an emergency blood transfusion service using donors had been set up in London and the Home Counties with 50-60,000 enrolled volunteers having been blood group tested by this time.<sup>437 438</sup> In 1940, Landsteiner and other co-workers discovered Rhesus antibodies whose significance was quickly appreciated and acted upon by clinicians with its implication in Haemolytic Disease of the Newborn.<sup>439 440</sup> Throughout the war, blood

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<sup>427</sup> Weiner A S, *Blood Groups*, , fig 17, p42

<sup>428</sup> Stansfield A E, 'Principles of the transfusion of blood', *The Lancet*, Mar 31<sup>st</sup> 1917, 488-91

<sup>429</sup> Mollison P L, 'Historical review: The introduction of citrate as an anticoagulant for transfusion and of glucose as a red cell preservative', *British Journal of Haematology*, Jan 2000, vol. 108, no. 1, 13-18

<sup>430</sup> Riddell V H, *Blood Transfusion*, (London, 1939, Oxford University Press), pp6-7

<sup>431</sup> Riddell V H, *Blood Transfusion*, *ibid*, pp306-8

<sup>432</sup> Stansfield A E, 'Principles', *op cit*, 488, 491

<sup>433</sup> Plummer N S, 'Blood transfusion – A report of six fatalities', *British Medical Journal*, Dec 12<sup>th</sup> 1936, 1186-9

<sup>434</sup> Autotransfusion is a process whereby a patient's own blood is collected and given back to them intravenously.

<sup>435</sup> Shamov W N, 'The transfusion of stored cadaver blood', *The Lancet*, Aug 7<sup>th</sup> 1937, 306-9 and Yudin Y S, 'Transfusion of stored cadaver blood; Practical considerations: the first thousand cases', *The Lancet*, Aug 14<sup>th</sup> 1937, 361-6

<sup>436</sup> Ellis R W, 'Blood transfusion at the front', *Proceedings of the Royal Society of Medicine*, Apr 1938, vol. 31, issue 6, 684-6

<sup>437</sup> Editorial, 'The emergency blood-transfusion service scheme to date', *The Lancet*, Jul 29<sup>th</sup> 1939, 363

<sup>438</sup> Editorial, 'The army blood transfusion service', *British Medical Journal*, May 15<sup>th</sup> 1943, 610-1

<sup>439</sup> Harding A J, 'A brief history', *op cit*, 1148

<sup>440</sup> Taylor G I, Race R R, 'Haemolytic disease of the newborn', *British Medical Journal*, Feb 26<sup>th</sup> 1944, 228-9

transfusion services continued to expand and the use of blood clinically increased in the civilian population so that by the end of the war it was proposed that a blood transfusion service be established.<sup>441</sup> As a result, in 1946 the Blood Transfusion Service was inaugurated.<sup>442</sup>

#### 4. 2. 2: Blood transfusion as a supportive treatment for haematemesis sufferers

As a supportive treatment for patients with haematemesis, blood transfusion began to be used from the beginning of the twentieth century. In 1900, Samuel Fenwick and W Soltau Fenwick suggested that intravenous treatment was indicated when life was threatened from blood loss from bleeding stomach ulcers but warned that the sudden injection of a large quantity of fluids carried with it the risk of dislodging the protective clot. They preferred saline solution to defibrinated blood.<sup>443</sup> In 1925 James Sherrin, surgeon to the London Hospital published a paper describing his use of blood transfusion as part of his treatment regimen where blood loss had been considerable.<sup>444</sup> By 1926 the treatment of haematemesis by blood transfusion was well accepted.<sup>445</sup> Despite this, Martin Rehffuss in 1927, speaking of his experiences of treating haematemesis, said, 'Blood transfusion has been rendered in some cases, but the use of this procedure requires nice discernment in judgement. Unless there has been a great loss of blood this method had better not be employed, as it tends to fill the vessels and continue haemorrhage.'<sup>446</sup> Ernest Bulmer's 1927 article published in *The Lancet* revealed a mortality rate of over 12% out of 526 patients treated in the medical wards of Birmingham General Hospital for haematemesis over a 24.5 year period with no mention made of blood transfusion in its treatment which illustrates the then current variation in opinion as to the usefulness of blood transfusion for haematemesis.<sup>447</sup>

There was a reluctance to used blood transfusion for fear that it might worsen gastric bleeding but this was opposed in 1926 by an editorial in *The Lancet*, which stated that, 'The fallacy of supposing that transfusion will encourage haemorrhage by causing too

<sup>441</sup> Editorial, 'Civilian blood-transfusion services', *The Lancet*, Nov 3<sup>rd</sup> 1945, 567-8

<sup>442</sup> <http://www.blood.co.uk/about-blood/> accessed 01.02.12

<sup>443</sup> Fenwick, Fenwick, *Ulcer of the Stomach*, op cit, p174. Defibrinated blood is blood which has had its clotting factors removed.

<sup>444</sup> Sherrin J, 'An address on acute haematemesis and melaena', *The Lancet*, Jan 24<sup>th</sup> 1925, 163-8

<sup>445</sup> Editorial, 'Blood transfusion', *The Lancet*, Jan 23<sup>rd</sup> 1926, 185

<sup>446</sup> Rehffuss M E, *Diagnosis and Treatment of Diseases of the Stomach*, (Philadelphia and London, 1927, W B Saunders Company), p624

<sup>447</sup> Bulmer E, 'The mortality from haematemesis: an analysis of 526 cases', *The Lancet*, Jul 23<sup>rd</sup> 1927, 168-71

great a rise in blood pressure is also losing ground.’<sup>448</sup> Sir Henry Tidy agreed, stating in 1934 that, ‘It will probably be accepted that blood transfusion and even repeated blood transfusion is generally desirable, for we need not now fear the supposed risk of a rise of blood pressure.’<sup>449</sup> The reluctance to transfuse blood continued in the form of its restricted use for only what were considered the more severe cases by which they meant that the haemoglobin levels of the patient should be less than 30% of normal. However, in 1937 it was reported that the most severely ill patients who were transfused had a higher mortality rate than the un-transfused patients in a Copenhagen hospital.<sup>450</sup>

Blood transfusion generally was known to cause reactions in patients who might even die from the effects of the transfusion. Edward Cullinan’s account of the treatment of haematemesis following peptic ulceration between 1925 and 1929 reported in the *St Bart’s Hospital Report* in 1932 showed that 23 out of 36 of the patients given blood suffered febrile reactions afterwards.<sup>451</sup> Cullinan’s report reinforced the view that blood transfusion could exacerbate the clinical conditions of the patient if not used according to criteria which he had based upon his experience. The *British Medical Journal* 1937 contains 11 reports of fatalities attributed to blood transfusion in the six month period from October 1936 until April 1937.<sup>452</sup> One such paper by Plummer has already been highlighted in this section of the thesis which recorded six deaths from transfusion reactions.<sup>453</sup> Despite these setbacks, blood transfusion was refined and improved and became an established part of treatment for haematemesis. By 1947, Francis Avery Jones was able to claim that the combination of early feeding and the liberal use of blood transfusion had halved the death rates from haematemesis in his medical unit compared with another series reported in 1932 in another hospital.<sup>454</sup> From the beginning of the NHS, blood transfusion became established as a major part of treatment of haematemesis and melaena.

#### 4. 2. 3: Changes in British life from 1900

As the nineteenth century neared its end, attitudes to the management of haematemesis changed with hospitalisation becoming an option and hospitals increasingly receiving

<sup>448</sup> Editorial, ‘Blood transfusion’, op cit, 185

<sup>449</sup> Tidy H L, ‘Severe gastric and duodenal haemorrhage’, *The Lancet*, Dec 15<sup>th</sup> 1934, 1365-6

<sup>450</sup> Hurst A F, Ryle J A, ‘The incidence, mortality and treatment of haemorrhage in gastric and duodenal ulcer’, *The Lancet*, Jan 2<sup>nd</sup> 1937, 4

<sup>451</sup> Cullinan E R, Price R K, ‘Haematemesis following peptic ulceration’, *St Bart’s Hospital Report*, 1932, vol. 65, 185-213

<sup>452</sup> *Web of Science* search in *British Medical Journal* using ‘blood transfusion’ between the dates 1930 and 1940

<sup>453</sup> Plummer N S, ‘Blood transfusion’, op cit, 1186-9

<sup>454</sup> Jones F A, ‘Haematemesis and melaena’, *British Medical Journal*, Sep 27<sup>th</sup> 1947, 477-83

haematemesis patients. Both in voluntary hospitals and in poor law infirmaries bed numbers increased for the benefit of the sick.<sup>455 456</sup> Ambulance services, initially designed for accident or fever cases increasingly transported ill people to hospital. Nursing became more professional providing a service adequate to the task of undertaking complex therapeutic measures including wound dressing, complex dietetic regimes and physical therapies including the supervision of blood transfusion.<sup>457</sup>

Hospitals now had become a relatively safe place to send an ill patient. Nevertheless, the wealthy continued to receive their medical care at home, including surgical operations, for the first three decades of the century employing their own nurses, but this effectively had ceased by the Second World War.<sup>458</sup> Hospital treatment was little different from that which a general practitioner could provide in terms of medication but it removed the patient from a busy crowded working-class home offering strict bed rest and diet with the possibility of surgical intervention if this failed.

#### 4. 2. 4: Dietary management of haematemesis

Diet was considered to be of the greatest importance in peptic ulcer disease with minor differences prescribed for severe dyspepsia, gastric ulcer and duodenal ulcer and haematemesis. Suitable diets were devised to avoid gastric stimulation, for the stomach had to be 'rested' and not be irritated by ingested food. Initially when food in anything other than small amounts was withheld, nutrition was supposedly to be maintained by nutrient enemata, whose worth was criticised by the Fenwicks as has already been recorded.<sup>459</sup> Dietetic treatment regimens were associated with the names of many physicians of the day as will be seen later. The simplest diet recommended by most nineteenth-century authors was a milk diet. Some added lime water or an alkali for up to three days before commencing a bland diet.<sup>460</sup> Food science had been established by the end of the nineteenth century and most common food substances had been chemically analysed and this information applied to designing patients' diets.<sup>461</sup> Physicians used nasogastric tubes to analyse food interactions with gastric juices.

<sup>455</sup> Toogood F S, 'The genesis of the modern infirmary', *The Lancet*, Aug 14<sup>th</sup> 1909, 446-9

<sup>456</sup> Cherry S, *Medical Services and the Hospitals in Britain, 1860-1939*, (Cambridge, 1996, Cambridge University Press), pp44-53

<sup>457</sup> Abel-Smith B, *A History of the Nursing Profession*, (London, 1960, William Heinemann Ltd), p50

<sup>458</sup> In 1904, more than half the registered nurses were employed in the homes of the wealthy. See Abel-Smith B, *A History*, *ibid*, p54.

<sup>459</sup> Fenwick, Fenwick, *Ulcer of the Stomach*, *op cit*, pp167-8

<sup>460</sup> Saundby R, 'Clinical lecture on chronic ulcer of the stomach', *The Lancet*, Feb 14<sup>th</sup> 1891, 353-5

<sup>461</sup> Riegel F, *Diseases of the Stomach*, (Philadelphia, New York, London, 1904, WB Saunders & Company), pp179-222

In 1906 Hermann Lenhartz advocated a new approach of complete bed rest with gradual increase in food intake over a four week period for the treatment of haematemesis sufferers. This differed from the then-current regimen of starvation.<sup>462</sup> He began feeding patients with egg and milk and after a week added mince, rice and other solid foods in increasing quantities. He also gave bismuth and iron by mouth as medication and applied ice packs to the epigastrium. This regimen was used both for the treatment of gastric ulcer and haematemesis.<sup>463</sup> Lenhartz's dietetic approach did not receive universal approval by hospital doctors. Arthur Hurst disagreed with any dietetic regimen which was subject to daily changes and put it in a forceful way, saying, 'If a certain diet is suitable for a certain day, it is absurd to assume that every ulcer, whatever its size or position or whatever the condition of the patient may be, will have improved in twenty-four hours to just the degree which justifies the addition of an egg or a zwieback to the diet.'<sup>464</sup> Hurst managed his haematemesis patients by starving them for up to forty-eight hours after the bleeding was deemed to have ceased before starting a diet of food sufficiently softened and diluted with saliva by mastication to avoid any mechanical, chemical or thermal injury to the mucous membrane.<sup>465</sup> Alkalis, atropine and olive oil were also added to the diet.<sup>466</sup> Arthur Hurst was a senior physician in Guy's Hospital and author of a much respected textbook on the subject as well as a frequent contributor to medical journals. He founded the British Society of Gastroenterology in 1935.<sup>467</sup>

Edmund Spriggs used Lenhartz's diet in the management of haematemesis with apparently good results, showing in 1909 that it was at least as good in its mortality rates as the traditional starvation and rectal feeding regime.<sup>468</sup> In 1933 Professor Einar Muelengracht in Copenhagen at the Sixteenth Scandinavian Congress for Internal Medicine reported results obtained by feeding all haematemesis patients from their initial admission to hospital. His report in *The Lancet* showed that death rates using his method of early feeding were much lower than other published results including those in another Copenhagen hospital which used the orthodox starvation regimen.<sup>469</sup> This hospital reported death rates of 7.9% as against Muelengracht's of 1% in a similar group of patients

<sup>462</sup> Haberman J V, 'The Lenhartz treatment of gastric ulcer at the Eppendorfer Krankenhaus, Hamburg', *The Lancet*, Jul 7<sup>th</sup> 1906, 25-6

<sup>463</sup> Lenhartz's dietary regime is described fully in Spriggs E I, 'Remarks on the treatment of gastric ulcer by immediate feeding', *British Medical Journal*, Apr 3<sup>rd</sup> 1909, 825-9.

<sup>464</sup> Hurst A F, Stewart M J, *Gastric and Duodenal Ulcer*, (London, 1929, Oxford Medical Publications), p390

<sup>465</sup> Hurst A F, Stewart M J, *Gastric and Duodenal*, *ibid*, p421

<sup>466</sup> Hurst A F, Stewart M J, *Gastric and Duodenal*, *ibid*, p269

<sup>467</sup> Hunt T, 'Sir Arthur Hurst. (Born 23<sup>rd</sup> July 1879, died 17<sup>th</sup> August 1944)', *Gut*, Jun 1979, 463-6

<sup>468</sup> Spriggs E I, 'Remarks', *op cit*, 825-9

<sup>469</sup> Muelengracht E, 'Treatment of haematemesis and melaena with food: the mortality', *The Lancet*, Nov 30<sup>th</sup> 1935, 1220-2

over the same time period. Despite the apparent superiority of Muelengracht's results, the topic of diet and early feeding in the management of haematemesis had not been fully settled by 1950 although early feeding had become accepted practice as soon as the haemorrhage ceased and when nausea and vomiting had subsided.<sup>470</sup> The appropriate diet which should be used remained contentious, with the Sippy diet being favoured in the USA of which more will be said later in this chapter.

#### 4. 3: The contribution of surgeons in the elective treatment of peptic ulcers

##### 4. 3. 1: Partial gastrectomy and gastroenterostomy

Understanding of diseases of the stomach grew rapidly from the last decade of the nineteenth century as a consequence of more abdominal surgery being done. Surgery became safer as problems associated with anaesthetics and hospital acquired infection lessened and the high operative mortality rates prevailing in the second half of the nineteenth century slowly declined. In a lecture published in 1910, Berkeley Moynihan claimed that he was dissecting many more bodies in his surgical practice than any pathologist at the time and he could see within the living abdomen what was actually going on in terms of pathology.<sup>471</sup> He coined the phrase, 'the pathology of the living', to make the point. At operation he found that the diseases which he specialised in treating were very different, both in type and numbers, than had been taught to his generation. Duodenal ulcer and gallstones, far from being rare diseases, were found to be much more common than previously believed.

By the second decade of the twentieth century, surgeons could increasingly safely stitch and patch holes in the stomach and duodenum, remove parts of the stomach and re-route its contents.<sup>472</sup> Initially most operations on the stomach and duodenum were performed in response to life-threatening situations but encouraged by their successes, surgeons began to devise operations to treat patients with peptic ulcers before they required emergency interventions.

For the first 25 years of the twentieth century, no consensus existed of how to deal surgically with chronic peptic ulcers. Some surgeons removed the ulcer by cutting or by

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<sup>470</sup> Ivy A C, Grossman M I, Bachrach W H, *Peptic Ulcer*, (Philadelphia and Toronto, 1950, The Blakiston Company), pp939-40

<sup>471</sup> Moynihan B G A, 'An Address on the Pathology of the Living', *British Medical Journal*, Nov 16<sup>th</sup> 1907, 1381-5

<sup>472</sup> Kirk R M, Jeffrey P J, 'Development of surgery for peptic ulcer: a review', *Journal of the Royal Society of Medicine*, Nov 1981, vol. 74, 828-30

cautery whilst others added the operation of gastroenterostomy to direct the food flow away from the ulcer site and to thereby ‘rest’ that part of the stomach coming into contact with the magenstrasse along which the stomach contents passed to the duodenum.<sup>473</sup> Most peptic ulcers were located along the magenstrasse or at the stomach outlet where the chyme came into contact with the duodenum. Uncomplicated gastroenterostomy brought symptomatic relief to duodenal ulcer sufferers becoming its main surgical treatment in the UK for the first three decades of the twentieth century with apparent good results.

Gastroenterostomy for peptic ulcer, however, did cause problems for some patients. Detailed explanations of the reasons for failures are given by Moynihan writing in the *British Medical Journal*,

*Every operation in surgery, even the best, most exquisitely performed, may bring its disappointments. The operation of gastroenterostomy, carried out in appropriate cases by a competent operator, is probably the most successful of all surgical procedures of equal magnitude and it is certainly among the safest of those entitled to the description of major operations.*<sup>474</sup>

Moynihan lists the reasons for failure under four categories: The operation has been performed in the absence of any organic lesion justifying it (the most frequent cause) or the operation has been incomplete or the technique is defective or late complications may develop after an operation has been performed in a case requiring it without any technical flaw. A gastroenterostomy operation was considered unsuccessful if the patient had symptoms of persisting pain, haemorrhage, vomiting and diarrhoea.<sup>475</sup> Severe vomiting could occur as a consequence of blockage soon after the surgical construction of a gastroenterostomy and was called ‘vicious circle vomiting’. It could be fatal.<sup>476</sup>

The problem of gastro-jejunal ulcer was an important complication of gastric surgery. It was an entirely iatrogenic condition which occurred as a consequence of surgically re-routing stomach contents via an opening in the stomach directly into the jejunum or first part of the small bowel. Although possibly more patients had the complication, its quoted incidence was given in 1936 as 4%.<sup>477</sup> Because the operation created a new gut opening, it

<sup>473</sup> The magenstrasse, German for ‘stomach street’, is the term used for the upper part of the stomach along the lesser curve which carries the food to the duodenum. It is at the point of contact of the partially digested food flow (chyme) of the magenstrasse with the stomach that most benign stomach ulcers occur and at its point of contact with the duodenum that most duodenal ulcers occur.

<sup>474</sup> Moynihan B G A, ‘Disappointments after gastroenterostomy’, *British Medical Journal*, Jul 12<sup>th</sup> 1919, 33-6,

<sup>475</sup> Moynihan B G A, ‘Disappointments’, *ibid*, 33-6,

<sup>476</sup> King C, ‘Vicious circle vomiting after gastro-jejunosomy’, *The Lancet*, Oct 19<sup>th</sup> 1907, 1083

<sup>477</sup> Joll C A, ‘The rôle of surgery in the treatment of chronic peptic ulcer’, *Postgraduate Medical Journal*, Sep 1936, vol. 12, 364-373

was called a 'stoma' giving the term, 'stomal ulcer' as an alternative to that of gastro-jejunal ulcer.<sup>478</sup> Yet another term used was 'anastomotic ulcer' because the ulcer occurred at the anastomosis, or join, of stomach and small bowel. Symptomatically it could be as severe a condition as peptic ulcer and could cause death from bleeding or perforation. In another series, stomal ulcer was quoted as a problem for 2% - 9% of patients who had had gastrectomy for duodenal ulcer.<sup>479</sup> In a proportion of cases, it was associated with internal fistula formation and surgery for its correction carried appreciable mortality rates.<sup>480</sup> In 1949 in England and Wales and in 1950 in Scotland, the Registrars General of Births, Marriages and Deaths of these respective nations began to include 'gastro-jejunal ulcer' as a separate cause of death in their Annual Returns.

By 1936, there was little change in surgical treatment of peptic ulcers.<sup>481</sup> The operation of ulcer removal by partial gastrectomy which removed the pylorus and antrum, had been used for the relief of both gastric and duodenal ulcers and good results were claimed.<sup>482</sup> In Germany, it was the operation of choice, being routinely performed in less than one hour.<sup>483</sup> However there was an emerging picture of the limitations of all operations. Approximately 80% of patients of surviving patients were 'cured' of their ulcers, 10% were 'improved', and 10% had 'little or no relief'.<sup>484</sup> Of the group with 'little or no relief', there were patients with severe surgically induced iatrogenic disease which would blight their lives, of which more later.

In 1945, Sir Henry Tidy published a paper in the *British Medical Journal* which revealed that crude death rates for peptic ulcer disease were rising in the period from 1912 and 1937 in England and Wales and between 1921 and 1937 in Scotland.<sup>485</sup> Surgeons had known success with the main emergencies discussed elsewhere (perforation, haematemesis and pyloric stenosis) but mortality rates were rising. Fordyce St John examined his results for surgical treatment of peptic ulcers in 1939.<sup>486</sup> Neither gastroenterostomy nor partial gastrectomy brought unqualified relief to his patients who had had surgery. There was a

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<sup>478</sup> Greek. Stoma - a mouth.

<sup>479</sup> Orr I M, Johnson H D, 'Vagal resection in the treatment of duodenal ulcer', *The Lancet*, Jul 19<sup>th</sup> 1947, 84-9

<sup>480</sup> Marshall S F, Knud-Hansen J, 'Gastrojejunal and gastrocolic fistulas', *Annals of Surgery*, May 1957, vol. 145, no. 5, 770-82

<sup>481</sup> Joll C A, 'The rôle of surgery', op cit, 364-3

<sup>482</sup> Broster L R, 'Gastric and duodenal ulcer: an analysis of 200 cases treated by operation', *British Medical Journal*, Nov 3<sup>rd</sup> 1928, 786-9

<sup>483</sup> Graves A M, 'Perforated peptic ulcer', op cit, 205

<sup>484</sup> Broster L R, 'Gastric and duodenal', op cit, 789

<sup>485</sup> Tidy Sir H, 'The course of the death rate from peptic ulcer in Great Britain 1912-1938', *British Medical Journal*, May 20<sup>th</sup> 1944, 677-82

<sup>486</sup> St John F B, Harvey H D, Gius J A, et al, 'A study of the results of surgical treatment of peptic ulcer', *Annals of Surgery*, Feb 1939, vol. 109, 193-18

10% mortality rate for gastroenterostomy overall and depending on the clinical indication for the operation (bleeding, obstruction, pain) there was a variable outcome in terms of satisfactory results. In the 12 months following operation, 79% were classified as 'satisfactory' but all those patients in the 'satisfactory' groups when followed up for up to 15 years saw a steady proportion becoming 'unsatisfactory' and needing medical therapy.<sup>487</sup> In addition, the surgeons' efforts did not prevent recurrent perforation or bleeding. Partial gastrectomy patients fared better at 88% satisfactory in the first post-operative year but had a mortality rate of 14.8%. Their long-term results were better in this study.

Other series had different results but generally partial gastrectomy had higher post-operative mortality rates but better long-term clinical outcomes.<sup>488</sup> Duodenal ulcer (and gastric ulcer) was known to be a recurring illness and usually surgery was suggested for patients with ulcers which were resistant to medical treatment.<sup>489</sup> Unfortunately these operations created a growing cohort of patients whose symptoms were, if anything worse, than they had been before surgery. However at the time, the extent of the suffering of these patients was not fully understood, although this observation had received some comment.<sup>490</sup> Further studies began to elucidate the long term effects of surgery.<sup>491</sup> In 1942 Arthur Allen and Claude Welch showed that 20% of all patients with duodenal ulcers eventually needed operations for symptoms or complications.<sup>492</sup> Surgeons in the UK seeking better results were increasingly turning to partial gastrectomy as a solution, especially for gastric ulcer when the ulcer and part of the stomach was removed.

As with gastroenterostomy as an elective procedure, partial gastrectomy was essentially an empirical technique, initially without much theoretical backing for the part played by acid secretion at the time was still contested by gastric physiologists. The part of the stomach removed was not the part which produced the acid but later physiological experiments showed that it did remove one part of the gastric stimulation process since the hormone gastrin was produced by the antrum of the stomach.<sup>493 494</sup> Partial gastrectomy which

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<sup>487</sup> Clark D H, 'Posterior gastroenterostomy in peptic ulcer: long-term-results', *British Medical Journal*, Jan 13<sup>th</sup> 1951, 57-61

<sup>488</sup> Orr I, Johnson H D, 'Vagal resection in the treatment of duodenal ulcer', *The Lancet*, Jul 19<sup>th</sup> 1947, 84-9

<sup>489</sup> St John F B, Flood C A, 'A study of the results of medical treatment of duodenal ulcer', *Annals of Surgery*, Jul 1939, vol. 110, 37-49

<sup>490</sup> This topic is extensively discussed later in the thesis.

<sup>491</sup> Martin L, Lewis N, 'Peptic ulcer cases reviewed after ten years', *The Lancet*, Dec 17<sup>th</sup> 1949, 1115-20

<sup>492</sup> Allen A W, Welch C E, 'Gastric resection for duodenal ulcer: follow-up studies', *Annals of Surgery*, Apr 1942, vol. 115, 530-43

<sup>493</sup> The acid producing part of the stomach is the part called the body of the stomach.

removes a variable amount of the stomach carried with it many problems which were capable of adversely affecting patients for the rest of their lives although most patients were satisfied with its results.<sup>495</sup>

In 1948, Hadley Visick suggested that an objective scale should be applied to the symptomatic outcomes of gastric surgery which he named after himself.<sup>496</sup>

Visick grades

Grade I: No symptoms

Grade II: Mild symptoms relieved by care

Grade III: Mild symptoms not relieved by care but satisfactory

Grade IIIu: Mild symptoms not relieved by care. Unsatisfactory

Grade IV: Not improved

(Grades IIIu and IV are considered failures)

The Visick grades (or scales) are still used today in a modified form as a means of assessment of surgical results, mainly in alimentary tract operations. Grade IIIu has been dropped and amalgamated with grade III as ‘unsatisfactory’. Visick’s own study of post-operative results of 500 patients for partial gastrectomy left eight percent of ‘failures’ which he attributed entirely to ‘patients with a marked neurotic overlay’.<sup>497</sup> Unlike St John’s 1939 paper mentioned above, his ‘failures’ reduced in number with the passage of time leaving a residue of five percent. Visick employed a method of gastrectomy called ‘Measured Radical Gastrectomy’ which removed up to three quarters of the stomach leaving only a tiny pouch of stomach. His operation series had a five percent mortality overall.

#### 4. 3. 2: Vagotomy research

In an attempt to improve surgical results for the treatment of peptic ulcers, surgeons experimented on the nerve supplies of the stomachs of laboratory animals. The mammalian stomach is innervated by the vagus nerve and the splanchnic nerves. The vagus nerve originates in the brain and the splanchnic nerves arise out of the sympathetic nerve supply from the sympathetic chain.<sup>498</sup>

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<sup>494</sup> The antrum is the muscular valve mechanism which controls the rate of flow of food out of the stomach. It also produces an alkaline secretion and hormones which regulates digestion.

<sup>495</sup> This will be discussed at length later.

<sup>496</sup> Visick A H, ‘A study of the failures after gastrectomy’, *Annals of the Royal College of Surgeons of England*, 1948, vol. 3, issue 5, 266-84

<sup>497</sup> Visick A H, ‘A study’, *ibid*, 276

<sup>498</sup> The splanchnic nerves lie deep within the abdominal cavity and are part of the unconscious nervous system (sympathetic nervous system) which maintains some of the body’s functions.

Galen in the second century AD, described the vagus nerve, which he called the ‘sixth nerve’, tracing it by dissection from the brain through the neck and thorax and into the abdomen as the nerve supply to the stomach and other organs.<sup>499</sup> Andreas Vesalius’s anatomical drawings of 1543 show the vagus nerve within the peritoneal cavity.<sup>500</sup> Despite proposals that the vagus nerve should be called the tenth cranial nerve, Benjamin Brodie in 1814 referred to it as the eighth nerve.<sup>501</sup> In 1921, André Latarjet accurately identified the distribution of the vagus nerve to the abdominal organs and the distinctive separate branches to the stomach are now called ‘the nerves of Latarjet’. The vagus nerve’s alternative name, used mainly in France, is the ‘pneumogastric nerve’. Latarjet showed that denervation of each part or all parts of the stomach could be achieved by cutting the vagus branches or its whole trunk.<sup>502</sup>

As discussed in chapter two of this thesis, Ivan Pavlov described the secretomotor effect of the vagus nerve.<sup>503</sup> His research on dogs’ vagus nerves revealed the ‘cephalic phase’ of digestion when dogs produced gastric juices, including hydrochloric acid, on sight or smell of food. In 1906, Walter Cannon did animal experiments on vagus nerve resection showing its effect on gastric motility.<sup>504</sup> He demonstrated that gastric motility could vary under physical or psychological stress and suggested that this effect was mediated via the vagus nerve.<sup>505</sup> However despite extensive experimentation by 1926 the physiological working of the stomach was not fully understood.<sup>506</sup> Cutting both splanchnic nerves seemed to have little effects on the stomach motility of some experimental animals but there was a notable hold-up of stomach emptying after complete vagotomy.<sup>507</sup> In humans vagotomy produced a more definite permanent effect of food hold up.<sup>508</sup> D’Arcy McCrea’s paper summarised the state of medical knowledge of the topic at the time:

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<sup>499</sup> Galen, *L’Anatomie des Nerfs, Tome viii*, (Paris, 2008, Les Belles Lettres), p38 According to Galen, there were seven cranial nerves.

<sup>500</sup> Vesalius A, *De Corporis Humani Fabrica, Libri Septem*, (Basel, 1543, Johannes Oporinus), p319

<sup>501</sup> Brodie B C, ‘Experiments and observations on the influence of the nerves of the eighth pair on the secretions of the stomach’, *Philosophical Transactions of the Royal Society of London*, 1814, vol. 104, 102-6

<sup>502</sup> Latarjet A, ‘Note préliminaire sur l’innervation et l’ennervation de l’estomac’, *Société Médicale des Hôpitaux, Lyon Med*, 1921, vol. 130, 166-7

<sup>503</sup> Secretomotor means the production of a secretion.

<sup>504</sup> Cannon W B, ‘The motor activities of the stomach and small intestine after splanchnic and vagus section’, *American Journal of Physiology*, Dec 1908, vol. 17, no. 4, 429-42. Motor activity (or motility) means muscular activity of the stomach.

<sup>505</sup> Cannon W B, ‘The influence of emotional states on the functions of the alimentary canal’, *American Journal of the Medical Sciences*, Apr 1909, vol. 137, no. 4, 485-7

<sup>506</sup> McCrea E D, ‘The nerves of the stomach and their relation to surgery’, *The British Journal of Surgery*, Apr 1926, vol. 13, issue 52, 621-48

<sup>507</sup> McCrea E D, ‘The nerves’, *ibid*, 629

<sup>508</sup> McCrea E D, ‘The nerves’, *ibid*, 534

*Whether nerve section has any real influence on secretion or acidity is doubtful. Psychic and reflex secretion disappears on vagal section and therefore the secretory curve is altered. This has been shown by Litthauer and he also finds that the secretion becomes continuous even in the fasting animal. It appears to be certain that an active juice is still secreted after denervation.*<sup>509</sup>

#### 4. 3. 3: Vagotomy as a therapeutic intervention

In 1899, Mathieu Jaboulay advocated removing the sympathetic nerve supply to the stomach, for relief of the pain caused by ‘gastric tabetic crisis’, a complication of chronic syphilitic infection.<sup>510</sup> In 1922, Latarjet, published a paper describing his experiences of vagotomy for relief of functional disorders of the stomach, often, but not always, related to an ulcer.<sup>511</sup> He discovered that vagotomy delayed gastric emptying which he relieved by a gastroenterostomy. However it appears that he was virtually the only advocate of vagotomy as an ulcer treatment until Lester Dragstedt began animal experimentation on the vagus in the 1930s and became convinced that it played a larger part in the secretion of stomach acid than had been appreciated. Dragstedt made no reference to Latarjet’s work in his research publications.

In 1943, Dragstedt performed a vagotomy on a patient with a severely symptomatic duodenal ulcer who had refused to submit himself to subtotal gastrectomy because of the bad experiences this operation had had on another close to him.<sup>512</sup> The patient’s symptoms were relieved within two weeks. In the following four years, Dragstedt performed one hundred and sixty more such procedures, publishing his results.<sup>513</sup> As had Latarjet before him, Dragstedt found that the vagus-denervated stomach did not empty spontaneously in about one third of cases and required a ‘drainage operation’ in the form initially of a gastroenterostomy.<sup>514</sup> Other surgeons began to perform this new operation for duodenal ulcer relief.<sup>515</sup> <sup>516</sup> There were dissidents who questioned the rationale and physiology of vagotomy for peptic ulcer but, undaunted, Dragstedt continued researching gastric acid

<sup>509</sup> McCrea E D, ‘The nerves’, *ibid*, 630

<sup>510</sup> McCrea E D, ‘The nerves’, *ibid*, 640. See also Woodward E R, ‘The history of vagotomy’, *The American Journal of Surgery*, Jan 1987, vol. 157, issue 1, 9-17. These papers discuss the work of other less well known clinicians and experimenters in this field of research.

<sup>511</sup> Latarjet A, ‘Résection des nerfs de l’ estomac. Techniques opératoire. Résultats cliniques’, *Bulletin de l’Académie Médicale, (Paris)*, 1922, 681-91

<sup>512</sup> Modlin I M, Darr U, ‘The centenary of Lester Dragstedt - 50 years of therapeutic vagotomy’, *Yale Journal of Biology and Medicine*, May-Aug 1994, vol. 67, 63-80

<sup>513</sup> Dragstedt L R, ‘Section of the vagus nerves to the stomach in the treatment of peptic ulcer’, *Annals of Surgery*, Nov 1947, 687-99

<sup>514</sup> Modlin I M, Darr U, ‘The centenary’, *op cit*, 73

<sup>515</sup> Editorial, ‘Vagal resection for peptic ulcer’, *The Lancet*, Jul 19<sup>th</sup> 1947, 95-6

<sup>516</sup> Orr, Johnson, ‘Vagal resection’, *op cit*, 84-9

secretion in his laboratory and in his surgical practice and by the end of the 1950s vagotomy combined with a drainage procedure had become one of the mainstays of surgical intervention for peptic ulcer.<sup>517</sup> It was believed that its main contribution was in reducing basal acid secretion. The operation gained great favour in the following years and was modified and refined using much of the knowledge gained earlier in the century by its pioneers.<sup>518</sup>

#### 4. 3. 4: Surgery for pyloric stenosis

Pyloric stenosis is the least common of the three major acute complications of peptic ulcer disease.<sup>519</sup> Many patients suffering its effects died after prolonged periods of vomiting when no nourishment was absorbed and their blood chemistry had become seriously deranged. In 1885, there was little any physician could do to help except to feed rectally but this was not sustainable for any length of time.<sup>520</sup> A surgical attempt to feed a patient suffering from pyloric stenosis was the fashioning of a gastrostomy on the abdominal surface into which it was hoped to introduce food.<sup>521</sup> Gastrostomies of this and other types were amongst the earliest elective operations attempted on the stomach and are briefly mentioned in chapter two of this thesis. Another reported technique was that of the patient who had survived for five years using a stomach tube to siphon out his stomach contents which had lain there since his last meal, before attempting to re-feed with fresh food.<sup>522</sup> The first reported surgical success in treating a patient with severe pyloric stenosis was achieved by Professor Loreta in Bologna in 1885. Some clinical details are helpful in the understanding of the severity of the patient's illness:

*He was a man, aged 47, named Cecconi, who had suffered from dyspeptic symptoms for twenty years, and had been treated at the hospital in Bologna, four or five years before the operation, for an ulcer of the stomach, near the pylorus (as then diagnosed). The symptoms were relieved, and for a time he returned to work, but soon relapsed; and, when admitted in August 1882, he was in the last stage of emaciation and exhaustion. The only food he could take was milk, in small quantity; every other species of food was at once rejected. Whenever he took any*

<sup>517</sup> Spira J, 'Vagal resection for peptic ulcer', *The Lancet*, Jul 26<sup>th</sup> 1947, 151-2

<sup>518</sup> Modlin I M, Darr U, 'The centenary', op cit, 73-4

<sup>519</sup> There is a form of pyloric stenosis which affects children in the first few months of life called 'infantile hypertrophic pyloric stenosis' which is usually corrected surgically and is not due to peptic ulcer disease.

<sup>520</sup> Robertson G J, 'A case of fibrous stricture of the pylorus: enterostomy: death', *British Medical Journal*, Feb 21<sup>st</sup> 1885, 376

<sup>521</sup> Robertson G J, 'A case', ibid, 376

<sup>522</sup> Russell J, 'Further report of non-malignant constriction of the pylorus: Use of siphon-tube through five years', *British Medical Journal*, Feb 21<sup>st</sup> 1885, 375-6

*food, he could feel its passage towards the right hypochondrium, whence it returned at once towards the left, causing eructations, and frequently vomiting. The man was as lean as possible, pallid, and with a rough skin entirely devoid of any panniculus adiposus.<sup>523</sup> The outline of the distended stomach could be seen through the abdominal walls and it felt tense and elastic; the resonance extended from the fifth rib to the umbilicus ... He was relieved by the emptying of the stomach and could better tolerate an examination. This revealed a tumour, not well circumscribed, extending from the pylorus towards the stomach, smooth, resisting, elastic, and not movable by hand, but following the up and down movements of the abdominal wall.<sup>524</sup>*

This account gives a clear clinical picture of how serious unrelieved pyloric stenosis could be. Professor Loreta took this man to theatre where he opened his stomach and dilated the narrowed pyloric canal using his fingers to allow progress of ingested food beyond the stomach. His post-operative course was uneventful and five months after his operation, ‘the man was in perfect health, and doing his ordinary work.’ It is of interest that Professor Loreta did not attempt partial gastrectomy and perhaps the reason was that such an operation carried very high post-operative mortalities.<sup>525</sup> Other surgeons followed Loreta’s procedure with success.<sup>526 527</sup>

By 1900, four methods of treating pyloric stenosis had been deployed. They were pyloroplasty, gastroenterostomy, gastrolysis and partial gastrectomy.<sup>528 529 530</sup> William Mayo confirmed that duodenal ulcers were the commonest cause of pyloric stenosis and records his experience of increasingly finding them from 1904.<sup>531</sup> He speculated on the diagnoses which had been made in cases of duodenal ulcer prior to the state of knowledge prevailing then and suggested that pyloric stenosis was frequently mistaken for cancer. By

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<sup>523</sup> Fat layer

<sup>524</sup> Holmes T, ‘On operative dilatation of the orifices of the stomach’, *British Medical Journal*, Feb 21<sup>st</sup> 1885, 372-5

<sup>525</sup> Editorial, ‘The surgery of the stomach’, *The Lancet*, Mar 24<sup>th</sup> 1883, 505-6

<sup>526</sup> Gardiner W, ‘A case of Loreta’s operation for dilatation of the pyloric orifice of the stomach’, *British Medical Journal*, Dec 14<sup>th</sup> 1889, 1322-3

<sup>527</sup> Bond C J, ‘On a case of digital exploration of the pylorus (Loreta’s method), with remarks of the relation of gastric ulceration to pyloric stenosis’, *British Medical Journal*, Dec 14<sup>th</sup> 1889, 1323-4

<sup>528</sup> A pyloroplasty operation involves enlarging the stomach outlet.

<sup>529</sup> Gastrolysis is the operative cutting of adhesions which are constricting the stomach or part of it.

Adhesions are fibrous bands to be found anywhere in the body where there has been a severe inflammatory response usually to infection.

<sup>530</sup> Moynihan B G A, ‘The surgery of chronic ulcer of the stomach and its sequellae’, *British Medical Journal*, Dec 8<sup>th</sup> 1900, 1631-5

<sup>531</sup> Mayo W J, ‘Chronic duodenal ulcer’, *Journal of the American Medical Association*, Jun 19<sup>th</sup> 1915, vol. 64, 2037-8

the twentieth century there was an adequate understanding that pyloric stenosis could be surgically remedied provided that the patient presented in a physical condition which allowed for safe surgery.

#### 4. 4: The contribution of the physician in elective treatment of peptic ulcers

##### 4. 4. 1: General management

By 1930, physicians and surgeons were both involved with the management and treatment of peptic ulcer disease as was the general practitioner in a ‘gatekeeper’ rôle whereby it was largely his or her decision as to whom a patient was referred for treatment.<sup>532</sup> The general practitioner would be involved with the treatment of day-to-day dyspepsia care and would refer in cases which he felt might benefit from specialist advice.<sup>533</sup> Whether surgery was considered appropriate or not might be based upon the general practitioner’s own experience of the services which were available to his particular patients.<sup>534</sup> Some doctors took the view that surgery should be a last resort because of its mortality and morbidity risks as well as incidence of poor results.<sup>535</sup> Others believed that medical treatment so often failed that surgery was inevitable and perhaps earlier operative intervention was more appropriate.<sup>536</sup> Moynihan was particularly anxious that physicians generally might be missing serious intra-abdominal pathology which might prove fatal to his patient from a number of causes.<sup>537</sup> The general practitioner provided a disease monitoring service and relief provision for patients in the form of ‘bottles’ which usually contained alkalis. Dietary advice similar to what the hospitals had enjoined was reinforced by them.<sup>538</sup>

A balanced view was expressed as a comment at the conclusion of a paper by William Hinton in 1931 which represented the ‘middle ground’ of discussions of the subject,

*From the study of this group of patients, one can see that a large percentage of both gastric and duodenal ulcers occurring in patients who seek treatment in a city hospital can be carried along under medical care with very satisfactory results,*

<sup>532</sup> Thorne R T, ‘General practitioner and consultant’, *British Medical Journal*, Jun 9<sup>th</sup> 1923, 997

<sup>533</sup> Bennett I T, ‘The medical treatment of peptic ulcer, part 1’, *British Medical Journal*, Jan 11<sup>th</sup> 1936, 69-71; Bennett I T, ‘The medical treatment of peptic ulcer, part 2’, *British Medical Journal*, Jan 18<sup>th</sup> 1936, 120-1; Wilson C M, ‘Treatment of functional dyspepsia’, *British Medical Journal*, Mar 21<sup>st</sup> 1936, 592-4

<sup>534</sup> Bennett I T, ‘Medical treatment, part 2’, op cit, 120-1; Walton Sir J, ‘The surgical treatment of peptic ulcers’, *British Medical Journal*, Jan 25<sup>th</sup> 1936, 172-3

<sup>535</sup> Short A R, ‘The treatment of gastric and duodenal ulcer: a statistical enquiry’, *British Medical Journal*, Mar 14<sup>th</sup> 1931, 435-40

<sup>536</sup> Moynihan B G A, ‘Some problems of gastric and duodenal ulcer’, *British Medical Journal*, Feb 10<sup>th</sup> 1923, 221-6

<sup>537</sup> Moynihan B G A, ‘Some problems of gastric and duodenal ulcer’, *ibid*, 223-6

<sup>538</sup> Bennett I T, ‘Medical treatment, part 1’, op cit, 69-71 and 120-1; Wilson C M, ‘Treatment’, op cit, 592-4

*and if one will refrain from operating on these patients early in the course of their disease and refer them only after every attempt at medical treatment has failed, the surgical results will be most gratifying with conservative types of operation, either gastroenterostomy or in selected cases, of pyloroplasties. Any attempt to call a patient cured after either medical or surgical treatment unless followed for a ten year period, and frequently examined, is most misleading.*<sup>539</sup>

Physicians devised diets and regimens which were directed at healing ulcers and little was available pharmaceutically, apart from antacids and some drugs which were believed to influence gastric secretion. A surgeon, Arthur Rendle Short in 1931, summed up medical treatment in one sentence: ‘The medical treatment adopted was, generally speaking, rest in bed, a milk diet and alkalinisation.’<sup>540</sup> At the time it was never fully understood how antacids worked since they were not powerful enough in normal doses to neutralise the stomach acid, but nevertheless they were the mainstay of treatment. The patients with the worst symptoms were admitted to hospital for special diet, bed rest and medication for a prolonged period of up to six weeks. This regimen worked to apparently heal ulcers as it had done for nearly 150 years.<sup>541</sup> It may have been that the mechanism of perceived healing was simply the placebo effect of medical attention combined with the well known intermittency of the natural course of the disease.

#### 4. 4. 2: Milk and alkalis

Milk was an accepted part of the dietary treatment for peptic ulcers and had been for generations.<sup>542</sup> One American physician, Bertram Sippy, used it in a dietary regime which became widely adopted in the USA and Europe.<sup>543 544</sup> His diet was intended to keep the contents of the stomach neutral and thereby prevent the acid juices of the stomach from attacking any ulcers in the stomach or duodenum, thereby promoting healing.

*The principle of the treatment consists in a thorough neutralisation of the acidity of the gastric juice over a prolonged period of time, and, secondly, in the taking of*

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<sup>539</sup> Hinton W J, ‘The management of patients with gastric and duodenal ulcers’, *Annals of Surgery*, May 1931, vol. 93, issue 5, 1082-5

<sup>540</sup> Short A R, ‘The treatment’, op cit, 435-40

<sup>541</sup> Rowlette R J, ‘The medical treatment of gastric and duodenal ulceration’, *British Medical Journal*, Aug 18<sup>th</sup> 1928, 290-3

<sup>542</sup> Cruveilhier J, in ‘Diagnosis of simple ulcers of the stomach: views of Messrs. Cruveilhier and Trousseau’, *Association Medical Journal*, Dec 6<sup>th</sup> 1856, 1040-1

<sup>543</sup> Sippy B W, ‘Gastric and duodenal ulcer – Medical cure by an efficient removal of gastric juice corrosion’, *Journal of the American Medical Association*, May 15<sup>th</sup> 1915, 1625-30

<sup>544</sup> Anon, ‘The Sippy treatment for gastric ulcer: (Compiled from directions of the Sippy Clinic)’, *Journal of the National Medical Association*, Apr 1924, vol. 16, issue 2, 105-7

*frequent small feedings of soft non-irritating foods that require very little gastric juice for their digestion and that combine easily with that gastric juice as is formed, thereby inhibiting the corrosive action of the juice on the inflamed mucosa.*

*As a preliminary to the treatment, it is necessary that all foci of infection, if any, be determined and eradicated, such as diseased tonsils, infected teeth, sinus infections, gingivitis, gallbladder infections appendicitis, etc.*

*During the first week of treatment it is necessary, if possible, to have the patient in bed except for attention to personal wants.<sup>545</sup>*

Weight gain was a recognised problem for this regimen which was very rich in dairy products for the patient was expected to swallow a diet of three ounces of half milk and cream hourly for twelve hours a day, later adding eggs and cereals and later still substituting custard for the eggs. There was some debate as to the length of bed rest, with some doctors prescribing up to two to three weeks.<sup>546</sup> Repeated gastric aspiration via a stomach tube allowed gastric acidity to be monitored and twice a week gastric lavage was performed throughout the six week period of admission. If acidity was high at night, then gastric aspiration was performed. Medication was prescribed on a regular strict regime in the form of powders dissolved in water containing ten grains of calcium carbonate with thirty grains of sodium bicarbonate initially taken hourly. When constipation was a problem, ten grains each of calcined magnesia and sodium bicarbonate were substituted.<sup>547</sup> Bismuth and dilute solutions of silver nitrate were added three times daily by some doctors.<sup>548</sup> By the fourth week the diet was relaxed sufficiently to allow some vegetables. Patients subjected to this regimen were expected to keep it up for at least a year.<sup>549</sup>

The diet was popular and many centres in the USA used it or a similar diet, with different added pharmaceutical compounds. Berkeley Moynihan in Great Britain in 1919 described it as, ‘the most rational of all methods is that introduced by Sippy which would appear to meet more combatantly those conditions in the stomach which we believe must be controlled before an ulcer can have a chance to heal.’<sup>550</sup> However by 1923, Moynihan recanted saying, ‘the practice has been carried to an extreme which in a very few instances

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<sup>545</sup> Sippy B W, ‘Gastric’, op cit, 105

<sup>546</sup> McNeill C B, ‘Nursing of cases of gastric and duodenal ulcer’, *The American Journal of Nursing*, Apr 1924, vol. 24, issue 7, 533-6

<sup>547</sup> McNeill C B, ‘Nursing’, ibid, 535-6

<sup>548</sup> McNeill C B, ‘Nursing’, ibid, 535

<sup>549</sup> Sippy B W, ‘Gastric’, op cit, 106-7

<sup>550</sup> Moynihan B G A, ‘The diagnosis and treatment of chronic gastric ulcer’, *British Medical Journal*, Dec 19<sup>th</sup> 1919, 765-9

appears to have been harmful.<sup>551</sup> In 1923, Arthur Hurst wrote to the *British Medical Journal* a letter warning of the possibility of ‘toxic manifestations’ caused by the Sippy diet and correctly linked them to cases where renal dysfunction was present.<sup>552</sup> This had been first noted in America by Leo Hardt and Andrew Rivers in 1923.<sup>553</sup> Charles Bolton, a respected English physician, in 1924 said of the Sippy regime, ‘the treatment by alkalis has been unnecessarily carried to excess by Sippy.’ Bolton asserted, ‘that the complete removal of acid from the stomach impairs digestion, it is not necessary for healing and that it may cause symptoms of intoxication.’<sup>554</sup>

Unfortunately while most patients with ulcers benefitted from an alkali regimen, a number of patients with renal impairment began to suffer from alkali poisoning. The symptoms were insidious beginning with a degree of personality change accompanied by melancholy, depression and delusions. The symptoms continued until headaches and muscle aches appeared and eventually the patient became drowsy with progression to coma possible. The diagnosis was made from a history of alkali ingestion and the changes of renal damage found on urine testing along with blood test evidence of renal damage. In 1936 Cuthbert Cope published a paper describing the condition, its causes, symptoms and management.<sup>555</sup> The condition became known as the ‘Milk-Alkali Syndrome’ and most patients recovered after stopping taking alkalis.<sup>556</sup>

In 1932, Asher Winkelstein, in New York, initiated a new variation on the Sippy diet principle by using a milk and alkali intragastric infusion to continuously bathed stomach or duodenal ulcers.<sup>557</sup> The patient was kept in bed throughout the treatment. The milk solution was delivered from a drip bottle via a nasogastric tube at a controlled rate and the patient received it day and night for up to several weeks. The milk drip treatment interrupted the rise in nocturnal acidity which many of the worst duodenal ulcer patients were noted to have. For the next thirty years, the milk drip was in use as a hospital treatment for peptic ulcers which had failed to respond to outpatient medical measures.

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<sup>551</sup> Moynihan B G A, ‘Some problems of gastric and duodenal ulcer’, op cit, 223

<sup>552</sup> Hurst A F, ‘Toxic symptoms following the alkaline treatment of peptic ulcer’, *British Medical Journal*, Jun 23<sup>rd</sup> 1923, 1074

<sup>553</sup> Hardt L L, Rivers A B, ‘Toxic manifestations following the alkaline treatment of peptic ulcer’, *Archives of Internal Medicine*, Feb 1<sup>st</sup> 1923, vol. 31, issue 2, 171-80

<sup>554</sup> Bolton C, ‘The principles of treatment of gastric ulcer in view of recent work’, *British Medical Journal*, Jan 26<sup>th</sup> 1924, 139-41

<sup>555</sup> Cope C L, ‘Alkali poisoning: a danger in the treatment of gastric ulcer’, *British Medical Journal*, Nov 7<sup>th</sup> 1936, 914-7

<sup>556</sup> Orwell E S, ‘The milk-alkali syndrome: current concepts’, *Annals of Internal Medicine*, Aug 1982, vol. 97, no. 2, 242-8

<sup>557</sup> Winkelstein A, ‘A new therapy of peptic ulcer: continuous alkalinized milk drip into the stomach’, *American Journal of the Medical Sciences*, 1933, vol. 185, 695-03

#### 4. 4. 2: Focal infection

Treatment of focal infection has been mentioned as part of the Sippy regime earlier in this chapter and it is discussed more comprehensively in chapter three. In the 1920s and 30s, focal infection was regarded as an important agent in ulcer genesis. Physicians were urged to seek out foci and subject their patients to appropriate surgery for their removal. They were also advised to vaccinate their patients against residual infection. However Robert Rowlette in a wide-ranging article on the medical treatment of gastric and duodenal ulceration in 1928 makes no mention of focal infection or of its treatment.<sup>558</sup> Hurst and Stewart's textbook of 1929 continued to suggest removal of teeth and tonsils as well as sinus surgery but used vaccines only in cases of severe focal infection where he doubted the ability to remove all the infection surgically.<sup>559</sup> Whilst others may have continued to give vaccines to heal ulcers as described before, no mention of vaccination or surgery for focal infection is mentioned by Izod Bennett in his parts of a series of papers published for the benefit of general practitioners in their management of peptic ulcer disease in 1936.<sup>560</sup>

#### 4. 4. 4: Bed rest and psychotherapy

In articles on gastric ulcer in the nineteenth century and on peptic ulcer generally in the twentieth century, bed rest is mentioned as being necessary in the medical treatment of peptic ulcer disease.<sup>561</sup> Charles Illingworth in 1952 said, 'In the absence of complications, the symptoms of peptic ulcer can usually be relieved quite easily by simple medication or at the most by a short spell of rest in bed.'<sup>562</sup> When a patient's symptoms were sufficiently severe to require more intensive investigation, an easy option was to admit the patient to hospital where they could rest. Stress of modern living was considered to play a major part in causing ulcers and this was supported by Susser and Stein's much quoted paper.<sup>563</sup> Psychotherapy itself did not seem to gain a strong foothold in the treatment of peptic ulcer disease in the UK although most doctors would enquire about stress and offer advice.

Opinions varied about formal psychotherapy for peptic ulcer therapy and it was not used in mainstream medicine in the UK. However in the USA in 1963, Eddy Palmer wrote, 'In the

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<sup>558</sup> Rowlette R J, 'The medical treatment', op cit, 290-3

<sup>559</sup> Hurst A F, Stewart M J, *Gastric and Duodenal*, op cit, p388

<sup>560</sup> Bennett I T, 'Medical treatment, part 1', op cit, 69-71, and 120-1

<sup>561</sup> Foster B W, 'On the treatment of ulcer of the stomach', *The Lancet*, Apr 25<sup>th</sup> 1868, 523; Wardell J R, 'On chronic ulcer of the stomach', *The Lancet*, Sep 2<sup>nd</sup> 1876, 316; Moynihan B G A, 'The diagnosis', op cit, 769; Bolton C, 'The principles', op cit, 140; Bennett I T, 'Medical treatment, part 1', op cit, 69

<sup>562</sup> Illingworth C F W, 'Refresher course for general practitioners: peptic ulcer', *British Medical Journal*, Jul 26<sup>th</sup> 1952, 206-7

<sup>563</sup> Susser M, Stein Z, 'Civilisation and peptic ulcer', *The Lancet*, Jan 20<sup>th</sup> 1962, 115-9

treatment of the uncomplicated duodenal ulcer, it is found that the emotional aspect of the illness is a great deal more important than the organic. ... for permanent help and even hope of a cure, the gastroenterologist must concentrate realistically on the patient's emotional problems through interview therapy.<sup>564</sup> Palmer reckoned that ten hours of interview therapy was required to treat the average duodenal ulcer patient.<sup>565</sup> In 1949, Francis Avery Jones wrote a lecture in the *British Medical Journal* for the benefit of general practitioners to help them treat peptic ulcer.<sup>566</sup> The article is an example of the state of knowledge about the treatment of peptic ulcers for the time. The recommended regimen of diet, alkalis, ascorbic acid, phenobarbitone and belladonna is detailed along with lifestyle advice about stress avoidance and stopping smoking. Laurence Martin and Ninian Lewis' ten year follow-up review of peptic ulcer treatment is more analytical concluding that in 1949:

*...medicinal ulcer therapy in the accepted form has resulted in almost complete failure ... It is undeniable that medical treatment relieves the discomfort of most relapses; but, from our present evidence we cannot believe that it is any protection against further trouble if this is destined by the ulcer.*<sup>567</sup>

#### 4. 5: Peptic ulcer in soldiers in World War II

After the onset of hostilities in World War II, 14.4% of soldiers who were withdrawn from active service in the British Expeditionary Force and admitted to hospital needed investigation and treatment for dyspeptic symptoms. Early in the assessment of these cases, it was found that the majority were organic, which is to say that a physical cause was found for the symptoms, and that psychological factors played a very small part in them.<sup>568</sup> A poor diet under field conditions and poor dental hygiene were implicated in causing the dyspepsia. It was also found that the majority had had dyspepsia or actual ulcer disease before enlistment. The army was unprepared for what they saw as a new problem and many of the soldiers were subsequently discharged as unfit for service. In World War I, the main reason for medical discharge from the army had been 'disorder of the heart' and peptic ulcer disease rarely featured.<sup>569</sup>

<sup>564</sup> Palmer E D, *Clinical Gastroenterology*, 2<sup>nd</sup> edition, (New York, 1963, Harper and Row), p211

<sup>565</sup> Palmer E D, *Clinical Gastroenterology*, ibid, p4

<sup>566</sup> Jones F A, 'Refresher course for general practitioners: The management of acute dyspepsia with special reference to gastric and duodenal ulcer', *British Medical Journal*, Dec 24<sup>th</sup> 1949, 1463-6

<sup>567</sup> Martin, Lewis, 'Peptic ulcer cases', op cit, 1117

<sup>568</sup> Payne R T, Newman C, 'Interim report on dyspepsia in the army', *British Medical Journal*, Dec 14<sup>th</sup> 1940, 819-821

<sup>569</sup> Bergman B P, Miller S A S St J, 'Unfit for further service: Trends in medical discharge from the British Army 1861-1998', *Journal of the Royal Medical Corps*, Oct 2000, vol. 146, 204-11

In 1941, it was reported, ‘In Army medicine, digestive disorders are presenting a large and increasing problem. Of 790 medical inpatients, 246 (31%) were admitted to a military hospital on account of gastro-intestinal complaints.’<sup>570</sup> Of these cases, 64% were found to be due to peptic ulcer with the majority being duodenal ulcers. It was noted that these patients rarely had haematemesis or perforations.<sup>571</sup> By 1943, 14% of all medical discharges were for peptic ulcer disease.<sup>572</sup> When the issue was further examined, in another series, it was found that, ‘The incidence of peptic ulcer was similar to that found in civil hospitals.’<sup>573</sup> Other researchers confirmed the above findings with some variation in the rates of diagnosis of peptic ulcers and the overall conclusion of the authors was that peptic ulcer disease was not a new phenomenon to appear as a consequence of army life rather it had been present in around 90% of soldiers who subsequently developed symptoms after their enlisting.<sup>574 575</sup> At first it seemed that the army was dealing with a new disease situation which had not been encountered before in the theatre of war but when carefully investigated, the outcome was of no surprise since it reflected the situation of peptic disease prevalence in civilian life.

## Conclusion to chapter four

In this chapter, the serious complications of peptic ulcer of bleeding, perforation and pyloric stenosis have been examined in detail with the response of medical practitioners to them. Blood transfusion and diet played the most important part in treating haematemesis but surgery was required for perforated upper gastrointestinal ulcers, for those patients with haematemesis who had failed to respond to medical regimens and for the relief of pyloric stenosis. It seemed that the surgeons had most to offer for the elective treatment of patients with chronic peptic ulcers but their success rates were limited by the health of their patients at the time of their intervention. In addition, their chosen operations for elective treatment were not as effective as first hoped because there was a legacy of serious after effects in a small proportion of patients. The work of the hospital physicians and general practitioners is also described as they used specialised diets to treat gastric and duodenal ulcers. The chapter ends with a brief account of wartime soldiers’ experiences of peptic ulcer which initially surprised the army before investigations of the circumstances led to an explanation.

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<sup>570</sup> Graham J G, Kerr O J D, ‘Digestive disorders in the forces’, *British Medical Journal*, Mar 29<sup>th</sup> 1941, 473-6

<sup>571</sup> Graham, ‘Digestive disorders in the forces’, *ibid*, 476

<sup>572</sup> Bergman, Miller, ‘Unfit for further service’, *op cit*, 204-211

<sup>573</sup> Hutchison J H, ‘The incidence of dyspepsia in a military hospital’, *British Medical Journal*, Jul 19<sup>th</sup> 1941, 78-81

<sup>574</sup> Hinds-Howell C A, ‘A review of dyspepsia in the Army’, *British Medical Journal*, Oct 4<sup>th</sup> 1941, 473-4

<sup>575</sup> Tidy Sir H, ‘Peptic ulcer and dyspepsia in the Army’, *British Medical Journal*, Oct 16<sup>th</sup> 1943, 473-7

The next chapter will depart from the stream of the narrative to reflect on the history of gastric and duodenal ulcers in the UK as it is currently understood. Based upon a closer examination of the history of the period and historical writing about it in the twentieth century, arguments are advanced to challenge the currently understood history of gastric and duodenal ulcers. This is brought up to date in the light of new clinical advances in the understanding of peptic ulcer disease.

## Chapter 5. The historical argument regarding the nature of duodenal ulcer

### Introduction to chapter five

Twentieth century authors, Denys Jennings, Jeremy Hugh Baron, Amnon Sonnenberg, Martin Blaser and David Graham take the view that peptic ulcer was a rare disease in the eighteenth century which became more prevalent in the nineteenth century. They believe that a change in the nature of the disease took place in the late nineteenth century when duodenal ulcer became more common than gastric ulcer. This view is also uncritically accepted by those who compiled the Welcome Witnesses Symposium, ‘Peptic Ulcer: Rise and Fall’, in the year 2000. The only author in recent times to challenge this is Ian Miller. This chapter challenges this proposition by closely examining some modern accounts and the statistics used in them which were written to reinforce this view. The current received history of peptic ulcer disease in the period is re-examined taking into account factors which have been overlooked by historians who have accepted it without question. It focuses on the nature of death certification, autopsy practice of the time, societal conditions and published data from other countries. The chapter ends with a discussion about the recent discovery of *Helicobacter pylori* and its place in the history of peptic ulcer disease.

### 5. 1: A history of peptic ulcer from the eighteenth century

When writing an article about peptic ulcer disease, some authors include a brief overview by way of an introduction.<sup>576 577</sup> Amnon Sonnenberg’s account is typical.

*Jennings gave a vivid and comprehensive account of the historic changes of peptic ulcer between 1800 and 1940. Peptic ulcer used to be a rare disease before the 19th century. In the beginning of the 19th century acute perforations of gastric ulcers were first reported in young girls. The disease had a dramatic course with sudden onset of severe pains, abdominal rigidity, and subsequent death within 24-48 hours. Necropsy would reveal a hole with sharp margins in the gastric wall. It is unlikely that the many fine physicians of the 18th century should have missed such an impressive clinical picture. It would rather seem that peptic ulcer did not exist or was quite rare before the onset of the 19th century. With progress of the*

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<sup>576</sup> Sonnenberg A, ‘Geographic and temporal variations in the occurrence of peptic ulcer disease’, *Scandinavian Journal of Gastroenterology*, Jan 1<sup>st</sup> 1985, vol. 20, no. 1, 11-24

<sup>577</sup> Sonnenberg A, ‘Time trends of ulcer mortality in Europe’, *Gastroenterology*, 2007, vol. 132, 2320-7

*19th century peptic ulcer became more frequent also in men. By the end of the century the incidence of duodenal ulcer had surpassed that of gastric ulcer. Since duodenal ulcer in young males affected a group which was fit for military service and responsible for the national income, interest in peptic ulcer disease grew and means were sought to master it. In the following decades peptic ulcer changed from a disease of the young ages to a disease of the middle and old ages. It also changed from a disease of the higher social classes to a disease affecting predominantly the lower social classes.*<sup>578</sup>

Thus stated, Sonnenberg's early history of peptic ulcer disease has five characteristics; it was a rare disease in the eighteenth and nineteenth centuries, it appeared first of all in young girls, presenting initially with gastric ulcers, before it changed into a disease predominantly of young men with duodenal ulcers, from the beginning of the twentieth century and, finally in the later twentieth century, it became a disease which affected mainly the lower social classes.

Two questions arise in the history: was peptic ulcer a new illness in modern times or was it always there, only in an unrecognised form? To answer these questions, it is necessary to seek evidence of the existence of the disease from the available records. The emergence of peptic ulcer disease in the eighteenth century as a diagnosis was discussed in chapter two from the clinical and pathological writings of Morgagni, Baillie and Cullen. In the nineteenth century, understanding of its nature grew and it began to be realised how common a problem it was, with much being written about it in books and medical journals. Samuel Fenwick's book, published in 1868, covering the spectrum of peptic ulceration is typical.<sup>579</sup> He asserted that at any time '236 persons in every 1000 were suffering from indigestion'. Dyspepsia as a diagnosis included peptic ulcer disease as well as all the other causes of upper gastrointestinal disorders in these writings as discussed in chapter one. Although it was always a common problem in society, it was never a major cause of death and was not noticed by the autopsy practitioners of the eighteenth and nineteenth centuries in large numbers, for reasons which will be discussed later in this chapter.

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<sup>578</sup> Sonnenberg A, 'Geographic and temporal variations', op cit, 17

<sup>579</sup> Fenwick S, *The Morbid States of the Stomach and Duodenum*, (London, 1868, John Churchill), p361

## 5. 2: Modern histories of peptic ulcer disease

### 5. 2: 1: 'A disease of civilisation'

Denys Jennings wrote two papers on 'perforated peptic ulcer' which used upper gastrointestinal perforation as an indicator of disease prevalence.<sup>580</sup> This has been discussed in chapter 1. He concedes in the first paper that there were fallacies in the collection of information from which a history of perforated ulcer can be constructed, because published material is of a selected sample. The type of patient on which necropsies were performed, the problems of transport, and diagnostic issues were important. Putting these difficulties aside, he used the published information available to him and his paper showed that there were appreciable changes in perforated ulcer prevalence in the published age and gender data over the period. His paper also discusses the rise in hospital activity in the treatment of peptic ulcer at the end of the nineteenth century. Unfortunately, his data does not distinguish between duodenal and gastric ulcer separately. Jennings' paper also repeated the statement that gastric ulcer in the mid nineteenth century was a disease of young female servants.<sup>581</sup> It has been the basis of many historical articles on peptic ulcer disease since.<sup>582</sup>

Mervyn Susser and Zena Stein were the first to argue that the number of those dying from peptic ulcer disease had reached its zenith in 1955 and was in decline by 1962.<sup>583</sup> Susser and Stein's article referred to the first of Jennings' papers in its historical introduction and appeared at a time when those in medical practice felt that it was an increasing clinical problem. Susser and Stein's research used the statistical method of cohort analysis, graphically plotting deaths from gastric and duodenal ulcer in cohorts by dates of birth and showed that the earliest cohort had the highest mortalities. Younger cohort death rates fell successively in time. They attributed the fall in deaths to a 'cohort effect' which Susser later defined as: 'Generation effects (cohort effects) are environmental effects attributed to the singular experience of each cohort antecedent to the time when the outcome of interest is observed.'<sup>584</sup> The Government Record Office (GRO) statistics of 1962 confirmed the

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<sup>580</sup> Jennings D, 'Perforated peptic ulcer', *The Lancet*, Mar 2<sup>nd</sup> 1940, 395-8; Jennings D, 'Perforated peptic ulcer', *The Lancet*, Mar 9<sup>th</sup> 1940, 444-7

<sup>581</sup> See chapter two

<sup>582</sup> An internet search using 'Denys Jennings' and the year '1940' on the World of Science database showed that it had been cited 55 times in journal articles

<sup>583</sup> Susser M, Stein Z, 'Civilisation and peptic ulcer', *The Lancet*, Jan 20<sup>th</sup> 1962, 115-9. An internet search on the World of Science database reveals that this paper has been cited 145 times in journal articles

<sup>584</sup> Susser M, 'Period effects, generation effects and age effects in peptic ulcer mortality', *Journal of Chronic Diseases*, 1982, vol. 35, 29-40

fall in aggregated deaths from both forms of peptic ulcer from 1955.<sup>585</sup> Susser and Stein concluded that peptic ulcers were caused by the stresses of modern living.<sup>586</sup> This paper was an early introduction to the concept of the birth-cohort as a factor in the aetiology of certain diseases as well as the concept of ‘a disease of civilisation’.

## 5. 2. 2: The ‘birth-cohort phenomenon’

Aaron Sonnenberg has published many articles on the subject of the birth-cohort phenomenon and its effect upon the history of peptic ulcer in particular. His hypothesis suggests that cohorts of the population grouped by age within the same societies shared common life experiences which had a bearing upon different illnesses. He explains it thus:

*Because genetically determined mechanisms stay unchanged during historical time periods, the marked temporal trends of gastric and duodenal ulcer disease indicated that their occurrence was largely influenced by exogenous risk factors. The simpler and most consistent pattern obtained by considering the patients’ period of birth rather than death implies that influences during or shortly after birth are very important. A birth-cohort pattern suggests that exposure to the relevant risk factors of the disease occurs during the early life between the prenatal period and adolescence.*

*... the occurrence of a birth-cohort phenomenon indicated that environmental factors were important in the etiology of gastric and duodenal ulcers.*

*... by plotting peptic ulcer death rates against the year of birth, one is given the opportunity to seemingly open a window and view most of the 19<sup>th</sup> century, even if the data themselves were generated during the 20<sup>th</sup> century.<sup>587</sup>*

If it is accepted that cohort analysis allows the historian to seemingly ‘open a window’ into a previous century, then its results must not conflict with the history of the period as it is understood by historians. At the beginning of the nineteenth century, the majority of England and Wales’ population lived in the countryside but by 1851 the majority lived in urban communities. It is known that the Industrial Revolution and the railways led to large population movements which might have had an effect of changing the disease prevalence should it be of an infectious or contagious nature. Other factors such as hygiene, housing

<sup>585</sup> See Figure 2 later in this chapter

<sup>586</sup> The paper is also known for popularising the concept of ‘a disease of civilisation’ although the authors did not make this precise claim for peptic ulcer disease preferring the phrase ‘a disease of early urbanisation’. The term ‘disease of civilisation’ was not coined by Susser and Stein and may be found in European literature from 1934.

<sup>587</sup> Sonnenberg A, ‘The meaning of the birth-cohort phenomenon’, in Marshall B J, *Helicobacter Pioneers*, (Victoria, 2002, Blackwell Science), pp57-61

overcrowding and poor food, which are often aetiologically implicated in peptic ulcer disease, were bad for a large section of the working classes, both in the countryside and the towns and cities, and food was often adulterated.<sup>588</sup>

The birth-cohort theory proposes that an exogenous risk factor was shared by the men and women of different class and prosperity, living in disparate parts of England and Wales, which made them increasingly susceptible to gastric and duodenal ulcers as the nineteenth century progressed, but no indication is given to explain what this exogenous risk factor was. Sonnenberg's statistical studies for his cohort theory used 'cause of death' statistics from the published GRO annual returns which further prejudices its likelihood of being valid in the light of how inaccurate the clinical diagnoses upon which they are based have been shown to be. This is discussed later in this chapter. Despite these objections, Sonnenberg's graphical representations of cohort mortality in peptic ulcer disease appear to support his hypothesis very elegantly and are accepted by most of those who have an interest in peptic ulcer disease history.

It may be suggested that the factor responsible for the appearance of peptic ulcer in the nineteenth century is the bacterium *Helicobacter pylori* which is now known to be the cause of most peptic ulcers and which would have been present in the stomachs of virtually the entire British population, possibly for many centuries.<sup>589</sup> However no satisfactory reason has been advanced to explain why increasing numbers of people died of peptic ulcers throughout the nineteenth century if *H. pylori* infection was its cause. This is discussed at greater length later in this chapter.

### 5. 2. 3: Other historical accounts

Jeremy Hugh Baron and Amnon Sonnenberg's paper, 'History of dyspepsia in Scotland', is an attempt to show that dyspepsia was an increasing clinical problem over the period from 1729-1830.<sup>590</sup> They used Guenter Risse's statistics from his monograph on Edinburgh Royal Infirmary as one source for their data.<sup>591</sup> Risse's book shows that when the Infirmary opened in 1729, it had six beds and admitted 35 patients in its first year. It was relocated and opened in 1741 and the numbers of beds grew gradually to approximately

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<sup>588</sup> This is discussed later in the chapter

<sup>589</sup> Blaser M J, '*Helicobacters* are indigenous to the human stomach: duodenal ulceration is due to changes in gastric microecology in the modern era', *Gut*, 1998, vol. 43, 721-7

<sup>590</sup> Baron J H, Sonnenberg A, 'History of dyspepsia in Scotland', *Scottish Medical Journal*, Aug 2008, vol. 53, issue 3, 42-4

<sup>591</sup> Risse G B, *Hospital Life in Enlightenment Scotland: Care and Teaching at the Royal Infirmary of Edinburgh*, (Cambridge, 1986, Cambridge University Press)

180 by 1800. Under such circumstances the numbers of patients admitted with any common disease could hardly have failed to rise.

‘Stomach complaints and dyspepsia’ was the fifth commonest admission complaint, occupying 4% of Risse’s sample. In the thirty years, 1770 to 1800, Risse’s quinquennial samples show that Edinburgh Royal Infirmary admitted an average of 17 patients (n. 12-26) a year with a diagnosis of ‘dyspepsia and stomach complaint’.<sup>592</sup> The sample numbers fluctuated but there was no rise over the period to suggest that dyspepsia prevalence was increasing for there were 12 patients admitted with ‘stomach complaint and dyspepsia’ in 1770 and 12 in 1800. In its first year there was no record of any admission for dyspepsia and the records for the period 1730-59 have been lost. Hospital admission was a new phenomenon in Edinburgh in 1730 and it cannot be assumed that the absence of an admission for any condition meant that it did not exist in the community. The authors’ graph begins in 1730 at zero and rises to 900 per million (12 patients) in 1770 when Risse’s data begins.<sup>593</sup> On the basis of this ‘rise’, the paper concludes with the statement that, ‘The rapid rise in admissions to the Edinburgh Royal Infirmary of patients diagnosed as stomach complaints or dyspepsia during the second half of the eighteenth century represented a real increase of this new gastric disorder that has persisted in a similar fashion since then.’<sup>594</sup>

The two authors supplement their argument by presenting data on MD theses from Edinburgh University on the subject of dyspepsia and gastritis which they assert grew numerically over the seventy year period from approximately 1750 and 1823. In all, 65 theses were submitted on this subject out of approximately 4000 submitted on all medical subjects between 1726 and 1823. Less than five were produced in any year on dyspepsia between 1750 and 1790. Then the numbers increase rapidly from 1790 until 1800 but with less than 50 out of the original 65 spread over the next 33 years. In reality all that can be said with certainty is that dyspepsia was a clinical problem which seemed to be an increasingly interesting topic for those writing MD theses at this period. It cannot be inferred from this that it was a newly emerging illness. A modern example of publications on *H. pylori* illustrates this point. No one would suggest that the rise in publications on *H. pylori* represented a rise in its incidence or prevalence from 1984.

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<sup>592</sup> Risse G B, *Hospital Life in Enlightenment Scotland*, *ibid*, p120

<sup>593</sup> It is not clear from either the data provided in the paper or from Risse’s data where the figure of 900/million has been derived from

<sup>594</sup> Baron J H, Sonnenberg A, ‘History of Dyspepsia’, *op cit*, 42-4

In another paper, ‘Three centuries of stomach symptoms in Scotland’,<sup>595</sup> Jeremy Hugh Baron, Amnon Sonnenberg and Fiona Watson wrote about dyspepsia in Scotland from 1750 until the late twentieth century. The outpatient data show that dyspepsia was a very common problem. The authors state that gastric and duodenal ulcer both showed a marked rise during the latter part of the nineteenth century.<sup>596</sup> Nosological difficulties surrounding the diagnosis of dyspepsia over the period were acknowledged and the authors ask, ‘Is it possible that those diagnosed as dyspepsia actually had peptic ulcers? However, in that case one would have expected reports of many complications from haemorrhage (there were few), many deaths from perforation (there were none) or many ulcers seen at necropsy.’<sup>597</sup> Elsewhere in this thesis I suggest that clinical diagnosis of peptic ulcer of any kind is inaccurate and that many peptic ulcers were in fact missed by clinicians.

### 5. 3: Death certification

By the mid-nineteenth century when patients presented with severe dyspeptic symptoms, doctors and surgeons believed that they were dealing with gastric ulcer, if these symptoms matched those which they had been taught as diagnostic. Other possibilities which were not considered as being the source of the pain included duodenal ulcer, gallstones, pancreatitis or other rarer conditions. The diagnosis was clinical and based upon the experience and opinion of the medical attendant and, unless the patient died in a voluntary hospital, an autopsy was rarely done. Even then, few autopsies were actually being done in voluntary hospitals although after around 1870, as may be judged by an examination of medical journals, they became much more common.<sup>598</sup> From 1851, the causes of death from upper abdominal conditions listed by Registrar General of Births, Marriages and Deaths for England and Wales in his annual returns were; gastritis, peritonitis, diseases of stomach and ulceration of the intestines. In 1881, dyspepsia, haematemesis, melaena, gastric ulcer, and gallstones were added. In 1891 appendicitis and perityphlitis appeared and duodenal ulcer was first included in 1911. Death certification was then as now, mostly a matter of clinical opinion.<sup>599</sup>

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<sup>595</sup> Baron J H, Watson F, Sonnenberg A, ‘Three centuries of stomach symptoms in Scotland’, *Alimentary Pharmacology and Therapeutics*, Sep 2006, vol. 24, 821-9

<sup>596</sup> Baron J H, Watson F, Sonnenberg A,, ‘Three centuries of stomach symptoms’, *ibid*, 828

<sup>597</sup> Baron J H, Watson F, Sonnenberg A, ‘Three centuries of stomach symptoms’, *ibid*, 827

<sup>598</sup> This statement is based upon a search by year for the words ‘post mortem’, ‘necropsy’ and ‘autopsy’ in the pages of *The Lancet* and the *British Medical Journal* from 1860-80. Post-mortem diagnosis included in case reports began to be steadily reported from 1872.

<sup>599</sup> Annual reports of the Registrar General of Births, Marriages and Deaths for England and Wales first appeared for the years 1837-8.

Of the several difficulties which made GRO cause of death statistics inaccurate, the most obvious one is that of diagnosis. In the nineteenth century, two particular diseases were problematic for different reasons. The first was typhus which was mistaken for typhoid on the basis of similarities of clinical presentations until the late 1860s.<sup>600</sup> The second was tuberculosis, for there were many confounding issues concerning the diagnosis of tuberculosis, some medical and others societal.<sup>601</sup> Some cases were genuinely mistaken and certified as cases of bronchitis. However, because of the opprobrium associated with a diagnosis of tuberculosis, some doctors used other diagnoses such as haemoptysis, bronchopneumonia, pleurisy or pleural effusion, but bronchitis was by far the most frequent diagnosis. A societal issue concerned the belief that a person with a family history of tuberculosis would not be admitted into an insurance scheme and for this reason, family doctors colluded in obfuscation of certification of cause of death by using a less obvious diagnosis than one which would point to a tubercular one.<sup>602</sup> The families of those who had died of tuberculosis were often socially ostracized and there was a belief that the condition was hereditary, which carried with it its own problems. Even today, sincere and honest certification can give an inaccurate diagnosis which is a problem for statisticians seeking quality data derived from death certification.<sup>603</sup>

The historian, John Eyler, wrote about the problem which the GRO faced with collecting data, ‘A large percentage of the deaths ... were still not medically certified even in the 1860s and among those that were, there were problems: doctors frequently saw the victim only in his last moments, or they would issue a certificate on a relative’s report of last symptoms. Sometimes they falsified death registrations to save respectable families embarrassment.’<sup>604</sup> Anne Hardy covers the issue of certification of causes of death in her paper, “‘Death is the Cure for all Diseases’: Using the Government Records Office Cause of Death Statistics for 1837-1920’.<sup>605</sup> Under-recording and over-recording of some causes of death was a common problem, worse in rural areas until the 1880s, as was accuracy of

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<sup>600</sup> Luckin B, ‘Death and survival in the city: approaches to the history of disease’, *Urban History*, May 1980, vol.2, 53-62

<sup>601</sup> Bryder L, “‘Not always one and the same thing’”: the registration of tuberculosis deaths in Great Britain, 1900-1950’, *Social History of Medicine*, Aug 1996, vol. 9, issue 2, 253-265

<sup>602</sup> Hardy A, “‘Death is the Cure for all Diseases’”: Using the Government Records Office Cause of Death Statistics for 1837-1920’, *Social History of Medicine*, Dec 1994, vol.7, issue 3, 472-92, esp p472

<sup>603</sup> Maudsley G, Williams E M I, “‘Inaccuracy’ in death certification: Where are we now?’, *Journal of Public Health Medicine*, 1996, vol.18, no. 1, 59-66

<sup>604</sup> Eyler J, ‘Mortality statistics and Victorian health policy: Program and criticism’, *Bulletin of the History of Medicine*, Fall 1976, vol. 50, 335-55, esp p352 Eyler is quoting the words of Henry Wyldbore Rumsey, a medical practitioner in Cheltenham who was opposed to abuses of mortality statistics especially by non-medical vested interests who could distort their meanings for their own ends.

<sup>605</sup> Hardy A, “‘Death is the Cure for all Diseases’” op cit, pp472-480

diagnosis. Not all deaths were certified by doctors and many were certified by a doctor who had not seen the patient before death.<sup>606 607</sup>

Clinical diagnosis can be seen to be highly suspect for acute abdominal conditions even in the hands of experienced surgeons.<sup>608</sup> One witness who was interviewed for this project told of his experience when he was medical student, seeing his first patient with acute peritonitis due to a perforation, one evening when he attended a receiving night in Glasgow Royal Infirmary around 1957. Students were taught by surgeons on ‘receiving nights’ about the conditions presenting as surgical emergencies:

*Mr ‘X’ was inspirational in that he took us callow students on his ward rounds and gave us a kind of continuous read-out of his thought processes. He told us exactly what he was thinking as he was thinking it and we had an amazing first receiving (night). We were up all night and a guy came in with board-like rigidity. ‘Look at this chap, there is board-like rigidity, classical perforated peptic ulcer, duodenal ulcer probably,’ he said. So we were duly impressed, went to theatre and the guy had a belly full of faeces and he had a perforated carcinoma of colon. That was impressive.*<sup>609</sup>

In 1859, the first Medical Register, published after the Medical Act of 1858, contained the names of approximately 15,000 medical practitioners in the UK whose population in 1861 was 24,525,000.<sup>610 611</sup> Only registered practitioners could sign certificates of cause of death and the 35<sup>th</sup> annual report (1871) of the Registrar General of England and Wales indicated that all but eight per cent of deaths were certified by practitioners, a figure not

<sup>606</sup> Hardy A, “Death is the Cure for all Diseases” op cit, p475

<sup>607</sup> Michael Stolberg’s paper, ‘National Statistics on the Causes of Death in Nineteenth-Century Bavaria’, shows that the problem of medical certification of death in Bavaria was much worse than that in England and Wales because of rural remoteness and paucity of doctors who could undertake the task. Lay persons with a very rudimentary training often undertook the task which at times included performing autopsies see Stolberg M. ‘National Statistics on the Causes of Death in Nineteenth-Century Bavaria’, *Journal of the History of Medicine and Allied Sciences*, Apr 1999, vol.54, issue 2, 210-225 The problem was similar in Denmark in the nineteenth century, see Johanson H C, ‘The development of reporting systems for causes of death in Denmark’, *Journal of the History of Medicine and Allied Sciences*, Apr 1999, vol.54, issue 2, 154-66

<sup>608</sup> See later in this chapter. Early clinical diagnosis was not accurate for cases of peritonitis in 1900 for up to one third of patients who were initially diagnosed as appendicitis pre-operatively had in fact had perforations. Moynihan himself had opened 18 cases of suspected appendicitis out of a series of 49 cases where perforation of the duodenum or stomach was the correct diagnosis. See Moynihan B G A, ‘On duodenal ulcer and its surgical treatment’, *The Lancet*, Dec 14<sup>th</sup> 1901, p1658

<sup>609</sup> From Testimony T21

<sup>610</sup> Porter R, *The Greatest Benefit To Mankind: A Medical History of Humanity from Antiquity to the Present*, (London, 1997, Fontana Press), pp355-6

<sup>611</sup> Bynum W F, *Science and the Practice of Medicine in the Nineteenth Century*, (Cambridge, 1994, Cambridge University Press), p179

improved upon by 1901.<sup>612</sup> Coroners who were also usually medically qualified, certified approximately six per cent, the remainder deaths being uncertified. There is evidence that the coroners were less than fully conscientious at times in the performance of their duties as indicated by correspondence in *The Lancet* under the title of 'Easy-going coroners', wherein three doctors complain of coroners' behaviour in inquests and their certification of deaths, which in their opinions merited more rigorous investigations.<sup>613</sup>

#### 5. 4: 1800-1940: living conditions and diet in Britain

Thomas McKeown wrote that in the eighteenth and nineteenth centuries the rise in the population of the British people was due to a decline in fatalities from infectious diseases as a result of improvement in diet and in living conditions, which was a result of higher incomes.<sup>614</sup> Population rise was used by McKeown as a surrogate measure of health. He asserted that medical practitioners achieved little to improve mortality in these two centuries. The 'McKeown hypothesis' has been contested and today, many historians reject McKeown's work on the grounds of his selective use of statistics and his expression of strong unsubstantiated opinions.<sup>615</sup> Despite this, McKeown's view that medicine had little to offer the British population in terms of health gain in the later nineteenth century is still taught and believed by a large section of the medical profession. In the case of peptic ulcer disease, if it did change its nature at around end of the nineteenth century, the factors which might have played a part in this change should be examined.

As has been stated, McKeown proposed that improvements in diet and in social conditions were the explanation of the rise in population. The sanitary improvements were acknowledged as playing a lesser part in the overall mortality of the century. Urban slum dwellers of the unskilled working classes saw no improvement in their circumstances, which worsened in Glasgow due to increasing overcrowding, but the burgeoning upper, middle and skilled artisan classes, who were increasingly retreating from the crowded urban centres to newly built suburbs, did experience great improvements in their living circumstances.<sup>616</sup> Between 1855 and 1925 deaths from the commoner forms of infectious

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<sup>612</sup> *Annual Report of the Registrar General of Births, Deaths and Marriages in England and Wales*, (London, 1901, H.M.S.O), Part 1, plxxx

<sup>613</sup> 'Correspondence', *The Lancet*, May 10<sup>th</sup> 1873, 683

<sup>614</sup> McKeown T and Record R G, 'Reasons for the decline of mortality of England and Wales during the nineteenth century', *Population Studies*, 1962, vol. 16, 94-122

<sup>615</sup> Szreter S, 'The importance of social intervention in Britain's mortality decline c.1850-1914: a reinterpretation of the role of public health', *Social History of Medicine*, 1988, vol. 1, 1-37; Johansson S R, 'Food for thought', *Historical Methods*, Summer 1994, vol. 27, no. 3, 101-26

<sup>616</sup> Chalmers A K, *The Health of Glasgow 1818-1920*, (Glasgow, 1930, Bell & Bain), p22

diseases fell dramatically both in Glasgow and in many major European cities.<sup>617</sup> Family size fell also from 1860 and has been linked to increasing prosperity but it is not possible to state categorically that this was its cause.<sup>618 619</sup>

The historical debate about the impact of the Industrial Revolution upon living standards continues with no certainty as to whether or not its influence had a positive or negative effect in its early years. Charles Feinstein analysed data for the period before and after the Industrial revolution and concluded:

*Most British workers and their families did not experience an actual deterioration in their standard of living during and after the Industrial Revolution. But neither did they enjoy the rapid progress which the super-optimists have discerned. For the majority of the working class the historical reality was that they had to endure almost a century of hard toil with little or no advance from a low base before they really began to share in any of the benefits of the economic transformation they had helped to create.*<sup>620</sup>

During the first fifty years of the nineteenth century, there were periods of famine at times in Britain and Ireland. The poor at this time lived on a diet of potatoes, bread and tea.<sup>621</sup> The average heights of adult males has been used as indirect evidence of nutrition and it fell between 1840 and 1860 gradually rising again by the end of the century to the levels of fifty years earlier.

Roderick Floud, writing of the period, states,

*There is little doubt that the second half of the nineteenth century, or more precisely the fifty-five years from 1860 to the outbreak of the First World War, saw significant improvements in the nutritional status of the British people and that these improvements were reflected in reductions of mortality and morbidity levels. The evidence of mean heights correlates so well with that of mortality that this inference is fully justified. Nevertheless, it would be inappropriate to overemphasise the scale of the change. Average male heights recovered from the very low levels which they had reached in the middle of the nineteenth century, but the recovery brought them by the First World War only to the levels which they had achieved*

<sup>617</sup> Chalmers A K, *The Health*, ibid, p88

<sup>618</sup> Chalmers A K, *The Health*, ibid, pp88-90

<sup>619</sup> The issues involved with falling family sizes are extensively discussed in Szreter S, *Fertility, Class and Gender in Britain, 1860-1940*, (Cambridge, 1996, Cambridge University Press)

<sup>620</sup> Feinstein C H, 'Pessimism Perpetuated: Real Wages and the Standard of Living in Britain during and after the Industrial Revolution', *The Journal of Economic History*, Sept 1998, vol. 58, no.3, 652

<sup>621</sup> Drummond J C, Wilbraham A, *The Englishman's Food*, (London, 1939, Jonathan Cape), p390

nearly a century earlier. This pattern, together with the different strands which go to make up nutritional status, suggests that it was only by the end of the nineteenth century that improvements in real wages, and in public health and other sanitary measures, compensated the British working class for the horrors of urban and industrial life which they had borne in the second quarter of the nineteenth century.<sup>622</sup>

Another factor which has to be considered is the cost to the environment occasioned by industrial activity and its effect on human health.<sup>623</sup> This was the time of rapidly expanding slum creation in the industrial towns and cities and overcrowding which continued well into the twentieth century in cities such as Glasgow.<sup>624</sup> Rural poverty associated with poor hygiene and overcrowding was also a feature of the times of early urbanisation associated with the beginnings of the Industrial Revolution.<sup>625</sup> It undoubtedly led to an acceleration of the emigration of country people into the towns and cities.

Martin Blaser, a contemporary American physician, who has written much about the history of peptic ulcer disease, states that, ‘the rise in peptic ulcer disease is related to improved nutrition of humans beginning in the nineteenth century due to the Industrial Revolution and the mass production of food.’<sup>626</sup> Dietary improvements were undoubtedly there for those who could afford them but food adulteration was commonplace, an example being the addition of non-food substances such as alum and chalk to bread. In 1851 Thomas Wakley, editor of *The Lancet*, began a campaign in its pages which lasted more than four years having been convinced of the evils of food adulteration by the chemist Frederick Accum who had been writing about food additives from 1820.<sup>627</sup> He set up the Analytical Sanitary Commission in the offices of *The Lancet* and provided laboratory facilities for the analysis of foodstuffs.<sup>628</sup> He ‘named and shamed’ shops in London in whose food produce his analysts had found all kinds of non-food substances and sometimes poisonous chemicals. His campaign for legislation to ban food adulteration was

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<sup>622</sup> Floud R, Wachter K, Gregory A, *Height, Health and History: Nutritional Status in the United Kingdom, 1750-1980*, (Cambridge, 1990, Cambridge University Press), p319

<sup>623</sup> Harris B H, *The Origins of the British Welfare State: Social welfare in England and Wales 1800-1945*, (Basingstoke, 2004, Palgrave MacMillan), pp28-39, esp37 quoting Hammond JL, ‘The industrial revolution and discontent’, *Economic History Review*, 1930, vol. 2, 215-228, esp pp220 and 225

<sup>624</sup> Chalmers A K, *The Health*, op cit, pp17-58

<sup>625</sup> Harris B H, *The Origins of the British Welfare State*, op cit, p29 also Hammond J L, ‘The industrial revolution and discontent’, op cit, 215-9

<sup>626</sup> Blaser M J, ‘*Helicobacters* are indigenous’, op cit, 721-7

<sup>627</sup> Drummond J C, Wilbraham A, *The Englishman’s Food*, op cit, pp341-5

<sup>628</sup> Dopson L. ‘*The Lancet’s* Analytical Sanitary Commission of 1851 and its effects’, *The Lancet*, Mar 10<sup>th</sup> 1951, 850-2

taken up by national newspapers and periodicals such as *Punch*.<sup>629</sup> <sup>630</sup> The food analyst Arthur Hassall added to the pressures, which led to the passing of the first Food and Drugs Act in 1860 but its regulations were largely ignored. In 1872, the Act was altered and strengthened and food adulteration diminished. Its demise also occurred because Victorian society was entering a period of mass production of food which put the corner shop bread and sweets adulterer out of business.

Then the food bought by the poor was generally not as contaminated as before. Milk remained a problem, being rarely fresh and often dirty and watered down. Pasteurisation was not generally used until the later 1930s.<sup>631</sup> Roller milling of bread flour began in Britain around 1880 and this process had the effect of removing much of its real nourishment. The poorer classes perceived brown bread to be less pure and resisted buying it. Canned vegetables and meat were available by this time and canned meat in particular became an important source of food for poorer people for a decade or more before frozen meat began to appear. Meat had been supplied mainly from local sources but by 1880 it began to be transported in refrigerated ships from the Argentine, Australia and New Zealand and was increasingly affordable. Refrigeration and the use of ice as a food preservative were not in use in Britain's homes, the frozen meat was taken to distribution points and defrosted there before reaching the butcher.

Before the arrival of frozen meat in Britain, salted foods such as sausages and salted herring were eaten. There is good experimental and epidemiological evidence that food high in salt is likely to be a contributing factor in the production of gastric ulcers.<sup>632</sup> In the context of British life, then peptic ulcer should have been predominantly a disease of the poor who would have been the main consumers of salted foods. It is this group who were the least likely to have had medical input with its attendant possibilities of hospitalisation and having autopsies performed on them after death. However it is noted that the 'servant girl class' patients whose deaths from perforated gastric ulcers were recorded by Crisp and others would have access to a better diet than poorer patients and would have been less

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<sup>629</sup> Drummond J C, Wilbraham A, *The Englishman's Food*, op cit, p347

<sup>630</sup> An examination of the Indexes to *The Lancet* which were published six-monthly at the end of each half year from 1851-55 give an indication of the extent of the problem of food adulteration and the volume of analytical work performed by the Analytical Sanitary Commission.

<sup>631</sup> The history of food contamination is to be found in Drummond and Wilbraham, *The Englishman's Food*, op cit, pp341-370

<sup>632</sup> Kato I, Abraham M Y N, Stemmermann G N, et al, 'A prospective study of gastric and duodenal ulcer and its relation to smoking, alcohol and diet', *American Journal of Epidemiology*, 1992, vol. 135, no.5, 521-30; Sonnenberg A. 'Dietary salt and gastric ulcer', *Gut*, Oct 1986, vol. 37, 1138-42 This proposition was also made in 1901 by James Braithwaite in 'Excess of salt in the diet, a probable factor in the causation of cancer', *The Lancet*, Dec 7<sup>th</sup> 1901, 1578-80

susceptible to the development of gastric ulcers, which suggests that the ‘salt hypothesis’ of gastric ulcer aetiology is unproven for all cases.<sup>633</sup>

Those in employment were enjoying improvements in living conditions as Britain’s towns and cities grew but dreadful slum areas persisted in their older parts, which were only removed in the nineteenth century when a railway company sought a new access through them or after Second World War bombing. Edwin Chadwick visited Glasgow and Edinburgh in 1840 and says, ‘The most wretched of the stationary population of which I have been able to obtain any account, or that which I have ever seen, was that which I saw in company with Dr Arnott and others in the wynds of Edinburgh and Glasgow’.<sup>634</sup> Friedrich Engels travelled around the country at the same time recording his experiences of the living conditions of the poor in the great cities of the UK and his descriptions of living conditions match those of Chadwick’s.<sup>635</sup> Professor Robert Cowan also described the conditions of the most wretched living in the slums of Glasgow in his paper published by *Journal of the Statistical Society of London* in 1840.<sup>636</sup> Seebohm Rowntree published his survey of the town of York in 1901 and showed that poverty and health were clearly related to income and living circumstances and that, even after all the improvements in sanitation over the preceding century, there were still people living in squalid and degrading circumstances.<sup>637</sup>

If the end result of a good balanced diet is a strong healthy population, then clearly this was not the case for the people of Britain born towards the end of the nineteenth century. During the Boer War, army recruitment issues surrounding the health of soldiers came to the fore, illustrating the poverty of the British people’s health when it was discovered that between 30% and 40% of the male population of army service age were unfit on account of ill-health.<sup>638</sup> This discovery was a major surprise to Britain’s leaders and ultimately played a part in the enactment of the National Insurance Act of 1911. After World War I, poverty and poor living conditions continued to affect the lives of the unskilled working classes. The researches published by John Boyd-Orr in 1937 stated, ‘According to the estimate

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<sup>633</sup> See ‘Gender issues’ in chapter 2 also Loudon I, ‘The diseases called chlorosis’, *Psychological Medicine*, Feb 1984, vol. 14, Issue 01, 27-36.

<sup>634</sup> Chadwick E, *The Sanitary Condition of the Labouring Population of Great Britain*, first published 1842, Flinn M, ed, (Edinburgh, 1965, Edinburgh University Press), pp97-9

<sup>635</sup> Engels F, *The Condition of the Working Class in England*, First published 1892, (St Albans, 1969, Granada Publishing), pp57-108

<sup>636</sup> Cowan R, ‘The vital statistics of Glasgow, illustrating the sanitary condition of the population’, *Journal of the Statistical Society of London*, Oct 1840, vol.3, no. 3, 257-92, esp p290

<sup>637</sup> Rowntree B S, *Poverty: A Study of Town Life*, (London, 1901, Macmillan), pp182-221, 299

<sup>638</sup> Soloway R, ‘Counting the degenerates: The statistics of race deterioration in Edwardian England’. *Journal of Contemporary History*, Jan 1982, vol. 17, no.1, 140-3

given here, the diet of nearly one-half of the population, though sufficient to satisfy hunger, is deficient for health.’<sup>639</sup>

In the light of the sociological factors mentioned above, little emerges to explain a change in the incidence of peptic ulcer from gastric ulcer to duodenal ulcer except the issue of high salt intake and its association with gastric ulcer formation which might explain why gastric ulcer could have been commoner in the nineteenth century than duodenal ulcer for a portion of the population. Such an observation does not constitute proof of cause for this proposition, for so little is known about the diets of the people of the time.

David Graham, an American gastroenterologist has attempted to explain the change from gastric ulcer to duodenal ulcer predominance at the turn of the nineteenth century by suggesting that its explanation is to be found in factors which promote ‘non-atrophic gastritis’.<sup>640</sup> He lists these as the use of refrigeration in the home to preserve food, the reduction of seasonality in the diet and the increased use of fresh fruit and vegetables.<sup>641</sup> Perhaps if this were true, the young women whose deaths were reported in the 1850s should have had duodenal ulcers and not gastric ulcers for their superior living conditions should, according to Graham, have promoted non-atrophic gastritis. ‘Non-atrophic gastritis’ is a specific modern pathological diagnosis based upon microscopic criteria. There is no empirical evidence to support his hypothesis that this condition became more prevalent in the later nineteenth century for no one has done the histo-pathological work on corpses of the period to prove the point in any kind of way which would satisfy an epidemiologist. Furthermore his hypothesis does not fit the time scale for Britain where home refrigeration was not in common use in Britain until the middle part of the 1950s.

## 5. 5: Autopsies

The dominance of perforation of gastric ulcer compared with duodenal ulcer as a cause of death found at autopsy and reported in the medical journals in the nineteenth century has been discussed earlier. In France in 1894, Henri Collin’s book about duodenal ulcer reported 262 autopsy findings of duodenal ulcers in European-sourced medical literature

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<sup>639</sup> Boyd Orr J, *Food Health and Income*, A Survey of Adequacy of Diet in Relation to Income, 2<sup>nd</sup> ed, (London, 1937, Macmillan and Co. Ltd), p8

<sup>640</sup> ‘Non-atrophic gastritis’ is a diagnostic term which applies to inflammation of the stomach usually caused by infection of the stomach by the bacterium *H. pylori* and is normally confined to the part of the stomach before the pylorus called the antrum. This condition is known to stimulate high levels of acid production and is considered to be of great importance in the formation of duodenal ulcers. More will be written about this in later parts of the thesis.

<sup>641</sup> Graham D Y, Correspondence: ‘Changing patterns of peptic ulcer, gastro-oesophageal reflux disease and *Helicobacter pylori*: a unifying hypothesis’, *European Journal of Gastroenterology and Hepatology*, 2009, vol. 15, 571-2

which were unknown to English speaking authors. Collin nevertheless accepted William Brinton's statistics of 37 years earlier that gastric ulcer was fifteen times more common than duodenal ulcer.<sup>642</sup> Friedrich Brünner's search of the world literature quoted by Lennings reported 361 cases of deaths from perforated 'peptic ulcer' covering the period from 1890-1903 but he did not separate gastric from duodenal ulcers.<sup>643</sup> The problem of such statistics is that they do not give any indication of their incidence since there is no population denominator provided.

When trying to assess disease prevalence based upon autopsy reports it is accepted that they are only likely to represent a tiny fraction of deaths from these conditions over any period, especially the nineteenth century, since most patients died at home and did not undergo autopsy. Autopsies are not a good sample base for an epidemiologist. With reference to this, the epidemiologists Mausner and Kramer state:

*... autopsy results can be misleading for epidemiological purposes, because autopsies are done on a non-random sample of all deaths. Failure to obtain permission for some autopsies because of religious or other reasons adds yet another selective process to those already involved in gaining admission to a hospital. These selective processes make autopsy series quite unrepresentative of all deaths.*<sup>644</sup>

## 5. 6: The clinical presentations of gastric and duodenal ulcers

The clinical histories of patients with gastric and duodenal ulcers in the nineteenth century tended to differ in respect of the longevity of symptoms of each type of ulcer prior to hospital intervention. Both types of ulcers could be completely asymptomatic prior to complications, such as perforation or haematemesis. Symptomatic duodenal ulcer sufferers could get relief from ingested alkalis and unlike gastric ulcer sufferers could eat well and maintain their weight. Peptic ulcer disease is characterised by periodicity with often long periods of remission but sudden fatal complications were often the first intimation that the patient had an ulcer. Marmaduke Shield describes a case of perforation which he regarded as typical.

*A healthy and muscular (Scots) Guardsman aged thirty-eight years who was a bandsman and well able to perform his duties, played a game of racquets one*

<sup>642</sup> Collin H, *Étude sur L'Ulcère Simple du Duodenum*, (Steinheil G, 1894, Paris), p36

<sup>643</sup> Jennings D, 'Perforated peptic ulcer', op cit, 395-8

<sup>644</sup> Mausner J S, Kramer S, *Epidemiology - an Introductory Text*, Second Edition, (Philadelphia, 1951, B. Saunders Company), p73

*afternoon and afterwards proceeded to a music hall where he usually performed. He was suddenly seized with violent abdominal pain. The abdomen became tympanitic, but there was no urgent vomiting. He was conveyed back to bed, collapse supervened, and he died in about eighteen hours. At the necropsy an ulcer large enough to admit a crowquill was found about the centre of the duodenum ... This was not the least suspected during life, but it is stated that the man had been known to complain of epigastric pain and to press his hand there after laughing loudly.*

*... Writers on general medicine who refer to ulcer of the duodenum treat of the subject in general terms. The affection is classed with gastric ulcer, which in all respects it closely simulates and little or no attempt is made to distinguish between the pathology or symptoms of these two kinds of cases. There is a general opinion that gastric ulcer is rare in men and therefore when duodenal perforation occurs in the male sex the symptoms are peculiarly liable to be overlooked or entirely misunderstood, since they are identical with those of perforation of the stomach, which is so exceptional in the male sex.<sup>645</sup>*

It is of particular note that this man, a soldier who lived in a supervised environment with access to medical care, was not considered for surgery in 1895.

Gastric ulcer might suddenly perforate too, but their presenting symptoms usually were more insidious and associated with the signs of chronic ill-health and requiring hospital admission. Patients suffered weight loss, chronic abdominal pain, vomiting and pain after food and recurring haematemesis and melaena. As with duodenal ulcer, gastric ulcer symptoms could get better with or without medical care. The clinical differences described above between histories of the two ulcer types may account for the relative predominance of gastric ulcer in hospital admissions which led to death. Haematemesis was occasionally treated in hospital but was rarely a reason for admission and, if the patient died, then death would be assumed to have been due to a gastric ulcer. Nineteenth-century articles on the management of chronic ulcer of the stomach, such as that of Saundby's, suggest that haematemesis was an important diagnostic feature of gastric ulcer disease.<sup>646</sup>

Patients with duodenal ulcers could apparently manage their symptoms better than patients with gastric ulcers and remained more healthy and active. However patients with gastric

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<sup>645</sup> Shield M, 'Two cases of ulcer of the duodenum in which laparotomy was performed, with remarks on ulcers of the duodenum', *The Lancet*, May 11<sup>th</sup> 1895, 1169-74

<sup>646</sup> Saundby R, 'Clinical lecture on chronic ulcer of the stomach,' *The Lancet*, Feb 14<sup>th</sup>, 1891, 353-5

ulcers suffered pain after food and so tended to avoid eating and lost weight. Their health suffered and in severe cases patients took on the appearance of a cancer with wasting and debility. These patients more often found their way into voluntary hospitals and when they died, gastric ulcers were usually found at autopsy. In the absence of any kind of social security system, a man with a peptic ulcer might struggle on to support his family. When perforation occurred, a patient's clinical condition would have been recognised as hopeless by any doctor who would not consider admission to hospital. Dr Shields' example quoted above illustrates this perfectly. Doctors knew that surgery would not be attempted and that his duty was to keep the patient comfortable until death intervened. Poor people may not even have consulted regular practitioners perhaps until it was too late, if at all, as happens still in the developing world. Another issue was transport of the patient before recognised ambulance services were available, for the roads were in poor condition and cobbled streets would make any journey to a hospital for a patient with peritonitis an agonising experience, with little hope of recovery. Doctors in the nineteenth century could accurately diagnose what is now called 'peritonitis'; what they could not diagnose accurately were the many underlying causes of it, but the assumption was made that it was due to perforated gastric ulcer. Duodenal ulcer sufferers may have been less likely to have been admitted to hospital in their final illness for the reasons stated and as a result may not appear in the hospital autopsy accounts.

Another explanation for the low recorded death rates from duodenal ulcer is that it was simply being misdiagnosed. In 1882, William Osler's medical textbook stated: 'the symptoms (of duodenal ulcer) are in a great majority of cases identical with those of gastric ulcer and it is then impossible to distinguish between the two lesions.'<sup>647</sup> Although the mortality rates for surgical interventions for duodenal and gastric ulcer perforations remained high in the first two decades of the twentieth century following initial surgical successes, I suggest that the new hope that surgery might offer the chance of survival led to increasing numbers of admissions.<sup>648</sup> By 1920, major changes had occurred in British life and motorised ambulances had come into use and roads had considerably improved, so that patients could be transported with considerably more ease and over longer distances than in the previous century.<sup>649</sup> The 1911 National Insurance Act meant for the first time that a

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<sup>647</sup> Osler W, *The Principles and Practice of Medicine*, (Edinburgh and London, 1892, Young J Pentland), p374

<sup>648</sup> Graves A M, 'Perforated peptic ulcer in German clinics', *Annals of Surgery*, Aug 1933, vol. 98, no. 2, 197-09

<sup>649</sup> Pollock A C, 'Ambulance services in London and Great Britain from 1860 until today: a glimpse of history gleaned mainly from the pages of contemporary journals', *Emergency Medical Journal*, Mar 2013, vol. 30, issue 3, 218-22

working man would receive financial support for himself and his family so there was an incentive for him to seek medical aid. As a consequence, increasing numbers of patients appeared for medical and hospital care which would swell the statistics.

The surgeons Berkeley Moynihan in England and the Mayo brothers, Charles and William, in the USA, were in no doubt that duodenal ulcer always had been the dominant form of the illness and that there had been no rise in its incidence. Moynihan challenged the pathological evidence seen in the autopsy room as representing prevalence of ulcers, generally arguing that surgical operations offered a better source of medical knowledge because a surgeon could accurately observe the effects of pathology in the living body. These surgeons believed that autopsy results did not represent what had been happening in living patients and that the pathologists got much wrong in their concepts and conclusions.<sup>650</sup> As already stated in chapter one, historian Ian Miller in his PhD thesis and in his monograph, *A Modern History of the Stomach*, also questioned whether or not duodenal ulcer was a new disease or had always been prevalent.<sup>651 652</sup> He recorded the opinions of Berkeley Moynihan and his contemporary like-minded surgeons as evidence to refute those who were of the opinion that it was a new disease, and quotes extensively from his writings to support the assertion that it was not a new disease.

Francis Caird and his colleagues commented in 1913, ‘The difficulty in distinguishing the exact relation of a perforation to the pylorus on the operating table is well known, and it seems possible that cases of duodenal ulcer may have been classed as gastric ulcer.’ They also state, ‘We have no reason to suppose that the incidence of duodenal ulcer and its perforation have increased in recent years, and it must be admitted that in all probability some cases passed unrecognised.’ They further commented that the existence of the condition was only beginning to be recognised.<sup>653</sup> David Wilkie working in the same hospital a year later found 41 duodenal ulcers at necropsy out of 490 done in a three year period, only six of which had been diagnosed before death.<sup>654</sup> William Mayo increasingly

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<sup>650</sup> Moynihan B G A, ‘An address on the pathology of the living’, *British Medical Journal*, Nov 16<sup>th</sup> 1907, 1381-5

<sup>651</sup> Miller I R, *A Modern History of the Stomach: Gastric Illness, Medicine and British Society c. 1800-1950*, A thesis submitted to the University of Manchester for the degree of PhD in the Faculty of Life Sciences, 2009, pp143-150

<sup>652</sup> Miller I, *A Modern History of the Stomach: Gastric illness, Medicine and British Society, 1800-1950*, (London, 2011, Pickering & Chatto)

<sup>653</sup> Caird F M, Cotterill J M, Cathcart C W, et al, ‘Perforated Duodenal Ulcer’, *Edinburgh Medical Journal*, Nov 1913, vol. 11, 405-18

<sup>654</sup> Wilkie D P D, ‘Observations on the pathology and aetiology of duodenal ulcer,’ *Edinburgh Medical Journal*, 1914, vol. 13, 196-208

found duodenal ulcers after 1904, before which date he had found gastric ulcers more commonly at operation.<sup>655</sup>

With experience, general practitioners were beginning to diagnose the condition at an earlier stage and patients who were operated upon earlier had better survival chances. Francis Caird's comments confirm this and are reinforced by his statistics. Appendicitis was a frequently made diagnosis in cases of perforated duodenal ulcer. As already stated, in Moynihan's paper of 1901, 36% of the perforations operated upon were initially diagnosed as appendicitis.<sup>656</sup> Another frequent wrong diagnosis was made in the case of pyloric stenosis mistaken for cancer.<sup>657</sup> William Mayo was dismissive of William Brinton's book as a statistical source describing it as 'not necessarily representing the facts but their interpretation in the light of the time when the statistics were compiled.'<sup>658 659</sup> Moynihan concurs with Mayo's views stating, 'Ten years ago, ulceration of the duodenum was looked upon as a rare disease and its confident recognition during life was believed to be hardly possible. Today we know that the disease is common and its discovery in the majority of cases presents no great difficulty to the trained clinician.'<sup>660</sup> In a paper published later, he describes gastric ulcer as, 'a disease of comparative rarity; its diagnosis from the clinical evidence alone is difficult; its mimicry by other conditions extremely frequent'.<sup>661</sup>

Despite Mayo and Moynihan's opinions, in 1948, Donaldson Craig wrote, 'It is generally believed that the apparent rarity of duodenal ulcer until the present century was the consequence of failure to recognise the condition. Undoubtedly many cases were missed but when the situation is viewed against the broader background of earlier writings it is difficult to escape the conclusion that improvement in diagnosis was concomitant with an increased frequency of the disease.'<sup>662</sup>

The value of scrutiny of clinical work is seen in Malcolm Rawson's 1965 paper which shows just how inaccurate doctors were in making correct clinical diagnoses in peptic ulcer

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<sup>655</sup> Mayo W J, 'Chronic duodenal ulcer', *Journal of the American Medical Association*, June 19<sup>th</sup> 1915, vol. 64, 2036-40

<sup>656</sup> Moynihan B G A, 'On Duodenal ulcer and its surgical treatment', *The Lancet*, Dec 14<sup>th</sup> 1901, 1656-63

<sup>657</sup> Mayo W J, 'Chronic duodenal ulcer'. op cit, 2037-8

<sup>658</sup> Brinton W, *Lectures on the Diseases of the Stomach*, (Philadelphia, 1865, Lea and Blanchard)

<sup>659</sup> Mayo W J, 'Chronic duodenal ulcer', op cit, p2036

<sup>660</sup> Moynihan B G A, *Duodenal Ulcer*, (Philadelphia & London, 1910, W.B. Saunders Company), p11

<sup>661</sup> Moynihan B G A, 'The diagnosis and treatment of chronic gastric ulcer', *British Medical Journal*, Dec 13<sup>th</sup> 1919, 265

<sup>662</sup> Craig J D, 'The evolution of gastric and duodenal ulceration', *British Medical Journal*, Aug 14<sup>th</sup> 1948, 330-4

cases.<sup>663</sup> It should be noted that this research was conducted in Leeds General Infirmary, a hospital with a high reputation for its specialist interest in diseases of the alimentary tract, having earlier been the surgical domain of Berkeley Moynihan. Rawson's retrospective study looked at the records of 200 patients after they had had partial gastrectomies for defined clinical conditions deemed to be amenable to surgical amelioration. These operations allowed a direct visual inspection of the stomach and duodenum of the patients to confirm the correct diagnosis. Rawson examined the details of patient records to assess their pre-operative 'working diagnosis' which was the basis of the decision to perform the partial gastrectomy. His study divided the medical professionals who had been involved with these 200 patients into general practitioners, hospital doctors and radiologists. The resultant examination of data showed that hospital doctors had made correct diagnoses pre-operatively in 10% of cases of gastric ulcers where there had been no history of previous perforation or barium meal done, general practitioners fared a little better at 22% in the same group and radiologists were correct in 92% of cases, using barium meal examinations. The diagnosis of duodenal ulcers seems to have been easier with general practitioners and hospital specialists each making the diagnosis in the absence of previous history in 36% of cases. Carcinoma of the stomach diagnosed clinically 'without previous history pointing to a diagnosis' was also equally correctly diagnosed by the two groups in just over a third of cases. The diagnostic rates for each group were more successful where there was more information available to them. With reference to gastric carcinoma cases, another different study published in the same year showed that, when a gastric ulcer had been demonstrated in a barium meal procedure, it was not possible for the radiologist to state whether or not it was malignant in 10% of cases.<sup>664</sup>

## 5. 7: Death rates in England and Wales from gastric ulcer and duodenal ulcer from 1911 until 1969

In order to examine the 'rise' in death rates from gastric and duodenal ulcer which appeared to occur in the twentieth century, the graph in Figure 2 was constructed from the published data from the Registrar General for Births, Marriages and Deaths in England and Wales annual returns of death rates from 1911 until 1969. The data represents crude death rates (deaths per million of population) for each diagnosis over the period. As can be seen

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<sup>663</sup> Rawson M D, 'Accuracy in diagnosis of gastric and duodenal lesions by general practitioners, hospital clinicians and radiologists', *The Lancet*, Mar 27<sup>th</sup> 1965, 698-9

<sup>664</sup> Leading articles, 'Gastric ulcer or gastric cancer?', *The Lancet*, Dec 18<sup>th</sup> 1965, 1282-3

in the graph, certified death rates for gastric ulcer rose from 1911 and peaked in 1941 to fall thereafter. Death rates from duodenal ulcer rose from 1911 until 1955 after which year death rates for both forms of peptic ulcer fell at the same rate.

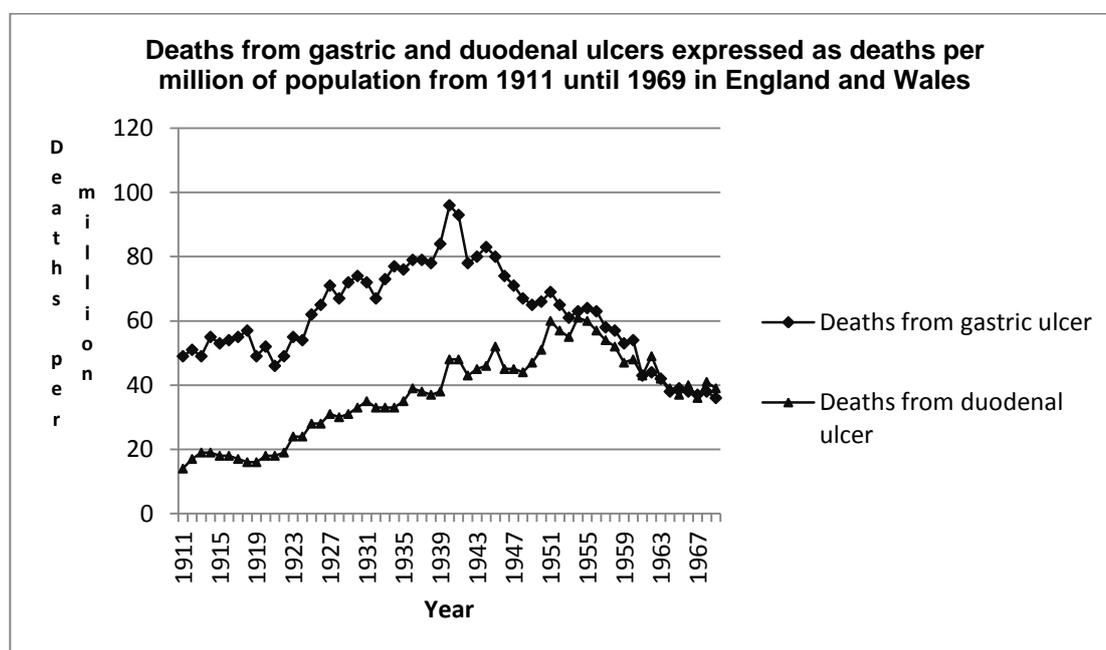


Figure 2

Crude death rates per million of population. Data extracted from the causes of death statistics of the Registrar General of Births, Marriages and Deaths in England and Wales from gastric ulcer and duodenal ulcer for the period 1911-1969

Although gastric ulcer was certified as the more frequent cause of death from peptic ulcer disease from 1911 until 1961, nevertheless duodenal ulcer had become the commonest surgical manifestation of peptic ulcer disease within the live population by the mid 1920s. The fact that duodenal ulcer was not the commonest certified cause of death from peptic disorders suggests that many of those suffering from its complications were being treated successfully. It will be seen later in the chapter that there was no similar rise in peptic ulcer rates in the first half of the twentieth century in France or in Japan. Japan however did experience a brief rise during WWII before reassuming the same rates as before.

## 5. 8: Diagnostic preference by doctors when certifying cause of death

After a disease has been included in a new nosology, it can take many years for doctors to use it in preference to a previously used diagnosis. The inherent difficulties in making a precise diagnosis within the dyspeptic spectrum of symptoms and presentations have been discussed in detail earlier in the thesis and this was recognised by the Registrar of Births Marriages and Deaths in England and Wales when he included the diagnosis of 'other

diseases of stomach (not malignant)’ as early as 1901. The numbers certified as dying from this category of disease, when added to those dying of ‘gastric catarrh’, were four times greater than those certified as dying from gastric ulcer which made its first appearance in these statistics that year. From 1901 until 1970, it can be seen from an examination of the tables of causes of death in England and Wales that by 1924, more people were being certified as dying from ‘gastric ulcer’ than from ‘other diseases of the stomach’. This trend continued in the following years and by 1970, deaths from ‘gastric ulcer’ were four times more commonly certified than for ‘peptic ulcer, site unspecified’.

Changes in practices of death certification can also occur as a result of doctors’ acceptance of new research advances. Surgeons such as Moynihan, the Mayo brothers and others who published their findings about the dominance of duodenal ulcer found at operation may have had this effect in the UK.<sup>665 666</sup> In the British causes of death tables the diagnosis of ‘duodenal ulcer’ may have been written on death certificates where once perhaps doctors wrote ‘gastric ulcer’ or a diagnosis which would be listed under ‘other diseases of the stomach’ such as ‘inflammation of the stomach’. In France, clinicians put ‘gastric ulcer’ on death certificates for the majority of deaths from presumed peptic ulcer from the time in 1925 when statistics in France began to be centrally collated until 2000.<sup>667</sup> In England and Wales, ‘gastric ulcer’ was the most frequent peptic ulcer diagnosis from 1911 until 1961 after which time death rates from gastric ulcer approximately equalled those from duodenal ulcer and this continued until 1969.<sup>668</sup> After 1948, Scottish Doctors favoured the diagnosis of ‘duodenal ulcer’ over ‘gastric ulcer’ although both remained relatively common as registered causes of death from peptic ulcer. From 1968 the Scottish Registrar General causes of death include ‘peptic ulcer site unspecified’ but the numbers recorded are a quarter of those diagnosed with duodenal ulcer and a third of those diagnosed with gastric ulcer.

## 5. 9: Peptic ulcer disease outside Britain

When looking at the history of a disease, it may often be helpful if we look elsewhere to other experiences of that illness. Africa, because of its remoteness and relative lack of Western lifestyle influences at the level of local rural living, may be thought of as a place where peptic ulcer could not have been modified to any great extent until relatively

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<sup>665</sup> Mayo W H, ‘Chronic duodenal ulcer,’ op cit, 2036-8

<sup>666</sup> Moynihan B G A, *Duodenal Ulcer*, op cit, p11

<sup>667</sup> See Fig 3

<sup>668</sup> See Fig 4

recently. It appears that peptic ulcer in Africa as described in the medical literature before 1992 was a relatively rare disease, especially gastric ulcer.<sup>669</sup>

The belief that peptic ulcer was rare in Africa was given the title, ‘the African Enigma’, but in recent years, this ‘enigma’ has been questioned and it has been demonstrated that Africans do suffer from peptic ulcer disease, as do Indians and Bangladeshis who were also thought to not suffer from it to any extent.<sup>670</sup> For all the same reasons that caused men in the UK not to seek help in the nineteenth century, discussed earlier in this chapter, the presence of ulcer sufferers in Africa and Asia may have been hidden from early statisticians. ‘Enigmas’ were postulated for India and Asia which have also been discarded.<sup>671</sup> Almost everywhere in the world, dyspepsia is suffered by people and peptic ulcer is common to a variable extent and the lesion most commonly found is duodenal ulcer. A predominance of gastric ulcer in young women was not found in developing countries as reported in England in the nineteenth century. Duodenal ulcer appears to be the commonest manifestation of peptic ulcer disease worldwide although exceptions are to be found, the best known of which being Japan.

Two non-English sources about peptic ulcer deaths gathered over long periods of time are now examined. Lothar Kusko’s study is based upon more than 100,000 autopsies performed in Vienna from 1850-1954.<sup>672</sup> The only constant factor in the numbers is that they were all obtained in the one place and no denominator of population statistics is given. The graphs of the autopsies show that death rates from ulcers of stomach and duodenum taken together remained steady in the first 50 years at around 1% of all autopsies. From 1906 the rate steadily increased for both types of ulcer to 4% in 1935 after which it rose to 8% at the height of World War II before declining in 1954 to 7%. There was little difference between gastric ulcer and duodenal ulcer in rates of rise. The graphs of deaths from both duodenal and gastric ulcers in the Kusko paper shows remarkable similarity to the graphs of peptic ulcer deaths for England and Wales as seen in Figure 2 of this thesis which also suggest that there was a rise in deaths from both types of ulcer over the period. For the first fifty-five years of the Viennese study from 1850, few duodenal ulcers were

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<sup>669</sup> Holcombe C, ‘*Helicobacter pylori*: the African enigma’, *Gut*, Apr 1992, vol. 33, 429-31

<sup>670</sup> Graham D Y, Lu H, Yamaoka Y, ‘African, Asian or Indian enigma, the East-Asian *Helicobacter pylori*: facts or medical myths’, *Journal of Infectious Diseases*, 2009, vol. 10, 77-84 ; Agha A, Graham D Y, ‘Evidence-based examination of the African enigma in relation to *Helicobacter pylori* infection’, *Scandinavian Journal of Gastroenterology*, 2005, vol. 40, 523-9

<sup>671</sup> The ‘Asian enigma’ has a slightly different meaning today tending to refer to the relationship with atrophic gastritis and cancer in those parts of the world.

<sup>672</sup> Kusko I, ‘Das Verhalten der Ulcuskrankheit auf Grund der Sektionsprotokolle des Wiener Pathologisch-Anatomischen Institutes in den 100 Jahren’, *Schweiz. Z. Path. Bakt.*, 1958, vol. 21, 433-7

found at autopsy. However between 1905 and 1935, gastric ulcers were discovered between two and three times more often compared with duodenal ulcers. Thereafter both types of ulcers were found in approximately equal numbers until 1954. It should always be borne in mind that the Viennese data were derived from autopsy material and for all the reasons stated elsewhere in this thesis, autopsy results only represent what is happening in a select hospital population which has given assent to a post mortem examination being performed.

The second non-English source was a Japanese paper which covered peptic ulcer deaths over a 62 year period from 1909 until 1971 and approached its subject in two ways.<sup>673</sup> Its first graph for the period was based upon medical certification. Over this time approximately 10% of deaths in Japan were certified as being due to peptic ulcer. Death rates rose during and shortly after the Second World War but with this exception the death rate varied little over the period. The main part of the study looked at autopsy results and on the basis of these, when gastric and duodenal ulcers were compared, the dominant ulcer by a factor of approximately five was the gastric ulcer and death rates did not change dramatically for either over the period. In particular there was no rise in deaths from peptic ulcer from 1911 until 1955.

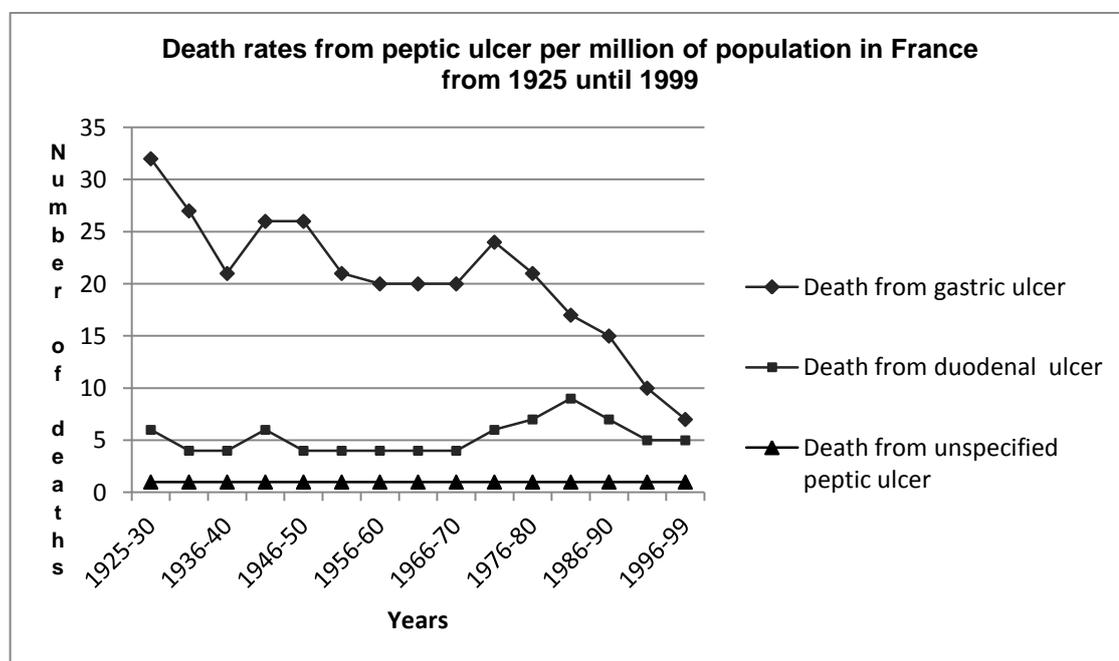


Figure 3

Crude death rates from peptic ulcer disease per million of population from official French government statistics, 1925-2000

<sup>673</sup> Gonoï T, Ueki Y, 'Historical changes in peptic ulcer', *Stomach and Intestine*, 1980, vol. 15, no. 1, 27-33

Figure 3 shows that in France, recorded deaths from peptic ulcer did not show any rises for gastric and duodenal ulcers over the period 1925-1955.<sup>674</sup> This is in contrast to the recorded rises in deaths from peptic ulcer in England and Wales over the same period which can be seen in figure 2 on page 153.

The Japanese data and the French graph are included in this discussion to illustrate that there was no steep rise in the prevalence and incidence of peptic ulcer in Japan and France from 1920 until 1955 as there appears to have been in one Vienna hospital and in the UK population as a whole.

## 5. 10: *Helicobacter pylori*

The hypothesis that *Helicobacter pylori* is the major implicating cause of peptic ulcer could possibly explain the history of peptic ulcer but this has not happened to date. *H. pylori* is an almost ubiquitous human pathogen of the stomach of humans which has affected mankind for millennia.<sup>675</sup> Hugh Baron writes,

*The occurrence of peptic ulcer showed a rapid increase in all Western countries from the turn of the 19<sup>th</sup> and 20<sup>th</sup> century. Because almost all patients with gastric and duodenal ulcer not caused by non-steroidal anti-inflammatory drugs are infected with Helicobacter pylori, it has been widely assumed that these time trends in peptic ulcer rates were due to an epidemic of H. pylori, a new pathogenic strain or a change in host susceptibility.*<sup>676</sup>

*H. pylori* is almost always acquired in very early childhood and if not eradicated, is carried in the stomach lifelong. It seems to be pathogenic to approximately 10% of those affected and may be carried asymptotically by the remainder. One study appears to show that there is a gender preference for infecting males.<sup>677</sup> *H. pylori* causes two different but specific pathologies in the stomach which predispose to the formation of peptic ulcer: for duodenal ulcer it is called 'non-atrophic gastritis' (or 'antral gastritis') and for gastric ulcer it is called 'atrophic gastritis'. Attempts were made to relate age at acquisition of *H. pylori* to the form of gastritis arguing that later infection led to the antral form of the gastritis and

<sup>674</sup> The data collected for this graph was obtained from the web site address, accessed 05.08.13:

[http://www.ined.fr/en/resources\\_documentation/detailed\\_data/death\\_causes\\_since\\_1925/the\\_menu/bd/d/tri/liste/](http://www.ined.fr/en/resources_documentation/detailed_data/death_causes_since_1925/the_menu/bd/d/tri/liste/)

<sup>675</sup> Linz B, Balloux F, Moodley Y, et al, 'An African origin for the intimate association between humans and *Helicobacter pylori*', *Nature*, Feb 22<sup>nd</sup> 2007, vol. 445, 915-8

<sup>676</sup> Baron J H, 'Hospital admissions for peptic ulcer and indigestion in London and New York in the 19<sup>th</sup> and early 20<sup>th</sup> centuries', *Gut*, Apr 2002, vol. 50, 568-70

<sup>677</sup> Replogie M L, Glaser S I, Hyatt R A, et al, 'Biological sex as a risk factor for *Helicobacter pylori* infection in healthy young adults', *American Journal of Epidemiology*, 1995, vol. 142, 856-63

thereby to the formation of duodenal ulcers but this hypothesis has been abandoned in the light of the knowledge that where early childhood infection occurs, it is associated with duodenal ulcers, as in Bangladesh.<sup>678</sup> David Graham confirms this, ‘Unfortunately the age of acquisition hypothesis has not withstood critical analysis; exceptions abound. ... It is now recognised that *H. pylori* is typically a childhood acquired infection ...’<sup>679</sup>

*H. pylori* is found in the stomachs of people all over the globe but to varying extents in terms of population percentages. The developed world generally has a lower prevalence of *H. pylori* within the stomachs of its populations than those in developing countries.<sup>680 681</sup> It has not been possible to explain the history of peptic ulcer in England and Wales on the basis of what is known about *H. pylori*. The suggestion that antral gastritis was a new phenomenon which swept through England to cause the ‘new’ disease of duodenal ulcer lacks the empirical evidence to substantiate it. It has also been suggested that a change in virulence of *H. pylori* is an explanation but again this does not fit for *H. pylori* of any virulence appears to be able to cause ulcers.<sup>682</sup> Throughout the world, there are considerable variations in the epidemiology of peptic ulcer which may be due to many causes.

## Conclusion to chapter five

In this chapter, the current view of one aspect of the history of peptic ulcer disease is challenged which states that peptic ulcer disease was rare in the eighteenth century and became relatively common in the nineteenth. The assertion is also challenged that gastric ulcer was the commonest manifestation of peptic ulcer disease in the nineteenth century, and that the situation changed for an unknown reason, so that duodenal ulcer became its commonest manifestation, in the following century. Some of the data which appears to support these assertions are examined and found to be derived from historically unreliable sources such as autopsy results, medical certification of death statistics, questionable hospital statistics and a technique of relating numbers of medical publications to disease prevalence. The view that there was an epidemic of peptic ulcers from the middle of the nineteenth century, as has been stated by contemporary authors, is also contested by

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<sup>678</sup> Blaser M J, ‘*Helicobacters* are indigenous’, op cit, 721-7

<sup>679</sup> Graham D Y, ‘*Helicobacter pylori* infection in the pathogenesis of duodenal ulcer and gastric cancer: a model’, *Gastroenterology*, 1991, vol.113, no 6, 1983-9

<sup>680</sup> Frenck Jr R W, Clemens J, ‘*Helicobacter* in the developing world’, *Microbes and Infection*, 2003, vol. 5, 705-13

<sup>681</sup> Parsonnet J, ‘The size of the problem’, *Gut*, Jul 1998, vol. 43, supp. 1, 6-9

<sup>682</sup> Graham D Y, Correspondence: ‘Changing patterns of peptic ulcer, gastro-oesophageal reflux disease and *Helicobacter pylori*: a unifying hypothesis’, *European Journal of Gastroenterology and Hepatology*, 2009, vol. 15, 571-2

tracing and challenging their supporting arguments. In this chapter and in other places in the thesis, it has been demonstrated that clinical certification of death in many cases of peptic ulcer disease was unreliable. It is also shown how peptic ulcer disease in Africa and other developing countries is now dominated by duodenal ulcer disease although some exceptions are noted in Japan and France. Finally, it is asserted that the most recent developments of the understanding of peptic ulcer disease, that of the discovery of *Helicobacter pylori*, take us no nearer to explaining the received view of the history.

The next chapter will begin with conditions in Britain after World War II showing how health care delivery changed dramatically after the inception of the NHS in 1948. It will show how patients sought relief for the symptoms of peptic ulcer disease, taking medications prescribed by doctors or obtaining them within the community without medical advice. It will be seen that a more analytical approach to the provision of healthcare grew in a period when new drugs for the treatment of peptic ulcers were examined by the newly invented clinical trial approach. Older regimens were also subjected to clinical trials and found to be of less worth than had hitherto been believed. Novel physical treatments will be discussed which were largely rejected after trials showed them to be deficient or dangerous. In the second half of the twentieth century a gradual change in the nature of the disease itself occurred at a time when specialist gastroenterologists were being introduced in the NHS to treat all gastroenterological diseases. Gastric and duodenal ulcer disease will be seen to have become a major health issue for the NHS

## Chapter 6. Medical approaches to the treatment of peptic ulcer from 1945 until 1976

### Introduction to chapter six

This chapter covers the period from 1945 until 1976 and briefly examines health services in Britain before and after the inception of the NHS. It discusses issues surrounding illness behaviour patterns regarding patients' decisions to seek medical help or to self-medicate, without medical input, often using community pharmacists as advisers. The medical treatments available to general practitioners and hospital doctors are also discussed, as are the results of trials of several new pharmaceutical substances and three physical treatments which were used, two of which were surgical. Over the period, it will be seen that major changes were occurring in the nature and severity of gastric and duodenal ulcer diseases, which were not noticed initially by doctors. In the early 1970s, the specialty of gastroenterology began to expand to meet a clinical need in the investigation of all gastrointestinal disorders and this is discussed.

### 6. 1: Life in Britain after World War II

The National Health Service (NHS) came into being in 1948 under the then Labour Government as a response to the perceived health needs of the British people only three years after the end of the Second World War. Large parts of cities had been bombed and still lay in ruins and slum dwellings still remained in the same places which Chadwick and Engels had written about a hundred years before, although, by comparison with the nineteenth century, living conditions there were much better.<sup>683</sup> From 1851 local authorities had used Parliamentary legislation to gradually reduce overcrowding and have unsafe housing removed.<sup>684</sup> They also provided community health services and care for those suffering from tuberculosis and insanity, and many old Poor Law buildings now served as hospitals, having been improved by them over the decades from the end of the nineteenth century. The temporary hospitals which had been built for wartime casualties were substantial enough to last for many years. Whilst poverty existed, no one died of starvation or severe neglect because of lack of provision: those suffering serious accidents and those suffering serious illnesses were accommodated in hospitals at their time of need.

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<sup>683</sup> Chadwick E, *The Sanitary Condition of the Labouring Population of Great Britain*, first published 1842, M Flinn, ed, (Edinburgh, 1965, Edinburgh University Press), and Engels F, *The Condition of the Working Class in England*, First published in 1892, (St Albans, 1969, Granada Publishing)

<sup>684</sup> Chalmers A K, *The Health of Glasgow 1818-1920*, (Glasgow, 1930, Bell & Bain), pp17-30

Aneurin Bevan was the Labour minister responsible for the steering of the National Health Service Bill through the House of Commons. His speech at the second reading of the bill to establish the NHS gives a flavour of the state of health provisions in Britain 1946 as he pointed to the major deficiencies of health care prevailing at the time. The then current National Health Insurance system provided a general practitioner service and catered for 21 million of the population, but the rest had to pay for the services of a doctor. The doctor had to use his own discretion and his own personal connections, to obtain hospital treatment for his patients and the services of a specialist were not available to poor people as a right. Hospital organisation had expanded with no plan, being unevenly distributed over the country, with very often the best hospital facilities available where they were least needed. Many were too small with 70 per cent having less than 100 beds, and over 30 per cent less than 30, which is too small to provide general hospital treatment. Bevan concluded his speech in Parliament:

*It is intended that there shall be no limitation on the kind of assistance given—the general practitioner service, the specialist, the hospitals, eye treatment, spectacles, dental treatment, hearing facilities, all these are to be made available free.*<sup>685</sup>

Employment was high nationally and in a city like Glasgow, the old industries such as heavy engineering and shipbuilding prospered as the nation tried to restore its fortunes by exporting manufactured goods. In Britain coal was the main source of power generation.<sup>686</sup> Politicians and people alike faced many challenges to transform Britain into a modern state where people would be well fed and enjoy good health. New housing was another priority but the war had severely depleted the British treasury and financial restraint was required. Rationing ended finally in 1954 after a period of two and a half years of gradual relaxation of its restricted range of foods.<sup>687</sup>

Despite wartime austerity, the British population in 1946 was in better health than at any time in the previous century and, because of rationing, had enjoyed a better balanced diet than was previously possible for the majority of its people. Chronic disease still blighted homes and tuberculosis was still prevalent although syphilis could at last be cured with penicillin. Fever Hospitals were still required for the containment of infectious diseases, but this was a lessening problem. In 1945, 71% of the nation's schoolchildren were

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<sup>685</sup> Abridged from, Bevan A, 'National Health Service Bill', House of Commons Debate, *Hansard*, April 30<sup>th</sup> 1946 vol. 422, 43-47

<sup>686</sup> Aneurin Bevan said in a speech in Blackpool in 1945, 'This island is made mainly of coal and surrounded by fish.'

<sup>687</sup> Rationing of food items which began at the outbreak of hostilities finally ended on July 4<sup>th</sup> 1954.

receiving free school milk.<sup>688</sup> Guided by the researches of John Boyd-Orr in the 1930s, the wartime efforts of Minister for Food, Lord Woolton, ensured that all children received a diet which was adequate in terms of nutritional requirements.<sup>689</sup>

The Second World War brought about massive changes in the life of the nation in terms of recognition of its health need provisions. This had happened after the First World War, there was a further erosion of laissez-faire political attitudes and Parliament enacted legislation, largely using local authorities as their agents to look at the problems of health care provision of its population.<sup>690</sup> During the War, the hospitals had come under the control of the Emergency Medical Service of the Ministry of Health and it became evident that most hospitals could not cope financially without state financial backing, so the stage was set for their absorption into the National Health Service.<sup>691 692</sup> Other agencies such as blood transfusion services and ambulance services and many of the local authority services were incorporated into the vision of a holistic health care system, as envisioned by Bevan. The NHS's free 'at-the-point-of-need' medical services were channelled through the general medical practitioners and it soon became evident that there was an enormous pent-up volume of hitherto unrecognised health problems. New medications such as antibiotics were beginning to appear which began to offer effective treatments for many illnesses.

It is difficult to find figures for rates of dyspepsia in the British population when the NHS came into being, but one study in London showed that approximately 17% of those interviewed suffered dyspeptic symptoms and 2% had peptic ulcers.<sup>693</sup> Estimates varied as to the relative proportions of each type of peptic ulcer but in Glasgow there were eight duodenal ulcers for every gastric ulcer. Gastric ulcers were slightly commoner in women and generally found in an older age group of patients. In London, the duodenal/gastric ulcers ratio was lower.<sup>694</sup> Subsequent studies indicate that the prevalence of dyspepsia to

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<sup>688</sup> Wilkinson E, 'Milk and Meals in Schools', House of Commons Debate, *Hansard*, Feb 27<sup>th</sup> 1946, vol. 419, 411-2

<sup>689</sup> Charman T, 'Imperial War Museum's Ministry of Food: Terry Charman explores food rationing', <http://www.culture24.org.uk/history+%26+heritage/war+%26+conflict/world+war+two/art76114>, Feb 15<sup>th</sup> 2010

<sup>690</sup> A good example of this was the provision of ambulances under the auspices of the newly formed Home Ambulance Service from the WWI battlefields for use throughout the nation and thereby providing a service which had been patchy at best until this time. See 'The Home Ambulance Service', *British Medical Journal*, May 22<sup>nd</sup> 1920, 716

<sup>691</sup> Bynum W F, Hardy A, Jacyna S, et al, eds, *The Western Medical Tradition 1800-2000*, (New York, Cambridge, 2006, Cambridge University Press), pp439-40

<sup>692</sup> Porter R, *The Greatest Benefit To Mankind: A Medical History of Humanity from Antiquity to the Present*, (London, 1997, Fontana Press), pp652-4

<sup>693</sup> Jones R, 'Leading article: dyspeptic symptoms in the community', *Gut*, Jul 1989, vol. 30, issue 7, 893-8

<sup>694</sup> Jamieson R A, Smith W E, Scott L D W, 'Peptic ulcer in Glasgow, a hospital survey', *British Medical Journal*, Feb 19<sup>th</sup> 1949, 298-300

be virtually unchanged in the second half of the twentieth century with up to 40% of the population suffering some kind of dyspepsia.<sup>695</sup>

## 6. 2. 1: Illness in the community, self-medication and the community pharmacist

Before the NHS was introduced, there was a ‘fear that state subsidized medicine and free choice of and access to a doctor for everyone would result in unutterable chaos, with the medical services swamped with trivial complaints ...’.<sup>696</sup> In reality, whilst there existed a problem with, ‘the frivolous demands from a small number of people’, the behavior of the majority of the British population was appropriate in their demands on their general practitioner. However, within the community, it was recognized that there existed a large amount of undiagnosed illness, some of which could be detected by screening.<sup>697</sup> It was called the ‘iceberg phenomenon’ whose ‘tip’ referred to those cases of illness known to the general practitioner. The classical example is that of diabetes where it is known that many more undiagnosed cases exist in the community than are under medical care.<sup>698</sup> A survey of ‘Medicines used for the five most common complaints’ in 1971, showed that in the treatment of digestive complaints, antacids were self-prescribed six times more commonly than medically-prescribed, ‘gastro-intestinal medicines’, were twelve times more commonly self-prescribed than medically-prescribed and analgesics almost twenty times more self-prescribed than medically-prescribed. This sample illustrates that far more of the population operated a system of self-care using their own concepts of how to control symptoms of digestive complaints than attended doctors.<sup>699</sup>

Most people self-diagnose and self-medicate for conditions which they do not perceive to be serious enough, ‘to bother the doctor with’, but a smaller proportion of people seek medical advice. David Mechanic proposed the concept of ‘Illness Behaviour’ to explain the differences between people in the ways they handled their illnesses.<sup>700</sup> He commented that an important incentive for some people not attending a doctor with an ailment, was to avoid adopting ‘the sick rôle’ in order to remain at work.<sup>701</sup> Mechanic studied a group of

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<sup>695</sup> Penston J G, Pounder R E, ‘A survey of dyspepsia in Great Britain, *Alimentary Pharmacology and Therapeutics*, Feb 1996, vol. 10, issue 1, 83-9

<sup>696</sup> Wadsworth M E J, Butterfield W J H, Blaney R, *Health and Sickness: The Choice of Treatment*, (London, 1971, Tavistock Publications), p1

<sup>697</sup> Last J M, ‘The iceberg: “completing the clinical picture” in general practice’, *The Lancet*, Jul 6<sup>th</sup> 1963, 28-31

<sup>698</sup> Wadsworth M E J, Butterfield W J H, Blaney R, *Health and Sickness*, op cit, p4

<sup>699</sup> Wadsworth M E J, Butterfield W J H, Blaney R, *Health and Sickness*, op cit, Table D, p105

<sup>700</sup> Mechanic D, ‘The concept of illness behaviour’, *Journal of Chronic Disease*, Feb 1962, vol. 15, 189-94

<sup>701</sup> Mechanic D, ‘The concept’, *ibid*, 190

American college students who could access medical care at no cost to themselves. He identified two groups of individuals with high and low stress levels in their lives which was expressed in difficult interpersonal relationships. Those with more difficulties at this level tended to seek medical help more often and for more trivial conditions. Mechanic was also able to show differences in behavior patterns based upon religious background. Some sought early medical intervention for most ailments and others were very slow to seek medical help. It should be recognized that his study sample were young, healthy and privileged but nevertheless Mechanic identified differences which played a part in decision making.

Thus, upbringing, expectations and life experience have been shown to play a part in understanding of illness and in decision making processes in matters of ill-health. Often people's concepts of illness are not recognizable within orthodox medical thinking but they could have their origins in the distant past, in cultural mores or in a misunderstanding of a medical idea.<sup>702</sup> Examples of health beliefs which were in common currency in the 1950s which were passed down in families included advice about not washing hair when menstruating or not getting one's feet wet or getting chilled, both of which were believed to make people susceptible to mainly respiratory infections. David Sharpe states, 'The non-medical diagnosis is often made by the person suffering the symptoms, on the basis of his own experience. Alternatively it can be made by, or on the advice of, a friend whose knowledge and experience is trusted by the patient; or more often still by someone who has had some training in health matters, normally a pharmacist.'<sup>703</sup> Sharpe's paper illustrates just how common it is for the public to seek advice from pharmacists. When pharmacists' advice was evaluated in terms of helpfulness, it was found to be very good. The worst advice came from 'impersonal sources such as women's magazines, home doctor books and television'.<sup>704</sup> When a doctor puts a diagnostic label on a patient's complaint, the patient may choose to self-medicate or seek medical prescriptions when appropriate, depending on the condition. A patient may buy over-the-counter (OTC) remedies available in the pharmacy but may also seek advice elsewhere. The pharmacist may be an excellent first-line advisor but alternative medicine may be another personal choice.<sup>705</sup>

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<sup>702</sup> Fleming G V, Giachello A L, Andersen R M, et al, 'Self care: substitute, supplement or stimulus for medical care services', *Medical Care*, Oct 1984, vol. 22, no. 10, 952

<sup>703</sup> Sharpe D, 'The general practice pharmacist viewpoint', *Royal Society of Health Journal*, 1977, vol. 97, issue 4, 165-6, 187

<sup>704</sup> Sharpe D, 'The general practice pharmacist', *ibid*, 165

<sup>705</sup> Moore J, Phipps K, Marcer D, et al, 'Why do people seek treatment by alternative medicine?', *British Medical Journal*, Jan 5<sup>th</sup> 1985, 28-9

## 6. 2. 2: Medical prescribing for peptic ulcer 1948-1975

When a patient went to their own general practitioner for a prescription for dyspepsia or peptic ulcer, a prescription for generic antacids might be provided.<sup>706</sup> The six commonest antacids prescribed were aluminium hydroxide, calcium carbonate, magnesium carbonate, magnesium oxide, sodium bicarbonate and magnesium trisilicate. Compound medications were also used which were mixtures of these alkalis, created to counteract individual side-effects. An example follows; because constipation occurs when calcium carbonate is taken, magnesium oxide, which has a mild laxative effect, can be added to produce an effective antacid which neither constipates nor loosens the bowels. Generic prescriptions at the time were not labeled with their ingredients, simply having on the container, ‘the tablets’ or ‘the powder’ or ‘the mixture’ and its dose stated.

Generic medication, labeled with the suffix ‘BP’, e.g. Magnesium trisilicate BP, indicated that that it had been produced by the method described in the *British Pharmacopœia*.<sup>707</sup> However this information was not available to the patient on his medicine container and often a patient would have several containers with different drugs all labeled, ‘the tablets’.<sup>708</sup> The general practitioner was allowed to prescribe proprietary drugs, including those which had been publicly advertised, which often were more palatable than a generic equivalent.<sup>709</sup> Many brand names enjoyed a strong popular support from the days before the NHS when patients had had to buy them.

Two other particular types of drug which were not antacids were used in the early 1950s in the treatment of peptic ulcer disease – barbiturates and atropine-like drugs. First marketed in 1912 by the Bayer pharmaceutical company as a sedative, phenobarbitone was believed to be helpful in treating peptic ulcer. Atropine, which was extracted from the naturally occurring plant belladonna and had been in use for many years, was known experimentally to reduce stomach secretion. The preferred form of atropine was belladonna extract which was often added to antacid mixtures. Both drugs were discussed by Arthur Douthwaite in a paper published in 1947 where he suggested the use of phenobarbitone as a ‘cerebral

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<sup>706</sup> ‘Generic drugs’ are named with their chemical contents as opposed to ‘proprietary drugs’ which usually had easily remembered trade names. An example is ‘cimetidine’ (generic name), its proprietary name being Tagamet. Antacids were mostly alkalis with the exception of bismuth containing medications.

<sup>707</sup> The *British Pharmacopœia* is a book originally produced subject to section 54 of the Medical act 1858 containing a list of medicines and compounds and descriptions of how they are to be accurately made up. It has been revised regularly since then.

<sup>708</sup> From Testimony T6

<sup>709</sup> Proprietary drugs have a trade name and are protected by a patent

sedative' and when this was unsuccessful in healing ulcers, he suggested using cannabis.<sup>710</sup> In the USA in 1950, a pharmacologically similar drug called 'Banthine', marketed in the UK as 'Probanthine', also had atropine-like properties and was thought to work by interfering with vagal stimulation of the stomach. It seems to have made little impact in the UK as a treatment for peptic ulcer, there only being one paper published over the period 1950-70 in the *British Medical Journal* on its use.<sup>711</sup> None were published in *The Lancet* over the same period. It made its first appearance in the *British National Formulary*, (BNF), in 1963.

Between 1952 and 1963, the *British National Formulary* listed sixteen antacid preparations based on the six basic antacids previously mentioned. However the pharmaceutical industry produced antacids in multiple variations of mixtures with belladonna or phenobarbitone added. *Martindale: The Extra Pharmacopœia*, was to be found in most pharmacies for everyday reference use, had fifteen pages devoted to antacids in its 1973 version.<sup>712</sup> *Martindale* as it was better known was preferred by pharmacists in the community to the *British Pharmacopœia* because it gave the contents of every proprietary and over-the-counter (OTC) medication. The fact of there being so many available preparations for the symptomatic treatment of peptic ulcer shows that it was big business for pharmacist and industry alike and gives an indication of peptic ulcer prevalence.

### 6. 2. 3: Other drugs and clinical trials for peptic ulcer

Other drugs and substances were evaluated in an attempt to promote ulcer healing by physicians. Enterogastrone and urogastrone were two theoretically-promising substances, occurring naturally in mammalian intestinal mucosa and urine respectively, which began to be used experimentally in 1938. When given by injection to dogs in laboratory conditions they inhibit gastric secretions.<sup>713</sup> Laboratory physiologists involved with the study of peptic ulcer disease began to study these substances and encountered favourable results which suggested that they could both heal ulcers and protect against future ulcer recurrence. They created peptic ulcers in dogs and then used enterogastrone to heal them. These substances had been demonstrated to have the capacity to reduce gastric secretion of acid and seemed to have a protective effect to prevent further ulceration, or delay further ulceration. Clinical trials using urogastrone were also undertaken which showed evidence

<sup>710</sup> Douthwaite A H, 'Choice of drugs in the treatment of duodenal ulcer', *British Medical Journal*, Jul 12<sup>th</sup> 1947, 43-7

<sup>711</sup> Editorial, 'Banthine and gastric acidity', *British Medical Journal*, Nov 17<sup>th</sup> 1951, 1205-6

<sup>712</sup> *Martindale, The Extra Pharmacopœia*, (London, 1973, The Pharmaceutical Press), pp124-39

<sup>713</sup> Sandweiss D J, Friedman M H F, 'The use of urine extracts in the treatment of ulcer', *American Journal of Digestive Diseases*, Jan 1940, vol. 7, 50

that ulcers could be healed by injecting it into patients, few of whom suffered reactions.<sup>714</sup>  
<sup>715</sup> However extensive investigation was unfruitful in taking this potential treatment into clinical practice because at the time the researchers were unable to isolate the active substance in sufficient purity and quantity to be clinically useful. Nevertheless urine and urine extracts seemed to be helpful in treating peptic ulcers and pregnant mare's urine seemed particularly promising as an injectable treatment.<sup>716</sup> However in 1950 a clinical trial of 'Robuden', an enterogastrone-like medication, showed that it was no better than placebo as a treatment for peptic ulcer and that placebo treatment was surprisingly effective in the healing of peptic ulcers.<sup>717</sup> This phenomenon of placebo effect in peptic ulcer disease will be discussed later in the thesis.

In a fourteen year period between 1950 and 1964, Richard Doll and his colleagues set up four series of clinical trials to assess the worth of the then current treatments for gastric ulcer. He summarised his work in the *Scottish Medical Journal* which refers to all the trial work done.<sup>718</sup> Four series of clinical trials took approximately two years each to examine the effects of hospitalization (bed-rest) with and without intragastric milk drips, the use of phenobarbitone, ascorbic acid, belladonna extract, Robuden, cabbage juice and carbenoxolone as treatments for gastric ulcer. The studies also looked at the worth of 'gastric' diets, and smoking. The outcomes of the four studies are summarized by his conclusion:

*In summary, therefore, it seems that we are now in a slightly better position to treat gastric ulcers scientifically than we were. Symptoms can usually be controlled by alkalis without admission to hospital; but if they fail to respond to ambulant treatment, they can always be relieved by bed-rest with continuous intragastric milk drip containing a sufficient quantity of sodium bicarbonate. Many ulcers will heal without any other special treatment within a few weeks; but many more can be assisted to heal by carbenoxolone in doses of up to 300mg a day. Some ulcers fail to heal on this regime and it may be that these should immediately be treated surgically. An attempt to heal the ulcer by bed rest in hospital combined with*

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<sup>714</sup> Sandweiss D J, Sugarman M H, Friedman M H F, et al, 'The effect of urine extracts on peptic ulcer: an experimental and clinical study,' *American Journal of Digestive Diseases*, Oct 1941, vol. 8, 371-82

<sup>715</sup> Greengard H, Atkinson A J, Grossman M I, et al, 'The effectiveness of parenterally administered enterogastrone in the prophylaxis of recurrences of experimental and clinical peptic ulcer with a summary of 58 cases', *Gastroenterology*, 1947, vol. 7, issue 6, 625-49

<sup>716</sup> Page R C, Heffer R R, 'Oral treatment of chronic duodenal and jejunal ulcers with an extract of mare's urine', *Gastroenterology*, Dec 1948, vol. 11, issue 6, 842-7

<sup>717</sup> Stolte J B, 'A therapeutic experiment in peptic ulcer', *The Lancet*, Dec 23<sup>rd</sup> 1950, 858-9

<sup>718</sup> Doll R, 'Medical treatment of gastric ulcer', *Scottish Medical Journal*, May 1964, vol. 9 no. 5, 183-96

*larger doses of carbenoxolone given by intragastric drip may, however, be justified.*

*Smokers should be advised to stop smoking, but dieting, apart from taking snacks between meals, is in my opinion, not necessary.*

*Phenobarbitone is not needed routinely and should be used only to treat the patient and not the ulcer.*

*Whether treatment along these lines will alter the long term outlook remains to be seen. Healed ulcers often break down within a few weeks or months and until we know the cause of the ulcer we can hardly hope to prevent its recurrence.*

These significant studies illustrate that most of the time-honoured means used by medical practitioners to treat gastric ulcers were of doubtful value, with the exceptions of bed-rest, intragastric milk drips and carbenoxolone. Carbenoxolone was a relatively new drug which had been little trialed until the early 1960s. It was eventually found to be a good treatment for gastric ulcers but unfortunately did not seem to work for duodenal ulcer sufferers. It had predictable side effects of which more will be said later in the thesis.

Gender has been implicated by clinicians in the formation of gastric ulcers since the mid nineteenth century.<sup>719</sup> Sidney Truelove, the first Professor of Gastroenterology at Oxford University, noted that duodenal ulcer seemed to have a predilection for the adult male but women relatively rarely developed duodenal ulcers during their reproductive years. However after the menopause, the picture changed and women began to suffer from the effects of duodenal ulceration. In 1953 Douglas Clark noted that duodenal ulcer symptoms improved in 88% of women while pregnant.<sup>720</sup> In 1960, Truelove designed a study to test the hypothesis that men suffering from duodenal ulcers might benefit from taking stilboestrol, a synthetic oestrogen hormone.<sup>721</sup> His double blind study also looked at the benefits of phenobarbitone and a 'gastric' diet. The trial result, which showed that none were of any short or long-term benefit in helping duodenal ulcer sufferers, agreed with Richard Doll's study in gastric ulcer sufferers.<sup>722</sup> Stilboestrol did offer both short and long-term benefits but only to those men who had had their duodenal ulcer for less than ten years, however stilboestrol causes the development of feminizing features, heart problems and impotence in men so few would choose it as an option. In 1965 and 1968, Richard

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<sup>719</sup> See chapter 2

<sup>720</sup> Clark D H, 'Peptic ulcer in women', *British Medical Journal*, Jun 6<sup>th</sup> 1953, 1254-7

<sup>721</sup> Truelove S C, 'Stilboestrol, phenobarbitone and diet in chronic duodenal ulcer: a factorial therapeutic trial', *British Medical Journal*, Aug 20<sup>th</sup> 1960, 559-66

<sup>722</sup> Doll R, 'Medical treatment', op cit, 183-96

Doll and colleagues also examined stilboestrol as a therapy for gastric ulcer in two studies whose results were inconclusive.<sup>723 724</sup>

In a paper in *Gastroenterology* published in 1977, Erik Christensen and others looked at randomized clinical trials of the treatment of duodenal ulcer for the decade 1964 to 1974.<sup>725</sup> They examined a number of trials of anticholinergic drugs, antacids, oestriol and deglycyrrizinated liquorice. The only drug in the trials which relieved symptoms and healed duodenal ulcers in men but did not prevent recurrence, was another oestrogen, oestriol, which could only be used short-term. The paper concludes with the statement that H<sub>2</sub> blockers and bismuth compounds were now being examined and ‘the preliminary results are favourable.’

By 1960, general practitioners managed patients with dyspepsia mainly using antacids and those who did not respond to their medications were referred to hospital, usually for a barium meal X-ray examination or consultant opinion which might include an endoscopy in some centres. Despite all the researches described above, the oral medications which general practitioners could prescribe were the same as those used by their consultant colleagues in the hospital service. Apart from carbenoxolone, any new drugs which appeared did not become established in the treatment of peptic ulcers and dyspepsia, leaving antacids as the main treatments until 1976.<sup>726</sup>

## 6. 3: Physical treatments for gastric and duodenal ulcer

### 6. 3. 1: Gastric Irradiation

Irradiation by X-rays (radiotherapy) to the acid producing part of the stomach works by suppressing acid production which allows the ulcers to heal in a relatively less acid environment. After its first use in 1917, radiotherapy of the stomach was used by a number of therapists in different countries in an attempt to modify gastric secretion which they believed played an important part in ulcer formation.<sup>727</sup> Walter Palmer in 1939 said, ‘There is an increasing amount of evidence that acid gastric juice plays a most important

<sup>723</sup> Doll R, Hill I D, Hutton C F, ‘Treatment of gastric ulcer with carbenoxolone sodium and oestrogens’, *Gut*, Feb 1965, vol. 6, issue 1, 19-24

<sup>724</sup> Doll R, Langman M J, Shawdon H H, ‘Treatment of gastric ulcer with oestrogens’, *Gut*, Feb 1968, vol. 9, issue 1, 46-7

<sup>725</sup> Christensen E, Juhl E, Tygstrup N, ‘Progress in gastroenterology: Treatment of duodenal ulcer’, *Gastroenterology*, Nov 1977, vol. 73, no. 5, 1170-8

<sup>726</sup> The antispasmodic drug dicyclomine appears in the 1968 *BNF*. It was little used. The 1971 *BNF* includes carbenoxolone without specifying its dosage regime.

<sup>727</sup> Ivy A C, Grossman M I, Bachrach W H, *Peptic Ulcer*, (Philadelphia and Toronto, 1950, The Blakiston Company), p929

rôle in both the pathogenesis and healing of peptic ulcer.<sup>728</sup> However there was no agreed X-ray dosage and the results were highly variable, although it was accepted that it was possible to depress gastric secretion by radiotherapy. A large scale series was published in 1948 which indicated that ulcer healing after radiotherapy was dose-dependent, with those receiving higher doses having fewer recurrences, but overall the results were disappointing and few other series were reported in the decade up to 1950.<sup>729</sup> It is difficult to assess how many peptic ulcer patients were treated by radiotherapy because so little published data are available.<sup>730</sup>

An Australian series published in 1956 compared two groups subjected to gastro-duodenal resection for duodenal ulcer.<sup>731</sup> Fifty-two patients had this operation with the addition of radiotherapy and a control group of 48 did not have radiotherapy following the same operation. Both groups were followed up for between 12 and 50 months. There was no apparent advantage to either group in terms of outcomes and there was an ulcer recurrence rate of 12% overall. The rationale of using radiotherapy in peptic ulcer disease was to avoid surgery in patients who were considered unfit for surgery but were nevertheless sufficiently symptomatic to require treatment. In Edinburgh, a series of 24 such patients were treated by radiotherapy for peptic ulcer disease from 1955 to 1972.<sup>732</sup> The results over the period studied were encouraging insofar as 16 patients achieved complete relief of symptoms on first treatment with three achieving partial relief. Of five patients who did not respond to a first course of radiotherapy, three had a second course with good results but two were no better. One benefit which emerged from this study was that the operative mortality for gastric operations of the hospital unit who organized the study on the over-60yrs age group was only 6% compared with an average of 16% for the same age group in other places. It was suggested that radiotherapy was a valid and useful treatment for treatment resistant patients unfit for surgery.

In 1979, two American physicians, Arthur Cocco and Albert Mendeloff who had treated a group of 463 patients over a 14 year period using the same clinical criteria as the Edinburgh series for patient selection reported good clinical results and an ulcer recurrence

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<sup>728</sup> Palmer W L, Templeton F, 'The effect of radiation therapy on gastric secretion', *Journal of the American Medical Association*, Apr 15<sup>th</sup> 1939, vol. 112, no. 15, 1429-34

<sup>729</sup> Ricketts W E, Palmer W L, Kirsner J B, et al, 'Radiation therapy in peptic ulcer-an analysis of results', *Gastroenterology*, 1948, vol. 11, issue 6, 789-05

<sup>730</sup> A search on Embase Classic + Embase for 'peptic ulcer/ rt [radiotherapy] from 1947-1980' only yielded 5 original research articles.

<sup>731</sup> This was a limited partial gastrectomy whereby the 1<sup>st</sup> part of the duodenum (which is where most duodenal ulcers are found) is removed with the outlet part of the stomach (the antrum).

<sup>732</sup> Findlay J M, Newaishy G A, Sircus W, et al, 'Role of gastric irradiation in the management of peptic ulceration and oesophagitis', *British Medical Journal*, 28<sup>th</sup> Sep 1974, 769-71

rate of 10%.<sup>733</sup> It should be noted with this paper that in the last three years of the study, cimetidine had become available and the authors recognized that their technique might be supplanted in the frail group of patients they were treating when the long-term safety of cimetidine could be established.<sup>734</sup> Melvin Greim's paper from the University of Chicago published in 1985, revealed that 2049 patients received therapeutic gastric irradiation to reduce gastric secretion for peptic ulcer disease between 1937 and 1968.<sup>735</sup> This paper was intended to assess how safe gastric irradiation was in the long term. Radiotherapy is known to be carcinogenic and one patient in this Chicago series, who received radiotherapy for peptic ulcer when he was 15 and again at 22, developed a sarcoma of stomach at the age of 51.<sup>736</sup> Two other patients, similarly treated, developed sarcomas, although they were both middle-aged at the time of their radiotherapy treatment. The use of radiotherapy for a benign condition is an indication of how troublesome a condition it was at the time, how desperate clinicians were to find an effective treatment for it and how dangerous it was to leave it ineffectively treated. Laurence Martin and Ninian Lewis's 1949 review confirms this showing that approximately 30% of both gastric and duodenal ulcer sufferers had a haematemesis or a perforation at some time in their lives with 10% of perforation sufferers and approximately 4% of haematemesis sufferers dying from these complications.<sup>737</sup>

### 6. 3. 2: Psycho-surgery

In chapter 3 of this thesis, the question about whether or not the brain itself could play a part in the formation of peptic ulcers was briefly considered. It had been reported by many pathologists that '[peptic] ulcer is seen fairly commonly in patients dying with brain tumours'.<sup>738</sup> Harvey Cushing had apparently demonstrated the pathway by which this might happen in a paper describing his personal experiences of operations for the removal of brain tumours in nine patients who had died from serious upper G-I complications found at autopsy.<sup>739</sup> This led Cushing to believe that he had found a neuronal mechanism for

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<sup>733</sup> Cocco A, Mendeloff A, 'Gastric irradiation of peptic ulcer: a 14 year follow-up', *American Journal of Gastroenterology*, 1979, vol. 71, no. 6, 577-81

<sup>734</sup> Cimetidine was the first oral medication of the H2 blocker type to be marketed. It first appeared in 1976. The history of its development and clinical use is described later in this thesis in chapter 8. 3. 1

<sup>735</sup> Greim M L, 'External irradiation at the University of Chicago' in Palmer W L, ed, *Gastric Irradiation in Peptic Ulcer*, (Chicago, 1974, University of Chicago Press) pp39-44

<sup>736</sup> A sarcoma is a relatively rare connective tissue cancer which is difficult to treat and often fatal.

<sup>737</sup> Martin L, Lewis N, 'Peptic ulcer cases reviewed after ten years', *The Lancet*, Dec 17<sup>th</sup> 1949, 1118-9

<sup>738</sup> Alvarez W C, 'Light from the laboratory and the clinic on the causes of peptic ulcer', *The American Journal of Surgery*, Nov 1932, vol. 18, no. 2, 207-231, esp p221

<sup>739</sup> Cushing H, 'Peptic ulcer and the interbrain', *Surgery, Gynaecology and Obstetrics*, Jul 1932, vol. 55, no. 1, 1-34

causing peptic ulcers. His paper gave a physical explanation as to how peptic ulcers may form, to those who believe in the psychosomatic theory of ulcer genesis and the worth of psychotherapy for treating peptic ulcer disease. In 1950, John Carmody reported two cases of patients with serious mental disorders unresponsive to all measures who were subjected to frontal lobotomy procedures which relieved their psychopathies and coincidentally cured their peptic ulcers which had been life-threatening because of repeated haematemesis.<sup>740</sup>

In 1952, in Paris, as a result of treating terminally ill patients with intractable pain by injecting the prefrontal cortex of the brain with the local anaesthetic solution procaine, Maurice Bucaille adopted this new technique for the treatment of diseases of the digestive tract 'in which the central nervous system, according to present theories, plays a part' which would not heal using recognized therapies.<sup>741</sup> This paper details two cases which are also mentioned in another paper jointly published with Drs Pierre Frumusan and Roger Cattan.<sup>742</sup> A 74 year old male patient with a giant gastric ulcer unimproved by medical treatment was cured by an injection into the left prefrontal area and remained well for the nine month period of follow-up. A 58 year old male with massive haemorrhage from a duodenal ulcer was treated similarly and the bleeding ceased. This man was declared completely cured after three months. It was felt that injection of a liquid in order to produce a lesion was insufficiently accurate to obtain optimal results so it was proposed to use electro-coagulation of both prefrontal areas of the brain. The paper details two new duodenal ulcer sufferers treated by prefrontal novocaine injection and one treated by electrocoagulation. One patient with a duodenal ulcer treated by injection was considered to be a failure because, although his ulcer was considered healed, he developed epilepsy. Bucaille re-published his five cases in a Belgian journal later that year and Marcos Meeroff a gastroenterologist working in Buenos Aires published a detailed summary of the initial paper by Frumusan and his colleagues, in Spanish.<sup>743</sup><sup>744</sup> In 1964, Bucaille returned to publishing about what he now called 'selective frontal surgery' for sixty patients in another

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<sup>740</sup> Carmody J T B, 'The effect of prefrontal lobotomy on peptic ulcer', *Surgical Forum*, 1950, vol. 1, 332-5

<sup>741</sup> Soupault R, Bucaille M, 'Procaine injection of the prefrontal lobe of the brain: technic and present indication', *Annals of Surgery*, Mar 1955, vol. 141, issue 4, 388-97

<sup>742</sup> Frumusan P, Cattan R, Bucaille M, 'Premières tentative chirurgicales sur le cerveau pour le traitement des ulcers gastriques et duodenum rebelles', *Semaine Des Hopitaux*, Fev 10<sup>ème</sup> 1957, nom. 9, 521-33

<sup>743</sup> Bucaille M, 'Electrocoagulations du cerveau préfrontal', *Acta Gastro-Enterologica Belgica*, May-Jun 1957, vol. 20, 506-14

<sup>744</sup> Meeroff M, 'Cirurgia cerebral en el tratamiento de las ulceras gastroduodenales rebeldes y en las haemorragias de origen ulceroso', *La Prensa Medica Argentina*, 1957, vol. 44, no. 17, 1332-9

Belgian journal and while he refers to his five original cases, the other 55 cases are not described in detail.<sup>745</sup>

This very brief excursion into the topic of psycho-surgery for patients desperately ill with gastrointestinal bleeding may have been undertaken by other surgeons but a literature search does not reveal their work. It should be remembered that the technique of frontal lobotomy was regularly practised by neurosurgeons on behalf of psychiatrists at that time and was considered to be ‘low-risk’ in terms of immediate mortality.<sup>746</sup> The long term personality changes produced were considered to be a price worth paying by its proponents who had no other means of treating serious psychiatric disorders until the era of good psycho-active medication.

### 6. 3. 3: Gastric freezing

Gastric cooling had been used for over a century in the treatment of haematemesis as seen earlier.<sup>747</sup> This principle was reintroduced by Owen Wangensteen in 1958 to control massive gastric haemorrhage in five patients.<sup>748</sup> He persuaded them to swallow a balloon through which he circulated water at 20°C to cool the stomach. Taking the concept further, Wangensteen devised an apparatus to achieve ‘physiological gastrectomy’ by gastric freezing so that the acid producing cells of the body of the stomach could be ‘switched off’ by subjecting them to a period of gastric freezing.<sup>749</sup> He used an intragastric tube arrangement which could be swallowed, into which he introduced a gastric coolant to reduce the temperature in the stomach to -20° C. By this means he showed that he could reduce gastric acid production for a time.

The technique was attempted by other clinicians who saw in it the prospect of an alternative to surgery for both haematemesis and as an elective treatment for gastric and duodenal ulcer in patients who had failed to respond to all medical regimens and were considered unfit for surgery. The ‘Wangensteen’ or ‘Minneapolis group’ enthusiastically employed the technique as an alternative to surgery and initial results claimed that out of

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<sup>745</sup> Bucaille M, ‘Chirurgie frontale en pathologie digestive’, *Le Scalpel*, Mar 7 1964, num. 10, 223-9

<sup>746</sup> A search using ‘pre-frontal lobotomy’ in the *Web of Science* search engine yields 349 articles published between 1940 and 1960.

<sup>747</sup> Budd G, *On the Organic and Functional Disorders of the Stomach*, (London, 1855, John Churchill), pp122, 124

<sup>748</sup> Wangensteen O, Root H, ‘Depression of gastric secretion and digestion by gastric hypothermia: its clinical use in massive haematemesis’, *Surgery*, 1958, vol. 44, 265-74

<sup>749</sup> Wangensteen O, Peter E, ‘Achieving “physiological gastrectomy” by gastric freezing’, *Journal of the American Medical Association*, May 12<sup>th</sup> 1962, vol. 180, 439-44

164 patients treated, 50% were symptom-free after one year. Within two years they had treated over 1000 patients ‘without mortality or serious complications’.

Others tried the technique. John Doyle and Edward Williams in 1964 reported early relapse rates of 30% after three months.<sup>750</sup> James H Lawrie and associates set up a trial of gastric freezing in duodenal ulcer patients and treated 13 patients, publishing their results in 1965.<sup>751</sup> They found that the results were unpredictable and variable due to the poor fit of the balloon apparatus to the stomach shape. One patient developed a gastric ulcer at the site where the coolant entered the stomach. Another who had had an ‘uneventful’ freeze suffered a severe intra-abdominal infection. The trial was abandoned because of the unacceptable and unpredictable side effects. The group’s conclusion was that, ‘In our opinion, gastric freezing is neither a reliable nor safe method of treating patients with duodenal ulcer and should not have widespread use in man until further experimental work has been carried out. ... Complications may be severe.’<sup>752</sup> In Stephen Wangensteen and colleagues’ New York study of 31 patients, three had melaena, three haematemesis and four developed new gastric ulcers.<sup>753</sup>

In 1969, the *New England Journal of Medicine* reported a double blind trial of gastric freezing by a team led by Julian Ruffin from the University of North Carolina.<sup>754</sup> They subjected two groups of patients to the gastric freezing procedure. Only one group actually had the coolant introduced into their stomachs while the ‘sham’ group underwent the procedure without realising that the coolant was not being circulated within their stomachs. The results were analysed and there was ‘no significant difference in the relief of pain, secretory (acid) depression, the number and severity of recurrences or the development of end points in the two groups.’ This study effectively ended yet another physical treatment for the duodenal ulcer patient who had not responded to conventional treatment and who was unfit for surgery.

## 6. 4: Zollinger-Ellison Syndrome

Possibly the worst form of peptic ulcer disease known to medicine clinically presented with increasingly recurrent ulcers, abdominal pain and the complications of perforation

<sup>750</sup> Doyle J C, Williams E J, ‘Elective treatment of duodenal ulcer by gastric freezing’, *British Journal of Surgery*, Oct 1964, vol. 51, no. 10, 778-83

<sup>751</sup> Lawrie J H, Smith G M R, Goodall P, et al, ‘Gastric freezing for duodenal ulcer’, *British Journal of Surgery*, Mar 1965, vol. 52, no. 3, 226-30

<sup>752</sup> Lawrie J H, Smith G M R, Goodall P, ‘Gastric freezing’, *ibid*, 230

<sup>753</sup> Wangensteen S L, Barker H G, Smith R B, et al, ‘Gastric freezing: an initial clinical study’, *American Journal of Medicine*, Jan 1965, vol. 38, 31-41

<sup>754</sup> Ruffin J M, Grizzle J E, Hightower N C, et al, ‘A co-operative double-blind evaluation of gastric “freezing” in the treatment of duodenal ulcer’, *The New England Journal of Medicine*, Jul 3<sup>rd</sup> 1969, 16-9

and/or haemorrhage and it defied all conventional means to alleviate its malign effects. In 1955 Robert Zollinger and Edwin Ellison first described ‘A clinical entity consisting of hypersecretion, hyperacidity and atypical peptic ulceration associated with non-insulin producing islet-cell tumours of the pancreas ...’<sup>755</sup> They called it the ‘Zollinger-Ellison Syndrome’. This tumour or tumours was located in the pancreas and sometimes could be tiny which makes surgical removal very difficult. These tumours produce a hormone which stimulates extreme acid production and later researches revealed that it was the hormone gastrin whose history is briefly described in chapter two. Before this discovery, total gastrectomy was the only solution to prevent further damage to oesophagus, stomach duodenum and small bowel and this led to enormous problems for the patient with no stomach. After 1991, an effective oral medication (Omeprazole) became available to block the effect of gastrin but surgery is recommended for removal of the tumour if possible, for it is malignant and may be ultimately fatal if it has metastasised before it is removed. It is a rarity and few doctors ever encounter a case.

## 6. 5: Gastric and duodenal ulcers from 1948 until 1976: a changing picture

In the previous chapter it is seen that certified death rates in England and Wales from gastric and duodenal ulcer varied from 1911 until 1969, initially both rising before falling at different times. By the fourth decade of the twentieth century, barium meal X-ray examinations were beginning to be accepted as reliable diagnostic aids for clinicians for the diagnosis of peptic ulcers although clinical enquiry and physical examination aided by other diagnostic methods discussed in earlier chapters still played an important part. In the period before the NHS, patients with possible peptic ulcers might have had this procedure but overall the numbers with accurate diagnoses confirmed radiologically was small. After the NHS came into being, radiology took many years to catch up with the size of the problem and Eric Wilkes’ paper, published in 1964, showed that 9% of patients dying at home of gastric cancer in the Sheffield area had not been to hospital for any form of investigation.<sup>756</sup> The diagnosis of peptic ulcer remained a clinical one for many patients until symptoms became sufficiently severe for a general practitioner to seek a second opinion and suitable investigations from a specialist.

The clinical incidence of perforation of peptic ulcers began to fall in the sixth decade of the twentieth century. In the West of Scotland, perforation rates fell between 1954 and 1963

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<sup>755</sup> Zollinger R M, Ellison E H, ‘Primary peptic ulcerations of the jejunum associated with islet cell tumours of the pancreas’, *Annals of Surgery*, Oct 1955, vol. 142, no. 2, 709-23

<sup>756</sup> Wilkes E, ‘Cancer outside hospital’, *The Lancet*, Jun 20<sup>th</sup> 1964, 1379-81

but in the following decade remained at the same levels.<sup>757 758</sup> In the Oxford area, the incidence of haematemesis did not change in the period 1953-67 as seen in a study which examined admissions for haematemesis in three successive quinquennial periods which found no change in its incidence between each period.<sup>759</sup> Another study of hospital admissions data from governmental statistics in England and Wales and Scotland for peptic ulcer, in the period 1958 to 1972, showed that admissions fell steadily for patients with non-perforated duodenal ulcer and with non-perforated gastric ulcer over the period by 12% and 33% respectively and rates of admission for perforations fell by 14% and 32%.<sup>760</sup> A similar analysis of statistics for the period 1958-1977 showed that the trend continued.<sup>761</sup> In 1967, Roger Sanger's study of perforations, again in Oxford, showed a falling rate of perforation due to peptic ulcers which illustrated a north/south difference in admissions rates, which by 1963 were four times lower in Oxford than in Glasgow.<sup>762</sup> There was no ready explanation for what was happening for, apart from the introduction of carbenoxolone, no new medication in widespread use had appeared and carbenoxolone seemed to have little effect on duodenal ulcer healing in any case.<sup>763 764</sup>

In 1968 Thomas Meade published a paper in the *British Medical Journal* which highlighted the observation that the incidence of duodenal ulcer in British medical practitioners had shown a substantial decline over the period from 1947 to 1965.<sup>765</sup> No explanation was offered. In 1974, Albert Mendeloff, a Baltimore physician, asked the question, 'What has been happening to duodenal ulcer?'<sup>766</sup> He noted a decline in diagnoses of duodenal ulcer of nearly 50% in the US work force and armed services from 1947 to 1965. He had no explanation for what he was seeing. In 1980, Janet Elashoff and Morton Grossman showed that admissions for duodenal ulcer to non-federal hospitals in

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<sup>757</sup> Mackay C, 'Perforated peptic ulcer in the West of Scotland: a survey of 5343 cases during 1954-63', *British Medical Journal*, Mar 19<sup>th</sup> 1966, 701-5

<sup>758</sup> Mackay C, Mackay H P, 'Perforated peptic ulcer in the West of Scotland 1964-73', *British Journal of Surgery*, Feb 1976, vol.63, no. 2, 157-8

<sup>759</sup> Schiller K F R, Truelove S C, Williams D G, 'Haematemesis and melaena with special reference to factors influencing the outcomes', *British Medical Journal*, Apr 4<sup>th</sup> 1970, 7-8

<sup>760</sup> Brown R C, Langman M J S, Lambert P M, 'Hospital admissions for peptic ulcer during 1958-72', *British Medical Journal*, Jan 3<sup>rd</sup> 1976, 35-7

<sup>761</sup> Coggon D, Lambert P, Langman M J S, '20 years of hospital admissions for peptic ulcer in England and Wales', *The Lancet*, Jun 13<sup>th</sup> 1981, 1302-4

<sup>762</sup> Sanger R, 'Incidence of perforated duodenal and gastric ulcer in Oxford', *Gut*, Feb 1967, vol. 8, issue 1, 58-63

<sup>763</sup> From Testimony T1

<sup>764</sup> Cliff J M, Milton-Thompson G J, 'A double-blind trial of carbenoxolone sodium capsules in the treatment of duodenal ulcer', *Gut*, Feb 1970, vol. 11, issue 2, 167-70

<sup>765</sup> Meade T W, Arie T H D, Brewis M, et al, 'Recent history of ischaemic heart disease and duodenal ulcers in doctors', *British Medical Journal*, Sep 26<sup>th</sup> 1968, 704-5

<sup>766</sup> Mendeloff A I, 'What has been happening to duodenal ulcer?', *Gastroenterology*, Nov 1974, vol. 67, no. 5, 1020-2

the USA decreased by 43% from 1970-78 and deaths from peptic ulcer fell by 31% over the same period.<sup>767</sup> Harvey Fineberg and Laurie Pearlman's article in *The Lancet* in 1981 confirmed this showing that the mortality rate for peptic ulcers in the USA declined by two-thirds between 1962 and 1979 and elective operations for its relief fell by 30% between 1965 and 1977.<sup>768</sup> In England and Wales, between 1958 and 1977 hospital admission rates fell for all non-perforation and perforation cases as did mortality rates for all age groups except for women over 40 whose admission and mortality rates rose with age.<sup>769</sup>

## 6. 6: Witness testimony to the decline in peptic ulcer disease

It was not so clearly evident in Scotland to clinicians in 1970 that peptic ulcer disease was declining, as surgeons and physicians continued to deal with large numbers of sufferers from it. Most witnesses interviewed for this thesis were unaware of what was happening at the time although when Professor Frederick Lee, who had worked in haematology between 1968 and 1973, returned to general pathology he noted a reduction in the amount of surgical biopsy material related to peptic ulcer in his laboratory.<sup>770</sup> Mr M K Browne, a witness, made the following comment which illustrates the point,

*From 1963-1970, the three of us in the (Glasgow) Royal Infirmary, Ian McLellan, J.S. Hutchison and I, did 1,000 vagotomies and pyloroplasties between the three of us, and in the succeeding seven years, I probably did another couple of hundred, and from 1977 I never did another one, I don't think.*<sup>771</sup>

Mr Browne appears to have stopped performing vagotomies earlier than other surgeons in Scotland over the period as illustrated in Figure 4 below.<sup>772</sup>

From 1968, the Information Statistics Division of the Common Services Agency of the NHS Scotland (ISD Scotland) began to monitor surgical activity for peptic ulcers by recording the number of vagotomy operations performed annually. The graph which they produced for the period 1968 until 2002 shows that between 1968 and 1976 there was a 30% decline in vagotomy operations. This was at a time when there had been no major

<sup>767</sup> Elashoff J D, Grossman M I, 'Trends in hospital admissions and death rates for peptic ulcer in the United States from 1970 to 1978', *Gastroenterology*, 1980, vol. 78, issue 2, 280-5

<sup>768</sup> Fineberg H, Pearlman L A, 'Surgical treatment of peptic ulcer in the United States: Trends before and after the introduction of cimetidine', *The Lancet*, Jun 13<sup>th</sup> 1981, 1305-7

<sup>769</sup> Coggon D, '20 years of hospital admissions', op cit, 1302-4

<sup>770</sup> From Testimony T16

<sup>771</sup> From Testimony T5

<sup>772</sup> Vagotomy operations were usually only used for those patients with duodenal ulcers who had failed to respond to medical intervention.

advances in treatment of the condition medically. Then from 1976 until 1990, the vagotomy rate fell from 2798 that year to virtually zero and much of this has been credited to the introduction of new effective classes of drugs which doctors could use to manage peptic ulcers.

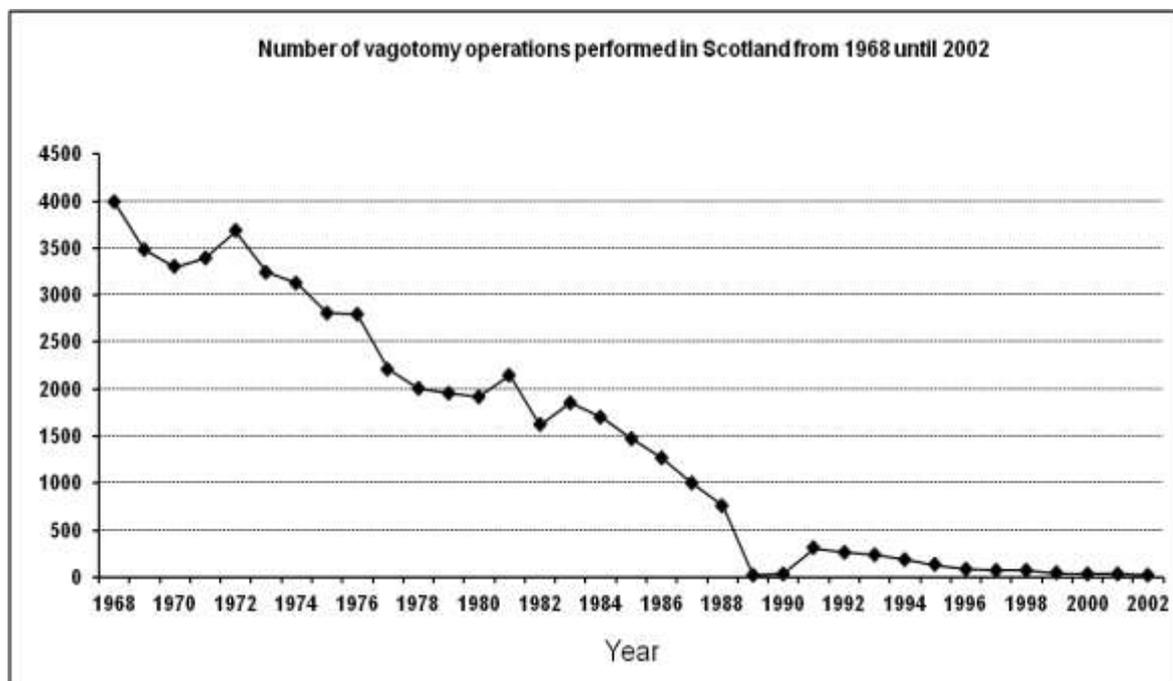


Figure 4

Data provided by Information Statistics Division of the Common Services Agency of the National Health Service in Scotland

No one had anticipated this change in disease incidence which occurred at a time of expansion of consultant numbers in the NHS in the UK. Between 1969 and 1973 the numbers grew from around 9,000 to 10,368 and it was projected that by 1978 there would be 11,386 consultants working in the NHS.<sup>773 774</sup> Gastroenterology as a specialty attracted many new recruits in response to its challenges which also included a large expansion of activity in the treatment of small and large bowel and liver conditions. The period also coincided with the introduction of the new Japanese and American fiberoptic endoscopes which were changing the understanding of peptic ulcer disease and other diseases of the intestines. This hitherto unavailable service promised better diagnostic results because lesions of the gastrointestinal tract at both ends could be directly visualised via endoscopes. This was the period when most witnesses interviewed for this thesis were in training and it was a time of change in the understanding and management of peptic ulcer disease.

<sup>773</sup> Editorial, 'Progress report on hospital staffing', *British Medical Journal*, Dec 6<sup>th</sup> 1969, supplement, 573

<sup>774</sup> Doran F S A, 'Expansion of the consultant grade', *British Medical Journal*, Mar 10<sup>th</sup> 1973, supplement, 74

## Conclusion to chapter six

This chapter has set the historical scene for the period after the war when the NHS came into being. Its main theme has been contemporary therapeutics both in terms of medication and of other treatments which were trialled. Despite much research, only one pharmaceutically useful drug was added to the physician's effective armamentarium over the period and doctors continued to rely on the old regimen of rest, diet and antacids. The development of promising new drugs has been discussed and few were found to be satisfactory when assessed using clinical trials. Of three new physical treatments attempted, only gastric irradiation showed any potential to be useful although it was inherently potentially dangerous and could only be recommended for those considered unfit for surgery. As a therapeutic answer to peptic ulcer was sought, the disease itself began to become more medically manageable and fewer people died from gastric ulcers from 1941 and from 1955 for duodenal ulcer. From 1970, the numbers of gastroenterologists grew as a part of a general expansion of consultants in the hospital service.

Chapter seven will approach the history of peptic ulcer disease from the beginning of the NHS until 1976 from the viewpoint of those who worked in it and will discuss aspects of treatments and patient care, interweaving the testimonies of witnesses who were involved at the time. The medical treatment of peptic ulcer in the community and in the hospital will be discussed before examining the rôle of surgeons in its treatment. It will be seen that in the absence of a unifying theory of the cause of peptic ulcer, doctors and surgeons treated it by trying to reduce the production of excess acid by the stomach. Surgical operations will be seen to be considered to be only effective solution for the patient who had chronic unremitting symptoms or whose life was in danger. A new operation will be discussed which had the promise of avoiding most of the serious after-effects associated with surgery but it did not receive universal acclaim. This period of the NHS will be seen to be a time when doctors from different medical disciplines began to work together in concert as a way of treating the complications of peptic ulcer disease.

## Chapter 7. NHS responses to the challenge of treating peptic ulcer diseases

### Introduction to chapter seven

The first six chapters of this thesis tell the history of peptic ulcer disease using published primary and secondary source material. Some oral testimonies are found in chapters five and six, but in this chapter the style of the history changes to allow those who played a part in it to give their accounts at first hand. It was not possible to find many witnesses from the early period of the NHS and there is no suggestion that experiences reproduced here represent a comprehensive account. However the witness testimonies, interspersed with the published record, bring life to the history and complement some of what has been written in the previous chapter in the period from the inception of the NHS up until 1976. This chapter discusses how patients received care for the treatment of their peptic ulcers in the hospitals and in the community and shows how gastroenterology emerged as a major specialty, at a time when surgeons were increasingly working with them in a new collegial manner. Throughout this period, surgeons were seeking to improve their operative results and towards its end, a new operation was introduced which promised better results than those which were regularly performed.

### 7. 1: The hospital experience

There is little doubt that peptic ulcer disease was a common and often dramatic illness in Britain as was seen in the previous chapter. It was calculated that in 1948, approximately 1,500,000 of the population of England and Wales had suffered from peptic ulcer at some time in their lives.<sup>775</sup> Estimates varied as to the relative proportions of each type of ulcer, but in Glasgow there were eight duodenal ulcers for every gastric ulcer, which was slightly commoner in women and generally found in an older age group of patients. In London, the duodenal/gastric ulcers ratio was lower due to there being relatively more gastric ulcers.<sup>776</sup> Richard Doll and Francis Avery Jones' 1951 survey of a sample of London patients showed that 6.5% of men and 1.7% of women had peptic ulcer based on their diagnostic criteria.<sup>777</sup> In the U.S.A., from 5 to 12 % of the population was affected.<sup>778</sup>

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<sup>775</sup> Avery Jones F, Pollak H, 'Civilian dyspepsia', *British Medical Journal*, Jun 9<sup>th</sup> 1945, 797-800

<sup>776</sup> Jamieson R A, Smith W E, Scott L D W, 'Peptic ulcer in Glasgow, a hospital survey', *British Medical Journal*, Feb 19<sup>th</sup> 1949, 298-300

<sup>777</sup> Quoted in Illingworth C F W, *Peptic Ulcer*, (Edinburgh, 1953, E&S Livingstone), pp69-70

<sup>778</sup> Ivy A C, 'The problem of peptic ulcer', *Journal of the American Medical Association*, Dec 28<sup>th</sup> 1946, vol. 132, 1053-9

Mr. M Kennedy Browne, a surgeon who started medical school in 1952, described his early experience of caring for patients with peptic ulcers.<sup>779</sup>

***MKB:** Well, in the early 50's and in the middle 50's, it was certainly the most common condition, I think, that one saw, although obviously most of it didn't come to the hospital, most of it was seen by the GP but, at that time, it was one of the commonest conditions presenting to the surgical person anyway. In these days, all one could give the patient, on the whole, was antacids in the way of medical treatment and vagal blocking agents and then if that didn't work or if the ulcer kept recurring, then surgery was the first line of treatment.*<sup>780</sup>

Margaret Haggart, a nurse, when asked of her first experiences of peptic ulcers recalled her first ward experience of patients with them in a male surgical ward in 1948.<sup>781</sup>

***MH:** Well I think probably it was of the gastrectomy, partial gastrectomy in a ward of thirty patients, I should think at any one time on the male ward (the females didn't have so many), I should think about eight patients for surgery. And we had an operating list twice a week on a Tuesday and a Friday. And each operating day I think the surgeons did two partial gastrectomies each operating day. So that was four, then they (the patients) would be in for about five or six days or a week ... they all went to a convalescent home for a week afterwards before they went home. Now of course the convalescent homes have gone.*

She remembers the problems associated with gastric surgery and gastric fistula was one particular post-operative complication which caused much distress to the patient and work for the nurses.

***MH:** ... I don't know whether it was the surgeons' technique or whatever, we had not a lot, but a few with a gastric fistula. Gosh, they were very hard to nurse and it took weeks sometimes for them to recover from this, they used to have it repaired and so on. And I suppose at any one time, no that's an exaggeration, possibly we would have about one every month or something like that.*

Isabel Duncan another nurse who started nursing in 1954 recalled her earliest experience of the management of peptic ulcer disease.<sup>782</sup>

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<sup>779</sup> The convention used by the author in this section of the thesis is to identify the witness by their initials in bold type and himself by his initials. The author is separately identified as **ACP**

<sup>780</sup> From Testimony T5

<sup>781</sup> From Testimony T19

<sup>782</sup> From Testimony T22

*ID: ... it was in that first ward I was in and we had a mixture of, in the gastrointestinal unit, patients coming in with massive haematemesis. And what was then just generally called peptic ulcers or they were duodenal or gastric ulcers. We had a lot of patients with oesophageal varices, which we didn't actually realise at that time I think, was due to a lot of alcoholism. ... we did always lose one or two patients with massive haematemesis that we just couldn't stop.*

*ACP: How were they being treated in the ward?*

*ID: They were being treated conservatively to start with, if you came in with a haematemesis you weren't operated on immediately because I think there probably wasn't enough blood in the way of blood transfusions.<sup>783</sup>*

*ACP: Did you transfuse early?*

*ID: Yes by that time we had bottles of blood coming in and the haematology unit was expanding. And we had proper blood transfusions coming in and that was in the middle fifties and before that patients who were bleeding came in and were put on drips.*

*ACP: Milk drips?*

*ID: Milk drips, saline drips and dextrose, that was the great thing, dextrose drips. And there was another one that was called Lehman's solution. And everybody was dripped because they were all dehydrated.<sup>784</sup>*

*ACP: And it was a 'wait and see situation'?*

*ID: It was a 'wait and see', to see if they could heal the ulcer first with milk drips and slowly introduce solids and hope... and of course they were all subjected to these ghastly barium meals, barium swallows etc.*

Another dramatic presentation of peptic ulcer disease was of patients with perforations being admitted as emergencies.

*ID: We saw perforations coming in.*

*ACP: Can you remember what kind of state these patients were in?*

*ID: Very poor and very dehydrated always. And very shocked.*

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<sup>783</sup> Miss Duncan is saying here that an 'expectant regime' was employed and that only those who did not respond to intravenous drip therapy and later by intra-gastric milk drip were operated upon.

<sup>784</sup> Milk drips were given via a naso-gastric tube into the stomach. The other substances were given intravenously.

*ACP: Were these late presentations?*

*ID: A lot of them were patients who also had other illnesses such as alcoholism and heavy smoking. Many patients presented with infections on admission.*

*ACP: Infections of?*

*ID: Terrible chest infections and pneumonia, the whole thing was complicated. A lot of patients with septicaemia just didn't make it. Some wounds would break down, this was the great thing too, trying to stop the wounds breaking down.*

*ACP: Can you remember another group of patients, just your ordinary chap of 25yrs, suddenly being struck down with a perforation, do you remember these chaps coming in?*

*ID: Yes that was often amongst the labouring classes who had poor diets and used to drink a lot and smoke a lot. And a lot of those young men did come in and a lot of the post war soldiers were ill and poorly you know. They used to come in very ill and very malnourished. I think money was very scarce.*

These testimonies give a flavour of the severe nature of peptic ulcer disease in the early years of the NHS.

## 7. 2: Medications for peptic ulcer disease and the rôle of the community pharmacist

The commonest medication used for dyspepsia was bicarbonate of soda and most homes would have a supply obtained from their local pharmacist, better known as a 'chemist' in Scotland. Mr. John Linn, a pharmacist who trained in 1950, spoke of its use in Glasgow, 'the standard then for any stomach upset in a Scottish household was baking soda. A teaspoon of baking soda stirred into water and as you know the side effect was CO<sub>2</sub> and a big belch and, "That's me, I'm off to work", that was the standard remedy for upsets.'<sup>785</sup> The *British National Formulary* of 1955 says, 'The lay public uses baking soda (sodium bicarbonate) freely in a dose of half to one teaspoonful to relieve gastric pain, heartburn and flatulent dyspepsia. The striking advantage of sodium bicarbonate is in the rapidity of its action. A sudden evolution of carbon dioxide is usually followed by voluminous eructations which contribute to the feeling of well-being by relieving the sense of

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<sup>785</sup> From Testimony T6. As can be seen in the section of 'dyspepsia' in chapter 1, patients had a vague understanding of that which was causing their upper abdominal discomfort and gave it many names, one of which, in the West of Scotland was, 'an upset tummy'. Today this is more likely to refer to an episode of diarrhoea.

fullness.<sup>786</sup> If patients could get relief of symptoms with their self medication, then it was unlikely that they would seek medical advice, but as a pharmacist, Mr. Linn always provided the advice, ‘Take this, try this and if it doesn’t get any better then you’ll have to go and see your doctor.’ There were many over-the-counter remedies available to patients who wished to self medicate.<sup>787</sup> Mr. Linn, talking of the period before the NHS began, said, ‘Doctors had to be paid (for their consultations), so people would ask for advice at the Chemist. The ingredients of products did not have to be stated, so the chemist could buy bulk quantities of analgesics, for example, put 25 in a bottle labeled, ‘Mr. Smith’s pain killer’ (aspirin) or ‘Mr. Smith’s strong painkiller’ (codeine compound). This was profitable for the pharmacist. At the start of the NHS, doctors’ prescriptions were provided free of charge. Ingredients were still not shown on labels and medicines were labeled ‘The Tablets; one, three times a day’ or whatever. Another was the famous, ‘The Mixture; as before’.

OTC medication sales were influenced by advertising. Mr. Linn tells of an advert for antacid tablets,

*The popular antacid was Rennie’s. Now Rennie’s had an advert and I think in later times they had to stop advertising, it was a picture of a carpet with a burn hole in it and it said, ‘There is enough acid in your stomach to burn a hole in your carpet, Rennie’s will stop this.’*

In the 1950s, Rennie’s advertised to the public with light-hearted cartoons and the product continues to this day as a remedy for indigestion.<sup>788</sup> The fact that there were so many products available for the treatment of dyspepsia and peptic ulcer suggests that there was no clear leader in the field. Word of mouth played an important part in the success of drugs. An example is that of ‘Roter tablets’ which first appeared on the market in 1948. Mr. Linn humorously recounts the tale of the man with an ulcer speaking in his shop for all to hear,

*Oh aye Willie, it was all fish and these milk puddings (before starting Roter tablets). He’s got these Roter tablets and now it’s all fish suppers, curries and stews.*

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<sup>786</sup> ‘Antacids’, *British National Formulary*, (London, 1955, The British Medical Association and The Pharmaceutical Society of Great Britain), p20

<sup>787</sup> The well-known antacids included; Rennies, Alka-seltzer, Milk of Magnesia, Bisma Rex, Bismag-Bisurated Magnesia, Moorland’s tablets and Queens Health and Liver Salts. There were many more available.

<sup>788</sup> Antacid adverts from the 1950s can be found at <http://www.historyworld.co.uk/admusem.php?l1=Medicines+%26+Health&l2=Indigestion> 4<sup>th</sup> April 2012

Such a commendation was bound to appeal to other patients whose lives were dominated by a medically-advised bland diet. Later he recalled the liquid mixture ‘Pepto-bismol’ which, originating in the USA, was imported and was similarly promoted by patients by word of mouth in his community. It is of interest that both Roter tablets and Pepto-bismol contained bismuth as an active ingredient. Both were also obtainable by prescription. There were many other proprietary antacids sold or prescribed, the choice of which was often a matter of patient preference.

At the start of his career as a pharmacist in Glasgow, Mr. Linn recorded that his job was very physical involving the mixing of ingredients to make up prescriptions. One of the most common remedies for dyspepsia was ‘the powder’. “‘The powder’...of course was prescribed in the old grains<sup>789</sup> and it was, I think, a ¼ grain of extract of belladonna, ¼ grain of phenobarbitone and 5 grains of magnesium carb pond. This is what they call nowadays “labour intensive” because these were prescribed in [packets of] 60’s and all the papers had to be laid and weighed out and folded.’

Mr. Joseph Smith was another pharmacist who worked in Glasgow who described a different powder which was available privately.<sup>790</sup> Dr Marlow was a Glasgow general practitioner in the 1950s who was well-known to patients for his particular stomach remedy and saw them for a fee, providing private prescriptions for a powder mixture which was dispensed by a pharmacist named Reynolds in Partick, a district of Glasgow.<sup>791</sup> The prescription was made up basically of five ingredients: there were three antacids, magnesium oxide, magnesium trisilicate, bismuth subnitrate mixed with phenobarbitone and belladonna. It is evident that this prescription was bought by patients dissatisfied with their general practitioner’s prescribing or OTC products. It is of particular interest that these powder prescriptions do not appear in any pharmacopœia and colleagues working in the hospital service who were interviewed were unaware of their existence. The pharmaceutical industry however was aware of the potential benefits of both belladonna and barbiturates since they produced the tableted products ‘Neutraddon’ and ‘Neutraddon Sed’. The former drug is a mixture of an antacid with belladonna alkaloids and the latter is the same but with a small dose of amylobarbitone (a barbiturate) and

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<sup>789</sup> Grains were imperial measures of weight used by pharmacists in the pre-metric era, one grain being equivalent to approximately 65mgs.

<sup>790</sup> From Testimony T27

<sup>791</sup> This type of private prescription was not unique to Glasgow. A photograph of an example from 1912 may be seen reproduced as figure 6 in Pounder R, *Wellcome Witnesses to Twentieth Century Medicine, volume 14, Peptic Ulcer: Rise and Fall*, edited by D.A. Christie and E.M. Tansey, (London, 2002, The Wellcome Trust), p54. Pounder’s illustrated prescription contained morphine as an ingredient.

ascorbic acid added. Other pharmaceutical companies made products using similar active ingredients for the treatment of peptic ulcers.

Towards the end of the decade, the work of the retail pharmacists changed and powders disappeared and the ‘making up’ of most prescriptions ceased. Dispensing largely became a matter of correctly providing and counting pills and lifting prepared liquids and creams and ointments off the shelf to give to customers.<sup>792</sup>

### 7. 3: Peptic ulcer disease in general practice

The general practitioners interviewed for this section were of a younger generation than the first five witnesses quoted above.<sup>793</sup> Their job was essentially the same as those of the generation who worked at the time of the inception of the NHS acting as a patient advocate in what has been called, ‘the gatekeeper rôle’, between community and hospital. In the period from 1948 and 1970, although many pharmaceutically active substances had been trialled, there was no new drug found to effectively treat duodenal ulcer although carbenoxolone and similar drugs had been shown to heal gastric ulcers. New operations were being trialed but their efficacy was still in dispute at this time. In the hospitals there were refinements in practice in terms of patient care with improvements in the management of seriously ill patients and death rates from peptic ulcers were beginning to decrease.

For the general practitioner, peptic ulcer disease was an issue of management and treatment in the surgery and of arranging hospital care in emergencies or as outpatients when complications arose. Most managed dyspepsia symptomatically, often using the same medications to treat duodenal and gastric ulcers, even though they were believed to be different diseases. A general practitioner might treat a dyspeptic patient for many years without further investigation but if the patient’s condition changed and was causing concern, because of such instances as uncontrolled pain, weight loss or a minor haematemesis, at this point the patient would be referred to a hospital consultant. The general practitioners working in the West of Scotland after 1970 had the right to order barium meals for their patients and had access to a full range of laboratory tests to give a clearer picture of his patient’s condition. In other parts of the UK this was not the case and the out-patient consultant-led hospital service was used as a filter to general practitioner requests for diagnostic imaging both by contrast X-ray and ultrasound. There is ample

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<sup>792</sup> Mr. Smith said that by 1958 after coming out of National Service in the army, he never made up any mixtures or powders or made any pills on prescription again.

<sup>793</sup> For a fuller account of how general practitioners work see testimonies T10, T14, T24 and T26.

evidence that this ‘safeguard’ to avoid unnecessary X-rays being ordered by general practitioners was not needed, for when the results of their directly referred requests were compared with those from hospital outpatients, their positive diagnostic rates matched those of the outpatient specialist requests and it was found that they requested repeat examinations less often.<sup>794</sup> Similar studies of diagnostic rates for general practitioner requests for ultrasound studies of the upper abdomen also compared favourably with those of their hospital colleagues.<sup>795</sup> Both articles referred to in this paragraph also emphasised the value to both general practitioner and patient of a negative result. Dr Ramsay Vallance, a consultant radiographer working in Glasgow from the early 1970s, spoke about general practitioner access for barium meals.<sup>796</sup>

*ACP: As the years passed, general practitioners got more and more access for outpatient investigations, could you say something about that?’*

*RV: Yes. ... we certainly welcomed that, I thought that anything that speeds up the patient journey, within reason, was to be encouraged, and to a large extent my experience of general practitioner referrals was very positive. Usually the clinical history was helpful and full and relevant so I think it was a very good development to a large extent.*

In an emergency the hospital referral pathway for the general practitioner was uncomplicated. Most hospitals regarded haematemesis as a medical problem. Patients with possible perforations would be admitted straight to the surgical wards. It is known that peptic ulcer perforations may present late and sometimes appear to be appendicitis and all the problems associated with septicaemia and other causes of shock may seriously threaten the life of the patient.<sup>797</sup> Elderly patients are at particular risk of adverse outcomes.<sup>798</sup> Dr David Ramsay, a general practitioner who worked in East Kilbride, spoke of the initial difficulty of distinguishing between a perforation and a myocardial infarction (heart attack).<sup>799</sup> The diagnostic problem was not unique to him as confirmed by the testimony of Dr Gordon Allan, a consultant gastroenterologist in Glasgow.<sup>800</sup>

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<sup>794</sup> Bury R F, ‘Editorial: General practice radiology – the poor relation’, *Radiology*, Oct 1990, vol. 42, issue 4, 226-7

<sup>795</sup> Charlesworth C H, Sampson M A, ‘How do general practitioners compare with the outpatient department when requesting upper abdominal ultrasound examinations?’, *Clinical Radiology*, May 1994, vol. 49, issue 5, 343-5

<sup>796</sup> From Testimony T11

<sup>797</sup> Mayer H W, ‘Perforations of the intestinal tract’, *Annals of Surgery*, Mar 1940, vol. 111, no. 3, 383-4

<sup>798</sup> Walt R, Katschinski B, Logan R, et al, ‘Rising frequency of ulcer perforation in elderly people in the United Kingdom’, *The Lancet*, Mar 1<sup>st</sup> 1986, 489-92

<sup>799</sup> From Testimony T10

<sup>800</sup> From Testimony T9

## 7. 4: Gastroenterology as a specialty in hospitals 1948-72

In the ‘medical side’ of the hospital service, there was slow but gradual development of specialties where interested individuals developed skills to treat specific illnesses. Specialisation was not new and had been introduced in the nineteenth century for treating diseases of the ears, the eye, the nose and throat, children and most of the organs of the body. Roy Porter records that, ‘by 1860 there were at least sixty-six special hospitals and dispensaries in London alone’.<sup>801</sup> The NHS drew the specialty hospitals under its wing and by 1948 there were specialties operating in the larger hospitals. However within general medicine, (and general surgery), a new wave of specialization was growing in response to a need for better understanding and treatment of common disorders. Gastroenterology was one such specialty which emerged in the 1960s.

The formation of what became the British Society of Gastroenterology in 1945 was first suggested by Arthur Hurst in 1936 as a kind of gentleman’s club, forty in number, of those interested in the subject.<sup>802</sup> It began to hold annual symposia and the numbers of interested doctors increased and international meetings were attended and hosted. In 1960, it began publishing its own specialized journal, *Gut*. In its opening editorial, Harold Edwards made the point that, ‘Though no one can doubt that gastroenterology demands special application for the better understanding of its manifold problems, it is not in itself a specialty.’<sup>803</sup> It may have been that in writing this, Edwards was reflecting one view of past years of specialists that, ‘their minds are narrowed, judgment biased and unbalanced by disproportionate knowledge of one subject’ and the patient would suffer because the specialist, ‘knows nothing of the constitutional idiosyncrasies of the individual, which are essential to correct diagnosis and treatment’.<sup>804</sup> Specialisation nevertheless had by 1960 become an accepted part of medical life which was to increase as new sub-divisions of practice appeared, often generated by new technological advances, which had opened new areas of study.<sup>805</sup>

In the next decade, doctors with ‘special interests in gastroenterology’ were appointed to the larger hospitals but these ‘specialists’ worked within a general medical setting taking their turns in emergency receiving work and doing the work of general physicians for

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<sup>801</sup> Porter R, *The Greatest Benefit To Mankind: A Medical History of Humanity from Antiquity to the Present*, (London, 1997, Fontana Press), p386

<sup>802</sup> Hunt T, ‘History of the British Society of Gastroenterology’, *Gut*, Mar 1960, vol. 1, no 1, 2-5

<sup>803</sup> Edwards H C, ‘Foreword’, *Gut*, Mar 1960, vol. 1, no. 1, 1

<sup>804</sup> Porter R, *The Greatest Benefit*, op cit, p388

<sup>805</sup> Bynum W F, *Science and the Practice of Medicine in the Nineteenth Century*, (Cambridge, 1994, Cambridge University Press), pp191-6

much of the time, as well as offering specialist clinics and services such as endoscopy, which distinguished them from general physicians. It should be noted in this context that the gastroenterologist's remit was the whole of the alimentary canal and liver but excluding the mouth and throat. Endoscopy was a skill used by surgeons too but some of whom were mistrustful of physicians' findings and often insisted in repeating endoscopy examinations on patients who had been endoscopically examined by gastroenterologists.<sup>806</sup> The history of the development of endoscopy was described in chapter three.

The initial clinical indication for gastroscopy was where there was a disparity between the clinical history and the radiological findings. At times when a serious lesion was suggested by patient history and physical examination and when barium meal did not confirm the diagnosis then gastroscopy was able to clarify the picture in at least a proportion of cases. Much later, gastroenterologists specialized within their specialty. Two of our witnesses exemplify this, Dr Gordon Allen developed an interest in inflammatory bowel disease and Dr Alistair Beattie's interest was liver diseases. They nevertheless were involved with all the other aspects of gastroenterology and had to do general medical work as well.<sup>807</sup> It must be emphasized that at this point the bulk of the work for gastroenterologists was with chronic duodenal ulcer.

## 7. 5: Peptic ulcer and the surgeon 1948-1972

At the same time as gastroenterology was developing, surgery was changing insofar as the operation used for the treatment of duodenal ulcers was switching from partial gastrectomy in its many forms to that of vagotomy and drainage. Mr. Colin Mackay, who qualified in 1961, had not seen partial gastrectomies done for chronic duodenal ulcers, only for gastric ulcers.<sup>808</sup> Under Professor Andrew Kay's leadership, the academic surgical unit in the Western Infirmary in Glasgow had moved on to vagotomy and drainage procedures.<sup>809</sup> It was recognized that, in terms of effectiveness of preventing ulcer recurrence, the partial gastrectomy combined with vagotomy brought the best results but it carried a higher mortality in non-specialist units. Many surgeons considered the small differences in outcomes to be so slight that they could offer partial gastrectomy if vagotomy and drainage failed. In most NHS hospitals, peptic ulcer surgery was performed by general surgeons and on every operating list, there would probably be two ulcer operations performed. Gall bladder surgery was common also. The thinking behind the move to vagotomy and

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<sup>806</sup> From Testimonies T28 and T13

<sup>807</sup> From Testimonies T9 and T8

<sup>808</sup> From Testimony T7

<sup>809</sup> 'Drainage procedures' refers to surgical reconstruction of the stomach outlet.

drainage has an experimental rationale which is outlined in the next few pages for there was an ongoing debate about the 'best operation' for different peptic ulcers diseases which divided surgical opinion.

In 1956, the Royal Society of Medicine published the contents of a symposium called, 'Discussion of the surgical management of uncomplicated duodenal ulcers'. Large published series had shown that recurrence rates of ulcer formation in operations for treatment of duodenal ulcer were high. Different series varied in their recurrence rates. Gastroenterostomy alone had a recurrence rate of 30 - 40%, Billroth I gastrectomy had a recurrence rate of 8-12%, Polya gastrectomy had a recurrence rate of 1-6%, and vagotomy and gastroenterostomy had a recurrence rate of 4.7-12%.<sup>810</sup> Mortality rates for any gastrectomy were twice those of vagotomy and gastroenterostomy operations. The Polya gastrectomy gave the least ulcer recurrences with Billroth I gastrectomy and vagotomy and gastroenterostomy being approximately equal. The Polya gastrectomy removed so much of the stomach that the long term problems of gastrectomy became an increasing problem with the passage of the years. In 1956, vagotomy and gastroenterostomy was a relatively new operation and its long-term sequelae were not fully understood, however Melville Capper showed that approximately 85% of patients were satisfied with its results three to five years afterwards. He added that satisfaction rates of 70% had been recorded for gastroenterostomy alone over the same period.<sup>811</sup>

In 1957, a study was made of three aspects of patient life following different operations for the relief of duodenal ulcer to ascertain the effects of the presence of biliary regurgitation, the ability to take a normal sized mixed meal and dumping.<sup>812 813 814</sup> The outcome showed that there was no difference with biliary regurgitation between partial gastrectomy and vagotomy and gastroenterostomy but dumping was less after vagotomy and gastroenterostomy, which caused fewer nutritional problems in the long term. Anaemia

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<sup>810</sup> Capper W M, in 'Discussion of the surgical management of uncomplicated duodenal ulcers', *Proceedings of the Royal Society of Medicine*, Section of Surgery, Aug 1956, vol. 49, issue 8, 503-6

<sup>811</sup> Capper W M, 'Discussion of the surgical management', *ibid*, 505

<sup>812</sup> 'Biliary regurgitation' or 'bile reflux' occurred after the protective valve mechanism of the pylorus had been removed or by-passed in a drainage procedure and allowed bile to back-flow into the stomach.

<sup>813</sup> Cox H T, Kerr D F, 'Comparison of side-effects after partial gastrectomy and vagotomy and gastroenterostomy', *British Medical Journal*, May 25<sup>th</sup> 1957, 1211-4

<sup>814</sup> Dumping. An unpleasant symptomatic complication of gastric surgery whereby uncontrolled amounts of food, usually not fully prepared, passes into the small intestine which reacts causing various discomforts including nausea, vomiting, diarrhoea and abdominal pain. They also may feel faint, dizzy, weak, tired and experience palpitations shortness of breath and sweating among other symptoms. See Hobsley M, 'Dumping and diarrhoea', *British Journal of Surgery*, Oct 1981, vol. 68, issue 10, 681-4

was a major problem following partial gastrectomy as was chronic weight loss.<sup>815 816</sup> In 1959, a relatively newly-noticed after-effect of vagotomy, that of diarrhoea, was mentioned in a Royal Society of Medicine symposium called a ‘Discussion on the surgical management of chronic duodenal ulcer’.<sup>817</sup> Three years after the 1956 symposium, surgeons were in a better position to evaluate different procedures for the treatment of chronic duodenal ulcer and from the discussions it appeared that the operation of vagotomy and gastroenterostomy was at least as good as partial gastrectomy in terms of results.<sup>818</sup> At the symposium, Lester Dragstedt reminded delegates that, ‘Death is the worst thing that can happen to a duodenal ulcer patient, and the mortality of even low gastric resection is four to eight times greater than that of gastroenterostomy.’<sup>819</sup> In 1960 Charles Illingworth reviewed the post-gastrectomy syndromes in *Gut*, which discussed the severe problems which 9.4% of ulcer patients suffered after surgical intervention.<sup>820</sup> The way was opening to vagotomy and drainage operations to become the standard operation for the relief of duodenal ulcer in the UK.

Professor John C Goligher of Leeds published several important studies concerning operations for duodenal ulcer from 1964 until 1972. Professor David Johnston who worked with him over the period summarised the very detailed outcomes as follows:

*... read Goligher’s perspective randomised controlled trial and look at the results and you will see that after five to eight years, the so called ‘Visick grades’ or function of these patients was better after gastric resection than after truncal vagotomy and pyloroplasty.<sup>821</sup> That is, the patients’ post surgery functional grades were better after partial gastrectomy and partial gastrectomy and truncal vagotomy than after truncal vagotomy and gastrojejunostomy or truncal vagotomy and pyloroplasty.<sup>822</sup>*

<sup>815</sup> Macintyre H W, Stent L, ‘Anaemia following partial gastrectomy’, *British Journal of Surgery*, Sep 1956, vol. 44, issue 184, 150-1

<sup>816</sup> Aldersberg D, Hammerschlag E, ‘The postgastrectomy syndrome’, *Surgery*, 1947, vol. 21, issue 5, 720-9

<sup>817</sup> Burge H, in ‘Discussion of the surgical management of chronic duodenal ulcers’, *Proceedings of the Royal Society of Medicine*, Section of Surgery, Oct 1956, vol. 52, issue 10, 835-46, esp p839

<sup>818</sup> Holt R L, and Feggetter G Y, in ‘Discussion of the surgical management of chronic duodenal ulcers’, *Proceedings of the Royal Society of Medicine*, Section of Surgery, Oct 1956, vol. 52, Issue 10, 837-9

<sup>819</sup> Dragstedt L R, in ‘Discussion of the surgical management of chronic duodenal ulcers’, *Proceedings of the Royal Society of Medicine*, Section of Surgery, Oct 1956, vol. 52, issue 10, 835-6

<sup>820</sup> Illingworth C F W, ‘Post-gastrectomy syndromes: a review’, *Gut*, Sep 1960, vol. 1, issue 3, 183-92

<sup>821</sup> Visick A H, ‘A study of the failures after gastrectomy’, *Annals of the Royal College of Surgeons of England*, 1948, vol. 3, Issue 5, 266-84

<sup>822</sup> Goligher J C, Pulvertaft C N, de Domball F T, et al, ‘The 5-8 year results of the Leeds/York Controlled Trial of elective surgery for duodenal ulcer’, *British Medical Journal*, Jun 29<sup>th</sup> 1968, 781-7; Goligher J C, Pulvertaft C N, de Domball F T, et al, ‘Clinical comparison of vagotomy and pyloroplasty with other forms of elective surgery for duodenal ulcer’, *British Medical Journal*, Jun 29<sup>th</sup> 1968, 787-9; Goligher J C, Pulvertaft C N, Irvin T

... the scientific facts in that trial were that truncal vagotomy and gastrojejunostomy didn't produce clinically superior results to gastric resection, whether with or without vagotomy. Of course, the lowest recurrence rate is with vagotomy combined with antrectomy, since it removes the acetylcholine and it removes the gastrin.<sup>823</sup> But it was also interesting that Goligher and his team did a huge number of truncal vagotomies and pyloroplasties and the results of truncal vagotomy and pyloroplasty were even worse than the results of truncal vagotomy and gastrojejunostomy, with a higher recurrence rate, and Visick grades which I think were about sixty four percent Visick one and two, which were the good grades, versus somewhere between seventy and eighty percent for gastric resection. These were the figures: I think at the level of statistical significance it wasn't very convincing in terms of p values but it was worse anyway. It certainly wasn't better. You could say very firmly that it wasn't better and it was probably worse.<sup>824</sup>

In 1968, Alan Cox published a paper examining the symptomatic results of 106 patients from Professor Kay's unit in Glasgow who had had either a partial gastrectomy or a vagotomy and pyloroplasty in the period 1954 and 1960.<sup>825</sup> The outcomes when statistically analysed showed little real differences between each operation but on clinical evaluation, approximately 10% of patients were encountering moderate and severe symptoms and this rose to over 16% when reported by patients themselves. Interestingly while there was no statistical difference for diarrhoea between the two groups, the figures indicate that 21% had episodic diarrhoea and others had frequent daily stools. Despite the fact that vagotomy and pyloroplasty was not the best operation in terms of all its outcomes, it became the routine operation for relief of chronic duodenal ulcer in many places in the UK in the 1960s and mid 1970s because it was perceived to be the most 'physiological' in its design and had relatively few post-operative symptoms referable to alimentary disturbance.<sup>826</sup> <sup>827</sup> Nevertheless in 1972, based upon his assessment of his results of performing truncal vagotomy and pyloroplasty for the treatment of duodenal ulcer, Professor Goligher said of it, 'Under the circumstances we feel considerable misgivings

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T, et al, 'Five to eight year results for truncal vagotomy and pyloroplasty for duodenal ulcer', *British Medical Journal*, Jan 1<sup>st</sup> 1972, 7-13

<sup>823</sup> Acetylcholine is a neurotransmitter substance which is secreted by the nerve endings in the stomach which stimulate gastric secretion.

<sup>824</sup> From Testimony T21

<sup>825</sup> Cox A G, 'Comparisons of symptoms after vagotomy with gastroenterostomy and partial gastrectomy', *British Medical Journal*, Feb 3<sup>rd</sup> 1968, 288-90

<sup>826</sup> Goligher J C, Pulvertaft C N, de Domball F T, 'Clinical comparison of vagotomy and pyloroplasty' op cit, 789

<sup>827</sup> Goligher J C, Pulvertaft C N, Irvin T T, 'Five to eight year results', op cit, 7-13

about continuing to accord to this operation pride of place in the elective surgical treatment of duodenal ulcer.<sup>828</sup>

## 7. 6: The emergence of a new surgical approach

Duodenal ulcer continued to dominate surgical working time and research and after almost two decades of experience with vagotomy operations, it was evident to those treating peptic ulcers that if the production of acid within the stomach could be reduced surgically or medically, then gastric and duodenal ulcers would heal. Surgery offered a permanent cure whereas medication offered only continuous treatment but surgery could also cause iatrogenic pathology. Professor McColl, when asked his opinion of surgery for peptic ulcer in 2003, responded,

*The ulcer surgery was fairly effective in preventing recurrence of the ulcer ... it was a figure of something like for vagotomy and pyloroplasty, 80% of the ulcers would be prevented from recurring. If you went on to the more aggressive surgery, like partial gastrectomy, you used to get about 90-95% preventive recurrence. The problem though was that the surgery involved drastically altered the normal anatomy and physiology of the upper gastro-oesophageal tract and these patients ended up, ... many of them, with long-term morbidity related to the surgery. There would always be a small mortality but certainly long-term morbidity and a lot of these patients would have bilious vomiting, they'd have diarrhoea, they would feel full up after their meals, they often didn't really gain their normal weight. Certainly, after partial gastrectomy, they never did. They were subject to anaemia occasionally, iron deficiency, rare problems with dumping syndrome as we talk about, when they got very weak and faint after a meal and could become hypoglycaemic ...*<sup>829</sup>

In 1957, in an attempt to reduce dumping as a problem with gastric surgery, Charles Griffith and Henry Harkins in the Department of Surgery of the University of Washington School of Medicine in Seattle, performed some laboratory experiments on dogs to selectively cut the vagal fibres to the parietal cell mass of the stomach in an attempt to eliminate the cephalic phase of vagally mediated acid out-put.<sup>830 831 832</sup> The results showed

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<sup>828</sup> Goligher J C, Pulvertaft C N, Irvin T T, 'Five to eight year results', op cit, 12

<sup>829</sup> From Testimony T1

<sup>830</sup> The parietal cell mass is the part of the body of the stomach where all the parietal cells, which are those which produce acid, are located.

<sup>831</sup> The cephalic phase of digestion occurs where acid is secreted into the stomach before and during the start of eating and swallowing. It is a vagal response to the sight, smell and swallowing of food.

that in dogs, it was possible to reduce acid output by selective cutting of particular vagal fibres without having to do a drainage procedure. Griffith and Harkins' paper influenced many surgeons who later adopted selective vagotomy in an attempt to reduce after effects of vagotomy.<sup>833</sup> <sup>834</sup> A more refined operation was attempted in 1969 in the same laboratory where a more selective vagotomy was performed to block all vagal input to the parietal cell mass.<sup>835</sup> The results remained inconclusive in terms of reducing gastric secretion to the point of preventing the 'ulcer diathesis'. Nevertheless selective vagotomy began to offer the possibility of vagotomy without a drainage procedure which was believed to be responsible for most of the problems of dumping which occurred with vagotomy and pyloroplasty or gastroenterostomy and early experimental surgery looked very promising in this respect. It should be remembered that Latarjet and later Dragstedt had found that the stomach did not empty properly following truncal vagotomy and they solved this problem by adding a gastroenterostomy.

The drainage procedures of gastroenterostomy and pyloroplasty destroyed the sophisticated control outlet valve of the stomach provided by the pylorus and created what Sam McKelvey called 'an incontinent stomach'.<sup>836</sup> He was interested in post-vagotomy diarrhoea and dumping. A suggested answer to these two complaints might be a more selective form of vagotomy and the avoidance of destruction of the pylorus or of the creation of a different outlet. The operation of highly selective vagotomy (HSV) or parietal cell vagotomy (PCV) seemed to promise such a solution. David Johnston, who later became Professor of Surgery in Leeds, was one who took an early interest in highly selective vagotomy.<sup>837</sup> He described his experiences,

*That led me to do a great deal of background reading on duodenal and intestinal mechanisms of negative feedback on the stomach, both negative feedback on*

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<sup>832</sup> Griffith C A, Harkins H N, 'Partial gastric vagotomy: an experimental study', *Gastroenterology*, 1957, vol. 32, 96-102

<sup>833</sup> The vagus nerve innervates all of the different parts of the stomach including the pylorus which controls the rate of emptying of the stomach. It sends a branch to the liver and also to gallbladder which affects the timing of its function in the digestive process and branches to the duodenum where secretion is stimulated by it. The, pancreas and intestines are also vagally innervated. In selective vagotomy the surgeon isolates and spares the branch of the vagus to the liver and gallbladder before cutting the main trunk of the vagus supplying the whole stomach.

<sup>834</sup> Truncal vagotomy may lead to gallstone formation, see Ihasz M, Griffith C A, 'Gallstones after vagotomy', *American Journal of Surgery*, Jan 1981, vol.1, 48-50

<sup>835</sup> Amdrup B M, Griffith C A, 'Selective vagotomy of the parietal cell mass, Part 1', *Annals of Surgery*, Aug 1969, vol. 170, 207-14; Amdrup B M, Griffith C A, 'Selective vagotomy of the parietal cell mass, Part 2', *Annals of Surgery*, Aug 1969, vol. 170, 215-20

<sup>836</sup> McKelvey S T D, 'Gastric incontinence and post-vagotomy diarrhoea', *British Journal of Surgery*, Oct 1970, vol.57, no.10, 742-7

<sup>837</sup> From Testimony T21

*motility and stomach emptying, and negative feedback on secretion, because the two themes were intertwined, if you like.*

*So I studied in great detail the inhibitory mechanisms on the stomach and became aware of the needless effects of vagotomy. Take the gall bladder and biliary system for example, the gall bladder after a truncal vagotomy but not after selective and highly selective [vagotomies] becomes dilated, there is a greater chance of stasis and a higher incidence of gall stones ... And likewise pancreatic function is not as good, small bowel function is not as good and physiological regulation of gastric emptying is not as good. and showing quite definitely there was significantly more post vagotomy diarrhoea after truncal vagotomy than after selective vagotomy.<sup>838</sup>*

Johnston was not alone in being interested in reducing the potential harm done by surgeons as they treated duodenal ulcer. His testimony quotes others who used selective vagotomy as a solution, ‘Amdrup in Denmark, Terence Kennedy in Belfast, Harold Burge in London, and Grassi in Rome, these were some of the pioneers.’ David Johnston and Alan Wilkinson began to perform the operation of highly selective vagotomy and their first publication was a précis of a paper presented to the Joint Meeting of the Surgical Research Society, the Society of University Surgeons and the European Society for Experimental Surgery in June/July 1969 and published in the *British Journal of Surgery*.<sup>839</sup> The paper briefly outlined the results of their first 15 HSV operations and in 1970, a comprehensive paper in the *British Journal of Surgery* followed in which they added their experience of ten more patients. This paper illustrated the anatomy of the vagus nerve over the surfaces of the stomach and described the surgical technique of HSV.<sup>840</sup> Contemporaneously with Johnston, Erik Amdrup in Copenhagen was developing HSV and publishing parallel research papers but calling the operation ‘parietal cell’ vagotomy (PCV).<sup>841</sup> Along with others, Johnston and Amdrup published many research articles in medical and surgical journals over the next twelve years and confirmed that HSV was a safe operation in the right hands which considerably reduced the iatrogenic effects of both truncal and selective vagotomy. However it took time to assess the operation as a routine treatment for

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<sup>838</sup> Abridged quote from Testimony T21

<sup>839</sup> Johnston D, Wilkinson A, ‘Selective vagotomy with innervated antrum without drainage procedure for duodenal ulcer’, *British Journal of Surgery*, Aug 1969, vol. 56, no 8, 626

<sup>840</sup> Johnston D, Wilkinson A, ‘Highly selective vagotomy without a drainage procedure in the treatment of duodenal ulcer’, *British Journal of Surgery*, Apr 1970, vol. 57, no 4, 289-96

<sup>841</sup> See Testimony T21 and Amdrup E, Jensen H E, ‘Selective vagotomy of the parietal cell mass preserving innervations of the undrained antrum’, *Gastroenterology*, Oct 1970, vol. 59, 522-7

duodenal ulcer. Johnston also tested HSV for treatment of gastric ulcer but it did not displace more traditional approaches to its surgical treatment.<sup>842</sup>

The results of HSV were variable and seemed to depend on the surgeon performing the operation and Johnston found that some surgeons were poor vagotomists, something he had discovered early in his career with failed truncal vagotomy operations performed by others.<sup>843</sup> A study published in 1981 of HSV surgical results further demonstrated that results were dependent upon the skill levels of different surgeons.<sup>844</sup> Overall in Johnston's unit, a recurrence rate for ulcer formation was nine percent after 12 years, which is similar to their recurrence rate for truncal and selective vagotomy with pyloroplasty. However, to quote Johnston, 'After 12 years of clinical assessment, it now seems clear that, of all the alternative surgical procedures for duodenal ulcer, HSV has the lowest operative mortality and morbidity, interferes least with gastrointestinal function and so produces the fewest side effects and long term sequelae.'<sup>845</sup>

Post operative test results of stomach acid levels were broadly higher than those obtained by more radical operations but most ulcers only required significant lowering of stomach acid levels which it achieved and this explains some of its success. The claim that opening of the stomach surgically after HSV was unnecessary was found to be untrue in all cases insofar that 0.1% of a series of 5539 patients developed gastric stasis requiring surgical intervention post-operatively and 0.6% developed the problem later.<sup>846</sup> These very small numbers illustrate how effective the operation was in avoiding drainage procedures with their attendant problems. Besides this, HSV left the upper gastrointestinal tract intact for the surgeon who had at his disposal all the previously tried operations in cases resistant to its benefits.

The question arises as to how successful HSV was in terms of its use generally within the British and international surgical community for the treatment of duodenal ulcer. In 1975, David Johnston sent a questionnaire to 43 surgeons in 17 surgical units worldwide whom he knew were actively performing HSV operations for duodenal ulcer. He found that they had done 5539 such operations. No operations were recorded from Scotland and perhaps

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<sup>842</sup> Johnston D, Humphrey C S, Smith R B, et al, 'Treatment of gastric ulcer by highly selective vagotomy without a drainage procedure: an interim report', *British Journal of Surgery*, Oct 1972, vol.59, no. 10, 787-92

<sup>843</sup> Johnston D, Goligher J C, 'The influence of the individual surgeon and of the type of vagotomy upon the insulin test after vagotomy', *Gut*, Dec 1971, vol. 12, 963-7

<sup>844</sup> Blackett R L, Johnston D, 'Recurrent ulceration after highly selective vagotomy for duodenal ulcer', *British Journal of Surgery*, Oct 1981, vol.68, issue 10, 705-10

<sup>845</sup> Blackett R L, Johnston D, 'Recurrent ulceration', *ibid*, 709

<sup>846</sup> Johnston D, 'Operative mortality and postoperative morbidity of highly selective vagotomies', *British Medical Journal*, Dec 6<sup>th</sup> 1975, 545-7

part of the reason lay in the publication of an article published in April 14<sup>th</sup> 1973 by Professor Andrew Kay's unit in Glasgow in the *British Medical Journal*.<sup>847</sup> Professor Kay headed an internationally known peptic ulcer research programme established a generation earlier by his predecessor, Sir Charles Illingworth. His unit had a record of producing surgeons of the highest academic stature who left to work in the UK and throughout the world. Kay himself had the distinction of having published an article on gastric secretion which has been cited 548 times by other authors.<sup>848</sup> Kay's unit described a prospective surgical study of 547 patients with proven chronic duodenal ulcers, confirmed at operation. It involved 45 different surgeons, 61% of whom were of the rank of senior registrar or below (under supervision). Truncal vagotomy was chosen and the drainage procedure was either pyloroplasty or gastroenterostomy. The trial follow-up period was between two and four years and 17% of patients were lost to follow-up.

The results of the trial showed that of those interviewed later, 90% of patients had a good result, operative mortality was 0.5%, ulcer recurrence rate was 3% and bilious vomiting was 2%. Diarrhoea following vagotomy was carefully examined using a questionnaire which asked 15 questions about bowel habit. It affected 1.1% of cases. The reason given for the trial was that since duodenal ulcer was such a common condition then an operation should be available to a surgeon who did not have a specialized interest in gastric surgery.

The trial conclusion suggested that,

*... truncal vagotomy with drainage should be retained as the operation of choice in the surgical management of duodenal ulcer. The operation is simple, safe and able to be more quickly performed than the several variants of selective vagotomy. ... Finally while the results of carefully controlled trials including proximal gastric vagotomy will be awaited with interest, it is suggested that a success rate of 90% probably takes us to the point of diminishing returns in the quest for the ideal operation for the treatment of duodenal ulcer.*<sup>849</sup>

At the time of Kay's unit's paper, other researchers were still working on vagotomy and drainage operations including Terence Kennedy and his colleagues in Belfast.<sup>850 851</sup> The

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<sup>847</sup> Kennedy F, McKay C, Bedi B S, et al, 'Truncal vagotomy and drainage for chronic duodenal ulcer: a controlled trial', *British Medical Journal*, Apr 14<sup>th</sup> 1973, 71-75

<sup>848</sup> Statistic from *Google* search 16<sup>th</sup> July 2012. Kay A W, 'Effect of large doses of histamine on gastric secretion of HCl: an augmented histamine test', *British Medical Journal*, Jul 11<sup>th</sup> 1953, 77-80

<sup>849</sup> Kennedy F, McKay C, Bedi B S, et al, 'Truncal vagotomy', op cit, 75

<sup>850</sup> Kennedy T, Connell A M, 'Selective or truncal vagotomy? A double-blind randomised controlled trial', *The Lancet*, May 3<sup>rd</sup> 1969, 899-01

surgical academic units in Leeds and Sheffield were acknowledged as being eminent in the field of research into peptic ulcer also and their extensive published work on the results of different operations for duodenal ulcer in the Leeds/York controlled trial for the relief of duodenal ulcer, referred to earlier in this chapter, showed a considerable residue of iatrogenic pathology resulting from all operations to the stomach. However the majority of patients were satisfied with the result of their surgery.

Professor Goligher's concern was that surgeons should strive to continuously improve outcomes and his figures for the outcomes of same operations that Kay's group were reporting, were much less favourable. In an unusual step, Goligher wrote an open letter to Kay in the pages of the *British Medical Journal*.<sup>852</sup> Goligher disagreed with Kay's group that their suggested operations represented 'the acme of surgical achievements in the elective treatment of duodenal ulcer and that little scope remains for surgical achievement' and 'operations which returned from 25% to 30% of indifferent or frankly unsatisfactory results which would leave a fair amount of room for amelioration.' He agreed that the operation of parietal cell vagotomy took more time and required specific training for its performance and that further assessment of its effectiveness also required more time, but nevertheless he stated that current experience now of over 250 cases in his department had been highly satisfactory in their outcomes. He closed the letter with the reproachful comment,

*I think that it would indeed be a great pity if this new technique, which is based on such an idealised conception – after all it could be regarded as the realisation of Lester Dragstedt's original dream of a pure neurectomy for peptic ulcer without surgical intervention in the stomach itself – and which show so much initial clinical promise, should be extinguished in its first flickering phase by a blast of scepticism from such a distinguished and respected figure of British gastroenterology as Andrew Kay.*<sup>853</sup>

No public reply from Professor Kay to Professor Goligher was published in the pages of the *British Medical Journal*.

In the West of Scotland, many surgeons seem to have continued to follow the Kay route although two witnesses were aware of HSV being attempted by at least one of their

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<sup>851</sup> Kennedy T, Connell A M, Love A H G, et al, 'Selective or truncal vagotomy? Five year results of a double-blind randomised controlled trial', *British Journal of Surgery*, Dec 1973, vol. 60, 944-8

<sup>852</sup> Goligher J C, 'Elective surgical treatment of duodenal ulcer', *British Medical Journal*, May 19<sup>th</sup> 1973, 420

<sup>853</sup> Goligher J C, 'Elective surgical treatment', op cit, 420

colleagues with most unfortunate results. Mr Alan MacKay, a surgeon, when asked about the safety of the operation said,

*Yes, it was safe in that it did not involve opening the pylorus. That was its biggest benefit. There was no need to go inside the G-I tract and therefore you weren't destroying the physiology of the pyloric mechanism. However, in its early days and indeed throughout, it had a definite morbidity and mortality, mostly attributable to lesser curve ischaemia and there were one or two disasters that I can remember where people lost their lives, or lost their stomachs.*<sup>854</sup>

When asked of his experience of HSV, another witness, Mr M K Browne said,

*The first one I ever saw, or the first one I knew about, sloughed the lesser curvature of the stomach and died and that tends to influence your outlook in a big way.*<sup>855</sup>  
*The ones who had selective vagotomies, they sometimes needed their drainage procedure changed and then the fashion came in for highly selective vagotomy where there was no drainage, and they were just a menace because they nearly always had to go back and have drainage. They also had a high complication rate.*<sup>856</sup>

Post-vagotomy complications for vagotomy and drainage operations did not greatly concern two of the surgeons interviewed. Their comments included,

*The results of surgery on the whole were quite good. It depends how you looked at them. The patient satisfaction was usually high, although the medical satisfaction wasn't necessarily as high. ... the patient often, for instance, found their bowels moved more often than usual after vagotomy. In the West of Scotland, that was looked upon as a benefit for the patient, but we usually looked upon it slightly shamefully if they got post-vagotomy diarrhoea but the patients often were quite pleased to have regular bowel movements.*<sup>857</sup>

*The West of Scotland was slow to adopt the highly selective vagotomy. We felt that our results were really very good with truncal vagotomy. They did get some side-effects, there is no doubt about it. We perhaps argued that they weren't as much a trouble as perhaps some people were making out. There was a regional variation and it may be that the Glasgow punter was a kind of constipated individual anyway*

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<sup>854</sup> From Testimony T3

<sup>855</sup> Taylor T V, Torrance B, 'Ischaemic necrosis of lesser curve of stomach', *British Medical Journal*, Jan 24<sup>th</sup> 1976, 222

<sup>856</sup> From Testimony T5

<sup>857</sup> From Testimony T5

*and the fact his bowel moved a little bit oftener was perhaps a benefit. Now I am not saying post-vagotomy diarrhoea wasn't a problem but that was perhaps why we were a bit slow in taking HSV.*<sup>858</sup>

These opinions represent the views of two senior surgeons in the West of Scotland and reflected their practice, however many surgeons adopted HSV as their mainstay for vagotomy when it was required. This is confirmed by the large body of published cases of HSV follow-up in the surgical literature. Surgeons used vagotomy to reduce acid but it was known at the time that the hormone gastrin played a part in gastric secretion of acid and that 'G cells' which produced the gastrin were stimulated by the vagus and also by food in the stomach.<sup>859</sup> Some studies indicated that vagotomy prevented increased gastrin stimulation of acid in patients with duodenal ulcers by switching off G cells.<sup>860</sup> There is little in the literature of the time to suggest that gastrin levels in duodenal ulcer were a concern to surgeons. Dragstedt's view prevailed that 'the basic defect in duodenal ulcer is an increased vagal drive which causes hyperplasia of parietal cells'.<sup>861 862</sup> This view appears to have sufficed for surgeons.

As can be seen in Figure 4, between 1976 and 2002, in Scotland, the numbers of recorded vagotomies fell from 2798 to 23. There was a move away from truncal towards highly selective vagotomies and in the course of time it became apparent that HSV as an operation was not the complete solution to the problem of duodenal ulcer. When the statistics were examined in large series, there were problems of ulcer recurrence and surprisingly the two main issues which stimulated the development of the operation, dumping and diarrhoea, also were found albeit infrequently with the operation.

David Johnston's Leeds group paper from 1981 which reported the results of the first 12 years of HSV for duodenal ulcer has been mentioned briefly above.<sup>863</sup> They reported a recurrence rate of 9% in 433 patients operated upon between 1969 and 1980 with no deaths postoperatively and low rates of morbidity and side effects after surgery. Johnston's group reinforced an earlier statement that outcome in terms of recurrences continue to be surgeon-dependent and suggested that surgeons require to be trained specifically in the

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<sup>858</sup> From Testimony T7

<sup>859</sup> Dragstedt L R, 'Peptic ulcer: an abnormality in gastric secretion', *The American Journal of Surgery*, Feb 1969, vol. 117, 143-56

<sup>860</sup> Byrne D J, Young J D, Chisholm D J, et al, 'Serum gastrin in patients in patients with peptic ulceration', *British Medical Journal*, Jun 13<sup>th</sup> 1970, 626-9

<sup>861</sup> Hyperplasia is increased cell production in a normal tissue or organ.

<sup>862</sup> Hansky J, Korman M G, Cowley D J, et al, 'Serum gastrin in duodenal ulcer', *Gut*, Dec 1971, vol. 12, 959-

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<sup>863</sup> Blackett R L, Johnston D, 'Recurrent ulceration', op cit, 705-10

technique. In the same month, Erik Amdrup reported recurrence rates of 15% for PCV and 9% for selective truncal vagotomy with drainage at 5 years.<sup>864</sup> In 1987, a prospective 14-18 year follow-up study of patients who had had parietal cell vagotomy (HSV) reported that up to 30% of patients operated on in the series suffered an ulcer recurrence.<sup>865</sup> They concluded that longer studies of these patients brought increased numbers of ulcer recurrences but regarded the operation as safe and relatively free of post-vagotomy symptoms. David Johnston entered the debate about recurrence of ulceration in a letter to the *British Journal of Surgery* which was answered by H-E Jensen and J Hoffmann who repeated their concerns about the high recurrence rates of ulceration following PCV which can be as high as 46%. They repeat Professor Johnston's point that results are very surgeon-dependent.<sup>866</sup> In 1990, two long-term studies looked at HSV and its outcomes. The first reported recurrence rates varying between 5.3% and 25.6%.<sup>867</sup> There were no deaths in this series of 307 patients followed up for between 5 and 15 years and around 90% of those questioned reported satisfaction with the results. Dumping and diarrhoea were reported in 5% but the patients felt that they could cope with the symptoms. The second series compared truncal vagotomy and HSV in 137 patients all operated upon by one surgeon and the results were broadly similar at 12 years in terms of well-being (Visick grades). However 20% of the truncal vagotomy patients required a second operation compared with none of the HSV patients.<sup>868</sup> No patients in either group died post-operatively. The conclusion of this study was that HSV was a good operation in terms of long-term results.

These studies, whose outcomes are variable, suggest that there was merit in Andrew Kay's assertion that the operation he proposed of truncal vagotomy and drainage in 1973 was as good as any available if performed by an average non-specialist surgeon.<sup>869</sup> The weakness of Kay's group's study was that it only reported 2-4 years of operations and it is known from longer studies that recurrences increase with the passage of time. Goligher's series quoted earlier in the chapter suggested that the Leeds experience of the outcomes of truncal vagotomy and pyloroplasty were very different and that it was not a good operation.

<sup>864</sup> Amdrup E, 'Recurrent ulcer', *British Journal of Surgery*, Oct 1981, vol. 68, no.10, 679-81

<sup>865</sup> Hoffmann J, Oelsen J, Jensen H-E, 'Prospective 14-18 year follow-up study after parietal cell vagotomy', *British Journal of Surgery*, Nov 1987, vol. 74, 1056-9

<sup>866</sup> Johnston D, 'Parietal cell vagotomy' in 'Correspondence', *British Journal of Surgery*, Mar 1988, vol.75, no.3, 290; Jensen H-E, Hoffmann J, 'Author's reply', *ibid*, 290-1

<sup>867</sup> Macintyre I M C, Millar A, Smith A M, et al, 'Highly selective vagotomy: 5-15 years on', *British Journal of Surgery*, Jan 1990, vol. 77, 65-9

<sup>868</sup> Koruth N M, Dua K S, Brunt P W, et al, 'Comparison of highly selective vagotomy with vagotomy and pyloroplasty: results at 10-15 years', *British Journal of Surgery*, Jan 1990, vol. 77, 70-2

<sup>869</sup> Kennedy F, McKay C, Bedi B S, et al, 'Truncal vagotomy', *op cit*, 71-5

Despite the problems caused by surgery, it improved lives for the large majority although it did not solve all the problems of duodenal ulcers. The proponents of HSV pointed out their lower mortality rates and the very low incidence of dumping and post-vagotomy diarrhoea. It is ironic that as surgeons were getting on top of most of the problems of peptic ulcer disease, the arrival of a new drug would make their services virtually redundant for the elective treatment of ulcers of the duodenum.

## 7. 7: Collegiality within the management of peptic ulcer

Throughout this thesis, it has been emphasised how difficult a condition peptic ulcer disease can be to diagnose and treat and how at each stage in its management, a patient or a practitioner may have to seek more expert help. Today a general practitioner has the right to seek help from a specialist colleague. This is one example of collegiate working in the NHS, to achieve a common goal and as a topic it arose in the testimonies of those who treated peptic ulcers. Collegiality may be defined as the relationship between colleagues or those explicitly united in a common purpose and respecting each other's abilities to work toward that purpose. Two benefits of its practice are the avoidance of duplication of efforts and improved communication.<sup>870</sup> Today most professional groups recognise the importance of acting in a collegial way in order to achieve the best results for their client group but it was not ever thus. In the interview research for this thesis, it became evident that there was a wide range of attitudes to what constituted collegiality among those tasked with providing healthcare. The old competitions between the disparate branches of medicine referred to in chapter two gradually lessened in the twentieth century and as will be seen in chapter eight, physicians and surgeons in hospitals came together to work out a regimen for the best management of haematemesis. In the NHS, collegiality became increasingly necessary as patients presented with increasingly complex health issues. Nurses in particular were willing participants in any collegiality exercise which they saw as essential to patients' wellbeing.<sup>871</sup> However the testimonies showed that collegiality was a poorly understood concept for some, especially doctors, who have an expectation of leadership in any team setting and even within such a setting, there may be a hierarchy.<sup>872</sup>

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<sup>870</sup> Feiger S M, Schmitt M H, 'Collegiality in interdisciplinary health teams: Its measurement and its effects', *Social Science and Medicine*, Mar 1979, vol. 13A, 217-229

<sup>871</sup> Giankos D, 'Physicians, nurses and collegiality', *Nursing Outlook*, Mar/Apr 1997, 57-8

<sup>872</sup> Campbell-Heider N, Pollock D, 'Barriers to physician-nurse collegiality: An anthropological perspective', *Social Science and Medicine*, Mar 1979, vol. 25, no. 25, 421-5

In the nineteenth century when specialties evolved, there was initial hostility to their development, largely from an elite group of physicians and surgeons.<sup>873</sup> Those who opposed such specialisation nevertheless were always available to their colleagues for second opinions. In time, partly as a result of expansion in the hospitals and no doubt due to the success of the specialist hospitals, the different disciplines which emerged within medicine became incorporated into the large hospitals. This led to a form of collegiality between hospital doctors with general practitioners recognised as colleagues who fed the system with referrals. At the beginning of the NHS, while GP's were recognised as fellow professionals, it was not felt by their hospital colleagues that GP work was on the same level of importance as theirs. This is clearly stated by one witness who was particularly critical of GP's in his training days.<sup>874</sup> In addition, there was always a degree of subservience expected in the relationship which Michael Balint describes as 'the perpetuation of the teacher-pupil relationship' and explains it in these words,

*The general practitioner looks up with ambivalent respect to the consultants, who by their standing ought to, and often even do, know more about certain illnesses than he. If this is not confirmed by events, the general practitioner feels highly critical and dissatisfied but is prevented from taking appropriate steps because of the respect which the consultants inherited from their predecessors in the teaching hospital.*

*... Many consultants, being the successors of the doctors' teachers obviously feel obliged to pretend to know more than they actually do.<sup>875</sup>*

One witness, when asked about the relationship between hospital doctors and general practitioners in his early days as a medical registrar, put it much more colourfully,

**BD:** *GP's - almost we didn't think about GP's. GP's were out there, they sent us in patients. Often their referrals we thought were rubbish, they sent in people they shouldn't be sending in, they should have been dealing with them themselves. So the early... my early experience I had bought into, this notion that hospital doctors*

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<sup>873</sup> Bynum, *Science and the Practice of Medicine*, op cit, pp193-6; Porter R, *The Greatest Benefit*, op cit, pp381-8

<sup>874</sup> From Testimony T23

<sup>875</sup> Balint M, *The Doctor, his Patient and the Illness*, 2<sup>nd</sup> ed, (Edinburgh,1986, Churchill Livingstone), pp81-2

*were really good guys, knew what they were talking about and GP's were a slightly lower class of person.*<sup>876</sup>

He qualified these remarks later when talking about the request of a GP for admission of a patient with a severe dyspeptic problem,

**BD:** *I think back with horror at the way I spoke to GP's in those days.*

**ACP:** *Yes because perhaps there was a very good reason for the patient coming in?*

**BD:** *These guys had been treating dyspepsia for years and years and years, they had been relying on their own making of their own mixtures for it, they knew the patients symptomatology really well and they knew far more about it than we did. And if they thought a patient needed to come into hospital, I mean there is the odd rogue GP who doesn't get out of his bed, but if they thought a patient needed to come in because of the dyspepsia we should have listened to them.*

It became evident in the testimony that the rivalry between surgeons and physicians was also an aspect of collegiality in the hospitals at the time.

**ACP:** *... relationships with surgeons, how (did) the whole thing work?*

**BD:** *I suppose it's slightly different for me being a gastroenterologist, I had more of a connection with the surgeons because we were part of the endoscopy unit. I suppose as a student I was more aware of there being surgeons and there being physicians and the two didn't get on very well. And my impression was that surgeons were kind of dismissive of physicians who tried to deal with dyspepsia. They didn't really know what they were doing and really it was a surgeon's job and they should just ...*

**ACP:** *But that kind of disappeared the longer time went on?*

**BD:** *When I was ... particularly as a registrar, that had sort of gone away. I mean the surgeons are always going to be surgeons but it was more of a collaborative thing and joint clinics became a bit more in vogue, particularly with people with special interests in upper GI, particularly in oesophageal work. So it became much less of a 'them and us'.*

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<sup>876</sup> From Testimony T23

Another witness, a physician, in describing his interaction with a referring GP as a relatively junior doctor in an outpatient clinic said, ‘I put these people onto therapy, I sent a note to the GP and told them what to do.’<sup>877</sup>

Currently it would appear that relationships between hospital consultants and general practitioners have markedly changed as general practitioners are treated with greater respect by their hospital colleagues. High standards of training in general practice have raised the status of general practitioners, mainly due to input from their Royal College, for now all new aspiring candidates have to pass its examination as part of their professional assessment. General practitioners are now to be found in academic rôles in the universities, some have entered management positions in health boards and general practitioners generally are listened to by politicians who recognize their favoured position in society.

Looking at the wider picture, it is evident that others involved with patients who were suffering from peptic ulcer disease understood that there was a hierarchical structure in relationships with doctors which was never stated and never questioned. One such relationship existed between the pharmacist and the general practitioner which could become uneasy if a pharmacist made a therapeutic suggestion. It is illustrated in the words of Mr John Linn, a retail pharmacist who was trying to help a patient. This man was buying large quantities of antacids to unsuccessfully relieve his dyspepsia shortly after Cimetidine had become available and was being prescribed by many doctors with great success.

*One chap in particular, I said to him, ‘You know there is a new drug out, maybe you should make an appointment to see your doctor,’ and I couldn’t tell him the name of the drug because that was a ‘crime’ (laughter). (‘Mr Linn the chemist said you should prescribe this for me,’ (more laughter) that was not done.) But he came back and said, ‘I have been to see my doctor and my doctor said, ‘Oh no, I am not prescribing that, it’s far too expensive’, and she doesn’t think it has been properly tried.’<sup>878</sup>*

Doctors and nurses traditionally work in concert, but in hospitals until relatively recent years, the nurse has occupied a subservient role. Isabel Duncan a nurse who rose to become Chief Nursing Officer in Lothian Health board spoke of the professionalization of nursing in its early days,

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<sup>877</sup> From Testimony T13

<sup>878</sup> From Testimony T6

*... there was a feeling amongst the nursing profession that we had to move with the times, that we couldn't expect nurses to constantly just be a labour force in the Health Service and although it was an excellent basic training, the younger people coming in would be wanting degrees. Because by this time all the paramedical professions, the physiotherapists, chiropody, all of these had gone into colleges like the Queen Margaret and nursing was out on its own.*<sup>879</sup>

As nursing strengthened its professional status via the qualification route, it achieved a different status in collegial terms than it had enjoyed before. Nevertheless it can be seen from Isabel Duncan's testimony earlier in this chapter how intimately involved the nurses were with the management of seriously ill patients with peptic ulcers. Their collegiality played an essential part in the patients' journeys.

An example of how collegiality can be made to work well is described in what appears to be a mission statement published in the British Society of Gastroenterology (BSG) website welcome page. It states,

*The British Society of Gastroenterology exists to maintain and promote high standards of patient care in gastroenterology and to enhance the capacity of its members to discover and apply new knowledge to benefit patients with digestive disorders. Our members include physicians, surgeons, pathologists, radiologists, scientists, nurses, dietitians and others.*<sup>880</sup>

The web page continues by describing its status and influence both in the UK and overseas. It is a remarkable achievement by any standards considering its beginnings as an exclusive 'gentlemen's club' founded by invitation in 1937 for physicians with an interest in gastrointestinal disorders.

## Conclusion to chapter seven

This chapter has re-visited in more detail some of the history of peptic ulcer outlined in general terms in chapter six but on this occasion the power of oral history has been used to open up the difficulties and dilemmas which statistics alone cannot reveal. It is seen how peptic ulcer presented as a serious problem in the hospitals and how it was treated in the community and in general practice and the medications used. Surgery played an important part, for it was seen to be effective in the treatment of chronic ulcers, albeit with occasional severe after-effects which caused many problems for patients who had had operations. The

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<sup>879</sup> From Testimony T22

<sup>880</sup> BSG homepage, [www.bsg.org.uk](http://www.bsg.org.uk) (accessed 28.11.12)

chapter also shows that, within the surgical community, conflicting views as to the best surgical operation for peptic ulcers arose after the development of HSV and these views are expressed in the text by testimonies of surgeons on each side of the debate. The chapter concludes with descriptions of how healthcare professionals from different disciplines began and continued to work together in the clinical care of patients with peptic ulcers.

The next chapter will continue to open up the history of peptic ulcer in the last three decades of the twentieth century by using the witness testimonies of general practitioners and specialists. This was a period of increasing change as physicians and surgeons began to co-operate in new ways and gastroenterology expanded rapidly with the use of new endoscopes which increased the understanding of upper gastrointestinal disease and led to the virtual demise of barium meals as a first-line investigation of peptic ulcer. The chapter will describe the introduction of new effective drugs for the treatment of peptic ulcer and the relationship of the medical profession with the pharmaceutical industry will be explored. It will be seen that at this time that new prescription drugs ultimately brought peptic ulcer disease under control and provided an effective treatment for the majority of its sufferers for the first time.

## Chapter 8. New drugs are developed which effectively treat peptic ulcers

### Introduction to chapter eight

This chapter begins by describing how modern medical practice works to benefit the patient with peptic ulcer disease and in particular how physicians and surgeons began to work more closely together when serious complications of ulcer disease occurred. Improvements in endoscopes and increasing first-line use of them rendered barium contrast X-rays of the upper gastrointestinal tract obsolete in the investigation of uncomplicated peptic ulcer disease. A new class of effective drugs for the treatment for peptic ulcer and related disorders was developed and introduced and for the first time doctors could treat patients without resort to surgery. As new drugs were subjected to clinical trials, it was noted that the symptoms of many patients appeared to be helped by placebos and the subject of placebos is considered. The relationship of doctors with the pharmaceutical industry played an important part in the history of drug development and ethical considerations arose out of these interactions which are discussed. The chapter concludes with the introduction of a new class of drug which was superior to all which preceded them in terms of efficacy.

### 8. 1. 1: Peptic ulcer referral patterns 1970-2000

In earlier chapters it was seen that understanding and treatment of duodenal and gastric ulcers continued to expand and mortality rates from their complications declined in the second half of the twentieth century. Nevertheless there remained a hard core of patients for whom life with an ulcer remained an uncomfortable reality and some had been damaged by operations which designed to alleviate their illness. These patients were obliged to live with their symptoms despite all attempts to help them by surgeons, physicians and their family doctor often seeking solace from the pharmacist or alternative practitioners. Now they had to return to a life of regimented dieting and became a major part of the workload of the burgeoning new cadre of gastroenterologists.

As before, the majority of patients with dyspeptic symptoms continued to self-medicate using OTC products from their retail pharmacist and attended their general practitioners when they judged that their symptoms were sufficiently severe. GP's might treat the symptoms with or without investigations (usually blood tests and/or a barium meal) or refer the patient for a second opinion, if symptoms continued or the patient requested it. The choice of specialist for a second opinion was a pragmatic decision influenced by local

service availability and doctor preference.<sup>881</sup> By 1970, there was a greater likelihood of patients having operations if referred to a surgeon but gradually gastroenterologists were becoming a first line referral route. They had little more to offer than general practitioners but often their ‘authority’ as a specialist brought clinical rewards. A gastroenterologist, Professor Russell said, ‘We tended to see peptic ulcers when they had medical presentations such as dyspepsia, abdominal pain, and vomiting.’<sup>882</sup>

A surgeon, Mr Alan Mackay, described his experience of the referral system which was working from the early 1970s in the hospital he worked in,

*There are a proportion of patients who come with rather vague abdominal pain and GP’s will send them to their favourite doctor, whether he’s a physician or a surgeon, they just have people they like where they will get a common sense opinion but, if a young man came in with typical symptoms of peptic ulcer disease, by then they’d be going to the Peptic Ulcer Clinic which was run by physicians and the only people that would come for surgery would be the ones that the physicians had felt that their best management had failed on.*<sup>883</sup>

Gastroenterologists had other sources of patient referral apart from general practitioners, accepting patients with surgical complications not amenable to further surgical intervention. These tended to be patients with dumping or post-vagotomy diarrhoea. Dr Alistair Beattie when asked about such patients said,

*We had to deal with them to quite a large extent, yes. Dietary manipulation, increasing fibre, doing things to try and slow down gastric emptying, there weren’t many effective drugs that worked.*<sup>884</sup>

Professor McColl added,

*though the surgeon did cure the ulcers in most cases, in so doing, it produced long-term morbidity and these post-operative symptoms, you know, they persisted for many years of the lifetime of the patient and certainly later on in medical clinics, occasionally still we see patients with ongoing problems from ulcer surgery they had twenty, thirty or forty years ago.*<sup>885</sup>

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<sup>881</sup> Testimonies T10, T14, T24 and T26 illustrate this point

<sup>882</sup> From Testimony T4

<sup>883</sup> From Testimony T3

<sup>884</sup> From Testimony T8

<sup>885</sup> From Testimony T1

Dr Gordon Allan developed an interest for a time in seeing patients with post-vagotomy diarrhoea and as a consequence he probably saw many more cases of this than others.<sup>886</sup>

Gastroenterologists' testimonies tended to give the impression that surgery for duodenal and gastric ulcers was to be avoided if at all possible. They did however recognise that when they had little more to offer the patient, whose symptoms they could not relieve or who had complications, then the time had come to refer these patients for surgery. Surgeons recognised the problems associated with ulcer operations but tended to be more sanguine about them for they recognised that in the 'big picture' they were saving lives and getting rid of ulcers which had dominated their patients' lives for many years. Mr Colin Mackay recognised the issue and his unit devoted time and resources to helping affected patients.<sup>887</sup> In 1973, 3238 patients had vagotomy operations in Scotland and although surgery was not producing large numbers of affected patients in any given year, the numbers grew.<sup>888</sup> Professor Kay's unit reported a post-operative rate of only 1.1% of diarrhoea and of 2% of severe dumping.<sup>889</sup>

Dr Brendan Devine, a gastroenterologist, gave a vivid picture of the problem when asked about his experience of the after-effects of surgery,

*Yes, I saw a lot of that, diarrhoea, dumping syndrome. Because I was doing gastroenterology clinics for many years, I was treating those sorts of patients all the time. Patients who had had surgery many years before, who had had vagotomy and pyloroplasty and then come back for a second operation because that wasn't working or the vagus had come back again, or they hadn't done the operation properly the first time. That was very common in those days and your gastric clinics were full of those sorts of patients. Your wards were quite often full of those patients. And it's funny because I graduated more to specialising in gastro in the elderly patients. I followed those patients through because they became part of my patient load and I was 'scoping those patients when they were in their seventies/eighties/nineties sometimes, still seeing partial gastrectomy patients and pyloroplasty patients and seeing all the side effects that they had had from those things. The reflux gastritis, I mean acid reflux into the antrum, for these big pyloroplasties and drainage procedures, those who constantly had dyspepsia, who*

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<sup>886</sup> From Testimony T9

<sup>887</sup> From Testimony T7

<sup>888</sup> See graph of ISD Scotland Vagotomy statistics in Ch 6

<sup>889</sup> Kennedy F, McKay C, Bedi B S, Kay A W, 'Truncal vagotomy and drainage for chronic duodenal ulcer: a controlled trial', *British Medical Journal*, Apr 14<sup>th</sup> 1973, 71-75

*couldn't eat big meals, who couldn't get their weight up, so that was a very big part of my working life.*<sup>890</sup>

## 8. 1. 2: A new way of working

Before the inception of the NHS, surgeons and physicians tended to practice their professions independently with little reference to one another's activities, but gradually a multidisciplinary approach developed with gastroenterology. Both Professor Russell and Professor Bouchier spoke of the early co-operative approach to diseases of the gut pioneered by Francis Avery Jones in London. Of the situation in Glasgow, Professor Russell said,

*So Illingworth, although slightly blind to the importance of gastroenterologists or physicians in gastroenterology, did actually realise the need for them and one of the chaps that he brought in was Lawrence Scott who became a senior physician in the Southern [General Hospital] and I went to work in his unit and Andrew Melrose was there and we worked closely together.<sup>891</sup> Now, these people in the 50's and 60's had a very definite association with surgeons in the Western [Infirmery], like Illingworth, Kay and others. I was brought up in the thinking that, although there was a developing medical specialty which is gastroenterology, especially when it comes to peptic ulcer, we are required to work closely with surgeons because a number of them land up in their department. I was a founder member of the Glasgow Gastroenterology Club in the early 60's with these people. Melrose and Kay and myself and one or two others founded it, so from the beginning we had surgeons involved because we felt there was a need for surgeons to work closely with the gastroenterologists. So, we didn't have any problem about that and in London, when I worked with Avery Jones in his department, he actually had convinced his surgeon (Gunnar) to give him the beds of the surgical department, most of the beds, and Avery ran that department as an investigative type of area in gastroenterology, full-time gastroenterology, and the surgeons did the needful surgery. They did joint ward rounds together, so that was a combined medical/surgical department in the early stage.<sup>892</sup>*

At an every-day level physicians and surgeons had to agree what to do with the complications of peptic ulcer disease. For perforations there was no argument, they

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<sup>890</sup> From Testimony T23

<sup>891</sup> Professor, later Sir, Charles Illingworth, Regius Professor of Surgery in the Western Infirmery in Glasgow

<sup>892</sup> From Testimony T4

required surgical intervention. Most hospitals agreed that haematemesis and melaena should initially be handled by physicians and passed on to surgeons if it seemed unlikely that the bleeding was not going to stop. At first sight this seems simple but there were problems in deciding when to pass over the small group of non-responding medical cases to the surgeons. This could lead to tensions between physicians and surgeons as described by Mr Alan Mackay,

*Surgeons would be called across to medical wards and would find an exsanguinated patient with a drip going in with fluid going in eight-hourly, no nasogastric tube down, no blood cross-matched and just in the worst possible condition for surgery. That's what surgeons would say. Physicians would come to the surgical wards and find patients with the complications of peptic ulcer disease who hadn't been worked up, who hadn't been given proper drugs, who hadn't been re-hydrated and so there was an interesting conflict, and the end result of that was so called haematemesis management teams.<sup>893</sup>*

Under the leadership of Professor Andrew Kay in the Western Infirmary in Glasgow, physicians and surgeons agreed from 1972 that all patients admitted with haematemesis would be seen by a member of a specialist team working within an agreed protocol. This contrasted with what was happening elsewhere in other hospitals both in Glasgow and in the UK.

Dr John MacKenzie, a consultant gastroenterologist in Glasgow Royal Infirmary described a typical situation of the management of patients with haematemesis,

*there was no gastroenterology unit admitting policy of any kind. So if they went in under a general physician they took pot luck as to what that person would decide to do. But if they were admitted under a gastroenterologist, they would be transfused up and a surgeon would be called immediately, straight after admission.<sup>894</sup>*

Later in the decade, Glasgow Royal Infirmary followed the pattern which had been established in the Western Infirmary in Glasgow and had a consultant-led endoscopy team which saw each haematemesis on admission. Other centres were slower to respond in this way and Professor David Johnston reported that it was not until the 1980s that Leeds began to provide a haematemesis team.

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<sup>893</sup> From Testimony T3. One of the first ever haematemesis management teams was set up in the Western Infirmary in Glasgow in the early 1970s. It was well ahead of its time.

<sup>894</sup> From Testimony T28

This is a good example of interdisciplinary clinical endeavour or collegiality but long before such a practical approach evolved, doctors and surgeons of every kind were meeting regularly in specialty meetings in their hospitals, sharing clinical experiences and inviting comments on management. Several witnesses spoke well of the experience gained in these meetings and of the fellowship which they engendered as each made their contribution. They became part of the life of the hospital with additional inputs from radiologists and pathologists adding to the clinical scenario.<sup>895</sup> People continued to die from bleeding and perforations and still do. In 1970 in Oxford, the death rate from haematemesis and melaena was 10%, a figure unaltered for 15 years.<sup>896</sup> 4259 patients died of peptic ulcer complications, (perforation and bleeding) in England and Wales in 1983.<sup>897</sup> In Oxford the death rate from perforation of a peptic ulcer was 13% in 1984. Surgeons and physicians faced a considerable challenge to prevent these deaths.<sup>898</sup> These statistics give a measure of the problem and one of the solutions adopted by the NHS was the appointment of new consultants with an interest in gastroenterology.

## 8. 2: The growth in endoscopy and the gradual demise of the barium meal for first-line investigation of ulcers

Endoscopy began to distinguish the gastroenterologist from the general physician in the 1970s when it was applied to the diagnostics, and later the therapy, of diseases of the gastrointestinal tract, as gastroenterologists used both external gut orifices for access. The new generation of gastroenterologists appointed in the 1970s had studied under senior physicians who had started with the Wolf-Schindler or Hermon Taylor endoscopes and had progressed on to the more flexible early fibroptic endoscopes such as the Hirschowitz endoscope.<sup>899</sup> Like their predecessors, they were self-taught and learned by ‘slow accretion’.<sup>900</sup> Endoscopy took many years to develop in the UK into a service which could be considered first-line as an investigation. It received its final boost with the introduction of the new Japanese and American thin flexible endoscopes which were regularly improved and eventually could be sterilised.<sup>901</sup> Initially physician endoscopy results were not trusted by the surgeons.

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<sup>895</sup> From Testimonies T7, T15, T23

<sup>896</sup> Schiller K F R, Truelove S C, Williams D G, ‘Haematemesis and melaena with special reference to factors influencing the outcomes’, *British Medical Journal*, Apr 4<sup>th</sup> 1970, 7-14

<sup>897</sup> Taylor T V, ‘Deaths from peptic ulceration’, *British Medical Journal*, Sept 7<sup>th</sup> 1985, 653-4

<sup>898</sup> Watkins R M, Dennison A R, Collin J, ‘What has happened to perforated peptic ulcer?’, *British Journal of Surgery*, Oct 1984, vol. 71, issue 10, 774-6

<sup>899</sup> The development of the endoscope is covered in chapter 2

<sup>900</sup> From Testimony T28

<sup>901</sup> From Testimony T23

Dr John Mackenzie spoke of the situation in the early 1970s,

*... we were doing endoscopy and the results were being ignored, because it wasn't felt that physicians really knew what they were doing in that context. Gradually it became apparent that we did know what we were doing and eventually when therapies came in, the surgeons/physicians were like endoscopic therapists. But it was a hiatus in between in which we maybe make a diagnosis but endoscopic diagnosis wouldn't necessarily influence what the surgeon then did.*<sup>902</sup>

Professor Ian Bouchier had the same experience in the early years,

*... if we as a medical gastroenterologist saw an ulcer or possible cancer or something like that with an endoscope and you said to the surgeon, 'Now look, we think that this patient needs to have such and such a thing done', then the surgeon would immediately endoscope him as well. Now you could understand why, but that was illogical.*<sup>903</sup>

Until endoscopy became a fully trusted procedure, the mainstay for diagnosis of duodenal and gastric ulcers was a barium meal. There were two forms of this procedure; the plain barium meal which was most commonly used in the NHS, and the double contrast barium meal. The latter used far less contrast medium (barium) and by the addition of an effervescent agent, a gas was produced in the stomach which spread the medium over the stomach lining and gave the radiologist a far finer view of the stomach lining, and improved diagnosis.

Dr Ramsay Vallance learned his skills in gastroenterological radiology in a specialist unit in the Southern General Hospital in Glasgow and never used the routine barium meal, which was in general use elsewhere in most centres in the UK. Working in the Western Infirmary and Gartnavel Hospital, Dr Vallance was performing six to eight double-contrast barium meals per session and fifty or sixty of these procedures were done per week between the two hospitals.<sup>904</sup> Barium meals were estimated to be 80-85% accurate in the best hands in finding significant pathology of the stomach and duodenum and were better than endoscopes until they were developed to look back up into the top part of the stomach or into the second part of the duodenum.<sup>905</sup> Increasing use of endoscopy by 1980 led to a commensurate decline in requests for barium meals. Studies eventually confirmed the superiority of endoscopy as a first line procedure for the diagnosis of gastric and duodenal

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<sup>902</sup> From Testimony T28

<sup>903</sup> From Testimony T13

<sup>904</sup> The two hospitals were part of the same group

<sup>905</sup> From Testimony T11

ulcers.<sup>906 907</sup> Glasgow may have been more privileged in its supply of endoscopists than other areas.<sup>908</sup>

In 1970, the mainstay of medical treatment of peptic ulcer was antacids and diet but new drugs did appear which could be seen to heal treatment-resistant duodenal ulcers. In 1972, a successful trial using carbenoxolone to treat duodenal ulcer was reported but this drug was not widely used for this indication.<sup>909</sup> Three other drug types were developed at the same time as the newly launched H<sub>2</sub> antagonists, of which more follows.<sup>910 911</sup> Briefly these types of drug which worked in different ways: reduction of stomach acid (pirenzepine), coating the ulcers with a protective layer (Sucralfate and De-Nol) and protecting the gastric mucosal cells (synthetic prostaglandins). There is a sizeable body of literature to suggest that they healed duodenal ulcers but were not widely used outwith specialist centres.

### 8. 3. 1: Cimetidine and H<sub>2</sub> receptor antagonist drugs

In 1964 James Black led a research project for the pharmaceutical company ICI introducing the drug propranolol which selectively targeted nerve cell endings (beta adrenoceptors) in the heart which brought relief in the condition angina pectoris and saved many lives of those treated with the drug following myocardial infarctions.<sup>912</sup> After some years Black moved on to work with the pharmaceutical company Smith Kline and French (SKF) in England with the specific intention of finding a drug which would block the acid-producing cells in the stomach. Earlier physiological research had suggested that one way in which the stomach produced acid for digestion was via vagus nerve stimulation causing it to release histamine, thereby stimulating the parietal cells to secrete acid. This discovery was discussed by Frank Campbell McIntosh among many others in 1938 and confirmed by Charles Code in 1956.<sup>913 914 915</sup> Black proposed that in the stomach there should be a

<sup>906</sup> Dooley C P, Larsen A W, Stace N H, et al, 'Double contrast barium and upper gastrointestinal endoscopy: a comparative study', *Annals of Internal Medicine*, Oct 1984, vol. 101, no. 4, 538-45

<sup>907</sup> Colin-Jones D G, 'Endoscopy or radiology for upper gastrointestinal symptoms?', *The Lancet*, May 3<sup>rd</sup> 1986, 1022-3

<sup>908</sup> Scott B, Atkinson M, 'Gastroenterological services: a regional review over a five year period, (1981-86)', *Gut*, May 1989, vol. 30, issue 5, 695-700

<sup>909</sup> Sircus W, 'Progress report: carbenoxolone sodium', *Gut*, Oct 1972, vol. 13, issue 10, 816-24

<sup>910</sup> Weir D G, 'Peptic ulceration', *British Medical Journal*, Jan 16<sup>th</sup> 1988, 195-200

<sup>911</sup> Piper D W, 'Peptic ulcer', *Australian and New Zealand Journal of Medicine*, 1988, vol. 18, 237-44

<sup>912</sup> Stapleton M, 'Sir James Black and propranolol', *Texas Heart Institute Journal*, 1997, vol. 24 no. 4, 336-42

<sup>913</sup> McIntosh F C, 'Histamine as a normal stimulant of gastric secretion', *Experimental Physiology*, Jun 1<sup>st</sup> 1938, vol. 28, no. 1, 87-98

<sup>914</sup> Molinder H K M, 'The development of cimetidine: 1964-1976', *Journal of Clinical Gastroenterology*, 1994, vol. 19, no. 3, 248-54

<sup>915</sup> Parsons M E, 'Histamine and the pathogenesis of duodenal ulcer disease', *Gut*, Nov 1985, vol. 26, issue 11, 1159-62

specific type of nerve receptor which stimulated gastric acid secretion using histamine as a neurotransmitter.<sup>916</sup> After extensive research, Black showed that there were two kinds of histamine receptors in the body; one type found all over the body which played a major rôle in allergy and could be blocked by antihistamines, and others in the stomach which could not be blocked by antihistamines. He later called them H2 receptors and these were specific to the acid producing part of the stomach.<sup>917</sup> In 1972 Black and his team at SKF produced the first H2 blocking drug (a.k.a. H2 receptor antagonists) in experimental animals which reduced the stomach's output of acid. Having initiated and led this research to the point of producing drugs for trial, James Black moved to take the Chair of Pharmacology at the University College London in 1973.<sup>918</sup> Different compounds had been designed and one called burimamide was selected for trials as an H2 blocker. It worked somewhat but proved disappointing in volunteer studies because of poor oral absorption and so the team moved on to a modified molecule called metiamide. In the four years following, two other drugs went to trial, initially metiamide and subsequently cimetidine. Both proved effective in healing peptic ulcers and much investigative research was done and its results published in the medical journals of the time for this promising new type of drug.

In 1975, a six centre trial of metiamide proved its effectiveness in healing duodenal ulcers if continuously taken. Unfortunately reversible agranulocytosis occurred in a patient which was shown to be due to thiourea, a constituent part of its molecular structure<sup>919</sup> A patient who continued to bleed from a duodenal ulcer despite two operations to stop the bleeding was given metiamide which worked. He became seriously ill with agranulocytosis and when metiamide was stopped, the bleeding recurred to the point of being life-threatening. Supplies of cimetidine, which did not contain thiourea, were then given and the patient's bleeding stopped and his life was saved.<sup>920</sup> At the time cimetidine had only been trialled in a small group of healthy volunteers and although it was thought to be a 'cleaner' drug, its safety profile was still unknown.<sup>921</sup> Cimetidine was released as

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<sup>916</sup> A neurotransmitter is a chemical which transfers a nerve impulse across a structure at the end of the nerve called a synapse to stimulate a target cell.

<sup>917</sup> Black J W, Duncan W A M, Durant C J, et al, 'Definition and antagonism of H2 receptors', *Nature*, vol. 236, Apr 21<sup>st</sup> 1972, 385-90

<sup>918</sup> Gannellin C R, 'Personal reflections on Sir James Black (1924-2010) and histamine', *Inflammation Research*, 2011, vol. 60, 103-110

<sup>919</sup> Agranulocytosis is a blood condition where white cell production by the body is damaged, threatening the immune system.

<sup>920</sup> Burland W L, Sharpe P C, Colin-Jones D G, 'Reversal of metiamide-induced agranulocytosis during treatment with cimetidine', *The Lancet*, Nov 29<sup>th</sup> 1975, 1085

<sup>921</sup> Molinder, 'Development of cimetidine', op cit, 252-3

‘Tagamet’ tablets for prescription at the end of 1976, anticipated by gastroenterologists who used it cautiously from the beginning, and within a year of its launch, over 300 articles about its use had been published.<sup>922</sup> As evidence mounted of its safety and efficacy, over the following years it became the most prescribed drug in the NHS despite its relatively high cost compared with established medications.<sup>923</sup> Cimetidine reduced the acid secretion into the stomach and at first it seemed to be as effective as a successful vagotomy in allowing healing of both gastric and duodenal ulcers. However more study revealed that gastric acid secretion was not a simple matter.<sup>924</sup> When compared with vagotomy, cimetidine produced similar healing rates but for those patients who did badly after surgery, it did not always help them.<sup>925</sup> <sup>926</sup> Continuously taken cimetidine healed duodenal ulcers and gastric ulcer to a lesser extent in the majority of patients.

Mr Browne’s memory of it follows,

**MKB:** *With the coming of Cimetidine and Omeprazole and so on, we hardly ever saw duodenal ulcers again, they were just gone, and we certainly didn’t operate on them any more.*

**ACP:** *Over what sort of timescale would that be?*

**MKB:** *Well, it was fairly sudden. 1977, I remember giving a talk to the GP’s in Monklands before the hospital opened and saying that the days of surgery on duodenal ulcer were over and that these new drugs were going to eliminate it virtually completely ...*<sup>927</sup>

Mr Browne’s prediction was correct and research showed that cimetidine had an effect upon vagotomy operations for duodenal ulcer in the UK.<sup>928</sup>

Cimetidine was launched in London at an international symposium in 1976 and became the first drug to reach sales of \$1 billion/year, ten years later.<sup>929</sup> A number of factors created the scenario which led to its early acceptance. From the start, it looked like a very safe and

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<sup>922</sup> *Web of Science* database search using ‘cimetidine’ with a time limit 1976-77

<sup>923</sup> From Testimony T6

<sup>924</sup> Debas H T, Carvajal S H, ‘Vagal regulation of acid secretion and gastrin release’, *Yale Journal of Biology and Medicine*, 1994, vol. 67, 145-51

<sup>925</sup> Pickard W R, Mackay C, ‘Early results of surgery in patients considered cimetidine failures’, *British Journal of Surgery*, Jan 1984, vol. 71, issue 1, 67-8

<sup>926</sup> Bardhan K D, Kapur B, Hinchcliffe R F C, ‘Cimetidine or vagotomy’, *British Journal of Surgery*, May 1984, issue 5, 402-3

<sup>927</sup> From Testimony T5

<sup>928</sup> Wylie J H, Clark C G, Alexander-Williams J, et al, ‘Effect of cimetidine on surgery for duodenal ulcer’, *The Lancet*, Jun 13<sup>th</sup> 1981, 1037-8

<sup>929</sup> Duncan W A M, ‘Some decisions in the development of cimetidine’, *Drug Development Research*, 1993, vol. 30, 18-23

effective medication for the treatment of both gastric and duodenal ulcers. The drug had been extensively tested before release and the trials published in the specialist journals ensured that there was both a high level of knowledge of the drug and an optimistic expectation of the drug's effectiveness.<sup>930</sup> In 1977, the BSG met in Cambridge on April 1<sup>st</sup> and 2<sup>nd</sup> and six papers were read on the use of cimetidine in the treatment of gastric and duodenal ulcers.<sup>931</sup> In Glasgow on April 7<sup>th</sup>, a similar symposium took place on use of cimetidine in the management of peptic ulceration.<sup>932</sup> In the UK, specialists began to prescribe the drug for proven ulcers with good effect and it was increasingly used.

There were known problems with interactions with other drugs which were metabolised in the liver, most notably warfarin, but such problems did not affect the majority who were given it.<sup>933</sup> Within a year, British GP's were asked to prescribe cimetidine by hospital specialists and, whilst many baulked at its cost, it became evident that its benefits far outweighed its cost-disadvantage, in terms of fewer hospital admissions for elective surgery for duodenal and gastric ulcers. In Scandinavia and in other countries, it remained a specialist-only prescribable drug for one of two reasons.<sup>934</sup> The first was cost and the second was a reluctance to use a powerful new drug which might have unforeseen side-effects. The main anxiety was that no one knew what would happen in the long term when acid levels in the stomach were so effectively reduced thereby potentially causing gastric cancer. Papers were published describing gastric cancers in patients treated with cimetidine but the link was refuted and the advice was given to make sure that patients did not have gastric cancer before starting treatment.<sup>935 936 937</sup> The success of cimetidine as a commercial property was due to the fact that when it was stopped, the symptoms recurred and the ulcers returned in a high percentage of cases.

Having used cimetidine with initial enthusiasm, after a time, Dr Brendan Devine slowly became less convinced of its efficacy overall,

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<sup>930</sup> A literature search on the *Web of Science* database displayed 88 articles on the subject of 'cimetidine' or 'H2 receptor antagonists' in the years 1975-6.

<sup>931</sup> 'Abstracts of papers, British Gastroenterology Association Spring Meeting', *Gut*, May 1977, vol. 18, issue 5, A419-A421

<sup>932</sup> 'Scottish symposium - the management of peptic ulceration - a report', *Scottish Medical Journal*, 1977, vol. 22, 287-305

<sup>933</sup> Warfarin is an anti-coagulant drug which 'thins the blood'.

<sup>934</sup> Molinder H, Wallander M A, Bodemar G, 'The introduction of H2-receptor antagonist to Scandinavia: effects of expert opinions', *Scandinavian Journal of Gastroenterology*, 1998, vol. 33, 224-30

<sup>935</sup> Elder J B, Ganguli P C, Gillespie I E, 'Cimetidine and gastric cancer', *The Lancet*, May 12<sup>th</sup> 1979, 1005-6

<sup>936</sup> Roe F J C, 'Cimetidine and gastric cancer', *The Lancet*, May 12<sup>th</sup> 1979, 1039

<sup>937</sup> Letters to the editor, 'Gastric cancer in patients who have taken cimetidine', *The Lancet*, Jun 9<sup>th</sup> 1979, 1234-6

*Tagamet (cimetidine) became a sort of wonder drug. Initially one was a bit dubious about it with the claims of its effectiveness but with experience, you realise that this was probably a major step forward but we still used a lot of antacids, particularly for reflux... Interestingly we were convinced it was a wonderful drug but the more we used it, the less effective it seemed to get. And when you look back in the trial data, you realise that we were slightly blinded by this new wonder drug, in fact, if you look back, the success was only fifty five to sixty percent. Not much better than placebo in retrospect, you know. But at the time, it seemed a really good drug and we used it a lot.*<sup>938</sup>

Cimetidine sales grew all over the world as it was increasingly used for the treatment of gastric and duodenal ulcers as well as other peptic disorders. Herdis Molinder's Scandinavian paper shows the steady increase in prescribing of cimetidine in Sweden between 1979 and 1986<sup>939</sup> and other historical accounts confirm that this was happening wherever cimetidine was introduced. Its manufacturer Smith Kline French (SKF), grew from being a small company later merging with Beechams to become Smith Kline Beecham (SKB) in 1989.

### 8. 3. 2: Ranitidine (Zantac)

In 1981 the pharmaceutical company Glaxo launched another H<sub>2</sub> blocker, Zantac (ranitidine), into the market with fierce marketing tactics and by 1988, it overtook and far exceeded the sales of cimetidine to become the most prescribed drug in the world at the time.<sup>940</sup> Ranitidine played an important role in the treatment of duodenal and gastric ulcers in the 1980s decade. However most gastroenterologists agree that it was only a marginally better drug for treating peptic ulcer diseases than cimetidine was. It had two advantages over cimetidine: it was 'cleaner' in the sense that there were almost no adverse drug interactions and the dosage regime was simpler with lower tablet strengths. SKB changed the dosage regimes and tablet strengths of Tagamet several times causing confusion for the patients and their doctors alike. Zantac was simpler to prescribe. A doctor ordered a twice daily dosage without the need to look up drug interactions for patients on large numbers of different medications. This was regarded by general practitioners in particular as a bonus at a time when there was a perceived increase in litigation against them which might have occurred if they had harmed a patient by missing a possible drug interaction. Ranitidine

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<sup>938</sup> From Testimony T23

<sup>939</sup> Molinder H, et al, 'The introduction of H<sub>2</sub>-receptor antagonists', op cit, Table ii, p227

<sup>940</sup> Wright R, 'How Zantac became the best selling drug in history,' *Journal of Health Care Marketing*, 1996, vol. 16, 24-9

worked in the same way as cimetidine to reduced acid secretion of the stomach allowing ulcers to heal and there were treatment failures from it also.

Two years of research publications of articles led to the introduction of ranitidine in competition with cimetidine in 1981.<sup>941</sup> For six years, cimetidine retained its market share as the use of ranitidine steadily increased eventually overtaking cimetidine, whose sales also continued to increase, but later slowly declined. Ranitidine research on all aspects of safety on such topics as carcinogenesis and long term side effects stood up to the scrutiny of rigorous drug trials.<sup>942</sup> As indications ‘softened’ for its use and general practitioners began to prescribe it freely for many of their dyspeptic patients who did not have ulcers. Years later, after it had come off patent, as had been the case with Tagamet, Zantac could be bought off the shelf in supermarket’s drug counters. Two other competitor drugs of H2 blocker type, famotidine in 1981 and nizatidine in 1987, were introduced but none could match the market share eventually achieved by ranitidine.

#### 8. 4: Placebos

The clinical testing of H2 blockers was done with double-blind trials of volunteers using placebos as controls and a curious fact emerged of the effectiveness of placebos in the treatment of gastric and duodenal ulcers. Traditionally, placebos are inert substances given to patients with the hope that they would alleviate symptoms in conditions where the doctor had no definitive therapy.<sup>943</sup> They worked well in some conditions but there was an element of deception involved which troubled many.<sup>944 945</sup> In a double-blind trial, patients are given coded medications, either an active drug or a dummy with no known effect (placebo), which are indistinguishable in appearance from one another and the prescribing doctor does not know which he or she is giving, to avoid any bias. When the trial is over, the codes are broken to reveal the results of treatment. In some trials, the active drug, while appearing to heal ulcers, was little better than the placebo it was being compared with. The subject of placebo response in trials of drugs for peptic ulcer was discussed by several witnesses. Mr Colin Mackay commented that peptic ulcer was a condition particularly responsive to placebo as seen in double-blind trials of cimetidine vs. placebo for the treatment of gastric and duodenal ulcer. This phenomenon was particularly

<sup>941</sup> A search in the *Web of Science* database using ‘ranitidine’ and the time limit of 1976-81, yielded 299 articles with the oldest being published in 1979

<sup>942</sup> Mills J G, Koch K M, Webster C, et al, ‘The safety of ranitidine in over a decade of use’, *Alimentary Pharmacology and Therapeutics*, 1997, vol. 11, 129-37

<sup>943</sup> Beecher H K, ‘The powerful placebo,’ *Journal of the American Medical Association*, Dec 24<sup>th</sup> 1955, 1602-6

<sup>944</sup> Ernst E, Herxheimer A, Editorial, ‘The power of the placebo’, *British Medical Journal*, Dec 21<sup>st</sup> 1996, 1569-70

<sup>945</sup> There is a large amount of published literature on the subject of the placebo.

noticeable in medical trials done by researchers in the early days after the introduction of cimetidine which attempted to assess the effects of dosage regimes and length of time required to heal duodenal and gastric ulcers and, later, its use as a maintenance therapy to prevent recurrence of them.<sup>946</sup> These trials gave placebo response rates of between 38% and 45% for ulcer healing.

Dr Beattie, another witness, when asked about these results, commented that that may have been due to the nature of the condition which he described as a ‘relapsing and remitting disease’. He further elaborated,

*Well it's a self limiting disease, peptic ulcer. You often heard patients say that they had an ulcer and they had it for years and I would say to them, 'Well you have not, - you have had recurrent ulcers. They get bad, this lasts for a few weeks and they get better.' Now if you've got a disease like that you're almost bound to get a placebo effect because the natural history is that they get better over a few weeks anyway. Hopefully more will get better with a successful treatment but you inevitably get a placebo effect.*<sup>947</sup>

Gunver Kienle and Helmut Kiene in their paper, ‘The powerful placebo effect: fact or fiction?’, give a list of factors which enhance placebo response which will be recognizable to any practicing doctor. Among them are; the natural course of a disease with spontaneous improvement, fluctuations of symptoms and regression to the mean. Patients themselves can play a part in bias with eagerness to please from politeness and ‘experimental subordination’.<sup>948</sup> Consciously or unconsciously doctors have recognized for many years that the environment of the clinic, its distinctive smell, its paraphernalia of testing equipment, the smartly dressed efficient nurses, the space and the specialist in his white coat, all working together towards the furtherance of healing, have a large part to play in the success of the whole consultation process. Michael Balint proposed the concept of the drug, ‘doctor’, where the doctor’s personality plays an integral part in the success of some clinical outcomes.<sup>949</sup> One witness commented upon this aspect of care in these terms, ‘the patients did matter. It still gets down to there are those of us who are good at

<sup>946</sup> Bardhan K D, Saul D M, Edwards J L, et al, ‘Double-blind comparison of cimetidine with placebo in the maintenance of healing of duodenal ulceration’, *Gut*, Feb 1979, vol. 20, 158-62

<sup>947</sup> From Testimony T8

<sup>948</sup> Kienle G S, Kiene H, ‘The powerful placebo effect: fact or fiction?’ *Journal of Clinical Epidemiology*, Dec 1997, vol. 50, no. 12, 1311-8

<sup>949</sup> Balint M, *The Doctor, His Patient and the Illness*, 2<sup>nd</sup> ed, (Edinburgh, 1986, Churchill Livingstone), pp5, 172-3

managing people and there are those of us who are not.’<sup>950</sup> The placebo effect, thought of as the result of the inert pill, may be better understood as an effect of the relationship between doctor and patient.<sup>951</sup>

Clearly with the H2 blocker drugs, times were better for the patient with a peptic ulcer for there was less surgery done, but duodenal ulcer and gastric ulcer were still poorly understood conditions beyond the knowledge that, if acid output in the stomach was reduced, many patients would cease to suffer from the effects of the ulcers and many would be cured. Gastroenterologists remained busy examining the upper gastrointestinal tract looking for pathology before beginning therapy and kept the pathologists equally busy with their samples taken at the time of endoscopy.

## 8. 5: The pharmaceutical industry and the success of Zantac

Zantac, manufactured by Glaxo, was a very similar drug to Tagamet which was manufactured by SKF, in both its efficacy and safety. There were only relatively minor differences between them, but Zantac was more expensive by approximately one third. In 1991, the year of the launch of Losec (omeprazole), one month maintenance equivalent doses of Tagamet cost £20.56p, Zantac £27.43p and Losec £36.36p. Cimetidine could be prescribed generically at this time for £18.00.<sup>952</sup> The question then arises, ‘How did Zantac achieve such a dominant place in the market?’

An end point of any pharmaceutical company’s endeavour is to produce a drug which will make a profit.<sup>953</sup> <sup>954</sup> It may take many years of testing to bring a drug to the market and once there, there is only a limited time available for the company to recover its research and development costs, making early clinical acceptance of the drug by doctors very important. Zantac’s sales dominance was the result of a carefully planned marketing strategy by its manufacturers.<sup>955</sup> In the two years before its launch, it was extensively trialled in many countries throughout the world and the results published in scientific and medical journals.<sup>956</sup> Clinical trials are necessary for pharmaceutical research and before any drug can be launched, large numbers of patients have to be recruited and enrolled in studies. Glaxo operated a team of clinical research assistants who recruited clinicians and

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<sup>950</sup> From testimony T07

<sup>951</sup> Spiegel D, ‘Placebos in practice,’ *British Medical Journal*, Oct 23<sup>rd</sup> 2004, 927-8

<sup>952</sup> British Medical Association and Royal Pharmaceutical Society of Great Britain, ‘Ulcer healing drugs’, *British National Formulary*, Sep 1990, No. 20, pp32-5

<sup>953</sup> David G, ‘New products help Glaxo products soar’, *The Times*, Tues, Oct 12<sup>th</sup> 1982, p15

<sup>954</sup> Prest M, ‘Zantac helps Glaxo to £86m profit’, *The Times*, Tues, Apr 12<sup>th</sup> 1983, p17

<sup>955</sup> Wright, ‘How Zantac became the best selling drug’, op cit, 24-9

<sup>956</sup> An internet search using ‘ranitidine’ and the years ‘1979-1981’ on the World of Science database showed that it had been cited 299 times in published articles.

helped to organise trials.<sup>957</sup> These are usually conducted in hospital outpatient clinics with the patients being recruited as volunteers. The drug company usually provides all the materials required for the study and the clinical unit receives a fee which may be paid into a research fund in the hospital to allow for other research expenses, such as research fellows' salaries or for travel/ accommodation costs for research meetings not funded by the NHS.<sup>958</sup>

In the years following the launch of Zantac, clinical researchers in the field of peptic ulcer disease compiled data on the clinical profile of the drug and researchers confirmed that the drug was safe and effective for its clinical indications. Clinical trials are subject to rigorous rules agreed between the medical profession and the Association of British Pharmaceutical Industries (ABPI).<sup>959</sup> They were often presented at symposia and published in medical journals by researchers whose reputations grew as they became recognised as having expert knowledge and experience of a drug and particular illnesses. Their reward was being asked to speak for a fee at prestigious meetings, sometimes in exotic locations with all expenses paid. These doctors became known as 'key opinion leaders' and were one of the main means used by pharmaceutical companies to promote their products.<sup>960</sup> Another way in which the pharmaceutical companies promoted their product was in the area of postgraduate medical education as they provided the funding for symposia and funded travel for specialists and their juniors.<sup>961</sup>

Glaxo were determined to make an impact with its launch of Zantac. One of our witnesses was present,

*All of Britain's gastroenterologists or a huge proportion of them were taken off by Glaxo to Lisbon, Estoril, for a big conference to launch ranitidine. And they spent a million pounds on that, I remember the figure. And they had to do that to try and persuade people to use it because cimetidine was so good. I'm not sure that there's any difference between these H2 antagonists but we did start using Zantac after that. I don't remember why actually, obviously being taken to Lisbon must have influenced us a little bit.*<sup>962</sup>

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<sup>957</sup> From Testimony T20

<sup>958</sup> From Testimony T13

<sup>959</sup> The ABPI has a published code of practice agreed with the medical profession which covers all aspects of their inter-relationships.

<sup>960</sup> These are now referred to in the pharmaceutical industry as 'key external experts'.

<sup>961</sup> For a more detailed description of clinical trials and the issues involved, see testimonies T1, T2, T4, T9, T12, T13, T18, T23, T28

<sup>962</sup> From a Testimony

Key opinion leaders from specialist practice formed an important interface with general practice as they were invited to give paid talks about their research to general practice audiences who tended to use such meetings for educational updates. These meetings were sponsored by drug companies, who, although they could not dictate to their speakers what to say, often provided presentational materials for the consultant to use in their talks. Before or after a good meal provided by the drug company, the general practitioners would be invited to visit displays advertising and promoting the drug in question. Not all speakers were experts in the field of research of any particular drug, many were local hospital consultants who spoke about their clinical management of particular diseases which could of course be helped by the drug which was being promoted by the sponsoring pharmaceutical company. General practitioners enjoyed these meetings since they provided a congenial and informal setting in which to learn and mix with hospital doctors whom otherwise they might only speak to on the telephone.<sup>963</sup>

Drug companies such as Glaxo had a well planned strategy for the promotion of their products, finely tuned over years of experience and directed by their marketing and sales divisions. The top-down approach using opinion leaders was one tactic but everyday sales promotion was in the hands of the drug company representatives. Their job was to keep the product in the forefront of the prescribers' minds as they saw patients in everyday contact. Glaxo representatives were usually recruited from a pharmaceutical or science based background, although other companies may have used those with purely sales skills. They were trained to have a good knowledge of their product and taught how to convey that information to doctors. Their task could be difficult since they were dealing with busy professionals who were time-pressurised for an activity which was not seen by them as essential to their working lives. Patience, persistence and deference were the key to success for the drug representative. The testimony of Mr Ian Davidson who worked for 36 years as a Glaxo pharmaceutical representative illustrates eloquently how he and his colleagues worked and summed it all up in a phrase, 'people buy people' meaning that when it came to selling anything, it was interpersonal relationships which mattered.<sup>964</sup> Mr Davidson described the lead-up to the launch of Zantac: the drug representatives were sent a distance learning pack and then brought to headquarters where they would sit an examination to ascertain their level of knowledge. They were then given a week's training to complete their learning on the product. Immediately before the launch, the whole Glaxo sales force met together in Deauville to complete their training.

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<sup>963</sup> The background to this section is all to be found in Testimonies T 17 and T20

<sup>964</sup> From Testimony T17

Drug company representatives' daily routine involved promoting their company's products by visiting general practice surgeries and hospital doctors on a regular basis. Basically it was a brief encounter as the drug representative tried to get across a message about particular products and they would leave appropriate literature including data sheets.<sup>965</sup> One technique used was to leave drug samples to allow a doctor to start a new medication course. Other promotional aide-memoires were left which had to be of some relevance to medical practice under ABPI rules. Doctors called them 'freebies' and generally enjoyed receiving them. Stationary products such as sticky pads, pens, headed notepaper, calendars and diaries were very popular and mugs advertising drugs could be found in most staff rooms. Between 1976 and 1996, gifts to doctors grew more sophisticated and valuable with such items as stethoscopes, sphygmomanometers, surgical instruments and tendon hammers being offered. Elastic tourniquets were particularly prized for phlebotomy. All these items advertised a product and were useful for practice.

Another inducement offered by drug representatives was that of entertainment which might be an invitation to a lunch at a local restaurant or an organized dinner. Golf outings on the general practitioner's half day were particularly popular. At its most extravagant, some pharmaceutical companies organized weekend educational symposia in European resorts in their off-season and paid for all the costs. All of these promotional activities were directed at facilitating face to face contacts with doctors, for it was very difficult for doctors to refuse to see a drug representative from whom he had enjoyed hospitality. In the hospitals, the representatives' jobs were little different and they used similar techniques. Contacts with junior doctors were important since they did a lot of the outpatient prescribing and it was known that they influenced their seniors. Mr Donald Dunn who worked as a hospital representative for Glaxo for many years used a similar approach and said that another function he performed was that of providing detailed scientific data on his products which was greatly appreciated by clinicians seeking important information which could be difficult in a time before computerized drug data could be easily accessed.<sup>966</sup>

The testimonies of the two Glaxo drug representatives interviewed indicated that they were not involved in organizing lavish hospitality for general practitioners and hospital doctors. Large scale entertaining of consultants or organizing of trials was handled by sales specialists in head office. The two drug representatives also emphasized how ethical a company it was when they worked for Glaxo and how strictly it adhered to ABPI regulations. Glaxo's approach was an educational one, sponsoring research, advertising in

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<sup>965</sup> These included detailed prescribing information.

<sup>966</sup> From Testimony T20

medical journals and mailings to doctors, using key opinion leaders and representative visits. Their large sales force and persistence bore fruit to the extent that Zantac became the market leader as an H2 blocker. Donald Dunn, talking about the differences between cimetidine and ranitidine and ranitidine's huge success said, 'Probably it shouldn't have done as well as it did if you just look at the two drugs on paper and the price differential. But it had a big company behind it, let me say.'<sup>967</sup>

## 8. 6: 'The Limited List'

In an attempt to reduce the costs of drug prescribing in the NHS, a 'Limited List' was produced by the Department of Health and Social Security in England and Wales and the Scottish Home and Health Department in 1985.<sup>968</sup> For the treatment of dyspeptic disorders, it meant the loss of 26 well known proprietary medications in the antacid group and favourites such as Aludrox, Actal, Asilone and Maalox, to name only a few, could no longer be prescribed on NHS prescriptions. Others remained available as generics which were cheaper. As a cost-reducing exercise, it was felt at the time to have been a futile gesture since many general practitioners began prescribing H2 blockers, which were more effective but more expensive.<sup>969</sup> When general practitioner witnesses were questioned about their experiences of the Limited List, all regarded it as relatively unimportant but it acted as another spur to prescribe generically, which was the message of the NHS as a cost-saving exercise. Later, all prescribing became generic in NHS practice but before drugs came off patent they were issued as proprietary products as before.

## 8. 7: Ethics, drug prescribing and the pharmaceutical companies

At the time of the launch of Zantac, there was little discussion about the relationship between the pharmaceutical industries and doctors.<sup>970</sup> It was assumed that doctors were people of integrity who behaved ethically. Unfortunately this was not always the case and doctors have been struck off the General Medical Register for fraudulent activities in medical research.<sup>971 972</sup> The situation is two-way, for it is not unknown for pharmaceutical companies to suppress adverse results.<sup>973</sup> In the new millennium there is a body of opinion which is rising against the power of the pharmaceutical industries or 'Big Pharma' as it has

<sup>967</sup> Abridged quote from Testimony T20

<sup>968</sup> Supplements, 'Mr Fowler's statement on limited list', *British Medical Journal*, Mar 2<sup>nd</sup> 1985, 724-6

<sup>969</sup> From Testimony T6

<sup>970</sup> An internet search using 'Pharmaceutical companies and doctors' and the years '1970-2000' on the World of Science database raised 16 journal articles concerning doctors prescribing decisions, fifteen of which appeared after 1986

<sup>971</sup> Dyer C, 'Consultant struck off over research fraud', *British Medical Journal*, Jul 26<sup>th</sup> 1997, 205

<sup>972</sup> Smith R, 'Misconduct in research; editors respond', *British Medical Journal*, Jul 26<sup>th</sup> 1997, 201-2

<sup>973</sup> Roth D, Boyle E, Beer D, et al, 'Depressing research', *The Lancet*, Jun 19<sup>th</sup> 2004, 2087

been called.<sup>974</sup> Des Spence writing in the *British Medical Journal* sees key opinion leaders as a particular issue which compromises the profession's integrity.<sup>975</sup> As far back as 1961, *The Lancet* carried an article from an anonymous American academic warning of the dangers of inappropriate relationships with the pharmaceutical industry and outlined some of the inducement practices to influence doctors, which burgeoned in the ensuing decades. Talking of drug representatives it says, '... the nature of their calling should make it very obvious that we cannot expect from them an impartial and unprejudiced statement of fact'.<sup>976</sup> In 1984 Michael Rawlins wrote a comprehensive essay in *The Lancet* covering all the techniques used by the pharmaceutical industry described earlier in this chapter.<sup>977</sup> In 1986, Richard Smith in the *British Medical Journal* wrote about the kind of excessive expenditure by the pharmaceutical industry on general practitioner drug promotion and mentioned one particularly notorious occasion, when the promotion of a drug to general practitioners who were taken on the Orient Express, reached the notice of the BBC television programme, *Panorama*. Other junkets mentioned were trips to the Balearic Islands in the name of further education. The *British Medical Journal* of 31<sup>st</sup> May 2003 devoted 20 articles to aspects of the relationship between doctors and drug companies. One of these articles written by Ray Moynihan, an American journalist, demonstrated that 'entanglement' between doctors and drug companies was widespread and that interactions with industry could influence doctors' behaviors and prescribing strategies. He also suggested that sponsored research tended to produce favourable results for the sponsor and that a culture of industry gift-giving could conflict with a doctor's primary obligation towards his or her patient.<sup>978</sup> This had become a major issue.

In the testimony research, it was obvious that many doctors were comfortable with their relationships with the drug companies at this time. Most denied that they were influenced in any way by any of their offerings and believed that drug companies were serving a useful purpose to medicine in bringing new products on to the market. Hospital specialists were happy to seek suitable sponsorship for educational events and research and did not feel compromised by their contacts with the drug companies. However two doctors expressed dissatisfaction at the way in which drug companies had insinuated themselves

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<sup>974</sup> Spence D, 'Medicine's Leveson', *British Medical Journal*, Mar 7<sup>th</sup> 2012, 1671

<sup>975</sup> Moynihan R, 'Key opinion leaders: Independent experts or drug representatives in disguise?', *British Medical Journal*, Jun 21<sup>st</sup> 2008, 1402-3

<sup>976</sup> Anon, 'The pharmaceutical persuaders: the industry, the doctor and the clinical trial', *The Lancet*, Aug 19<sup>th</sup> 1961, 421-3

<sup>977</sup> Rawlins M D, 'Doctors and the drug makers', *The Lancet*, Aug 4<sup>th</sup> 1984, 276-8

<sup>978</sup> Moynihan R, 'Who pays for the pizza? Redefining the relationships between doctors and drug companies: 1. Entanglement', *British Medical Journal*, May 31<sup>st</sup> 2003, 1189-92

into the whole educational scene and they felt helpless to do anything about it, expressing shame at being a part of it. One general practitioner avoided drug representatives completely for he felt uneasy at accepting any kind of emolument but others were happy to accept educational opportunities offered by them. The two Glaxo drug representatives said they could tell anecdotes about doctors who sought to try to take advantage of them by seeking inappropriate gifts but they were both firm that they had boundaries which they did not transgress.

Zantac was successfully maintained by its sales-force using the techniques described and when eventually challenged by a potential successor drug, responded with a massively expensive promotion, as described by one of my witnesses,

*I had a couple of very fancy trips without any question. To come back to it, the world of business came home to me big time when Glaxo took myself (I can't remember who else, there was people dotted about from all over Britain) to Berlin. Just at the time when the Berlin wall was coming down, or just after it actually but check-point Charlie was still there, that's how I remember it. And the reason it took everybody there on this monumental junket, was omeprazole was about to be released or had been released and they were there trying to just grease everybody's palms and also there was a lot of stuff about the dangers of these PPI's and all that sort of stuff. I mean they took us to Berlin Opera House.<sup>979</sup>*

## 8. 8: Omeprazole

In 1991, omeprazole (Losec) was the first proton pump inhibitor (PPI) drug to be released into the UK market by its manufacturer A B Astra. Losec began its clinical life in the UK in a storm of controversy over its safety. Like cimetidine and ranitidine before it, omeprazole had been extensively tested in drug trials for several years before it was released on to the market.<sup>980</sup> However at the time of its launch in the UK, letters began to appear in medical journals discussing its potential to produce cancer in stomach cells. The main originator of these data was Glaxo who reported a test which apparently could show abnormal cell growth in stomach mucosal cells in rats when given omeprazole and they described it as 'genotoxic'.<sup>981 982</sup> The research was immediately refuted on the same and following page of *The Lancet* by scientists representing the pharmaceutical companies A B

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<sup>979</sup> From a Testimony.

<sup>980</sup> *Web of Science* database search using 'omeprazole' with a time limit 1981-88, yielded 1039 articles.

<sup>981</sup> Burlinson B, Morriss S H, Gatehouse D G, et al, 'Genotoxicity studies of gastric acid inhibiting drugs', *The Lancet*, Feb 17<sup>th</sup> 1990, 386 and 419

<sup>982</sup> Jackson M R, Wood J R, 'Omeprazole', *British Medical Journal*, 9<sup>th</sup> Nov 1991, 1200

Astra and Merck, Sharpe and Dohme.<sup>983</sup> Others criticized the data as being seriously flawed on account of contamination of their specimens.<sup>984</sup> Astra Pharmaceuticals had a vast body of data which suggested that their new drug Losec was safe in both short and long term use having launched first in the USA in 1989. The advantage which omeprazole conveyed was far higher rates of ulcer healing. It was a very effective drug which was capable of switching off most of the parietal cell acid secretion compared with the H2 blockers which allowed more of a residual secretion of acid.

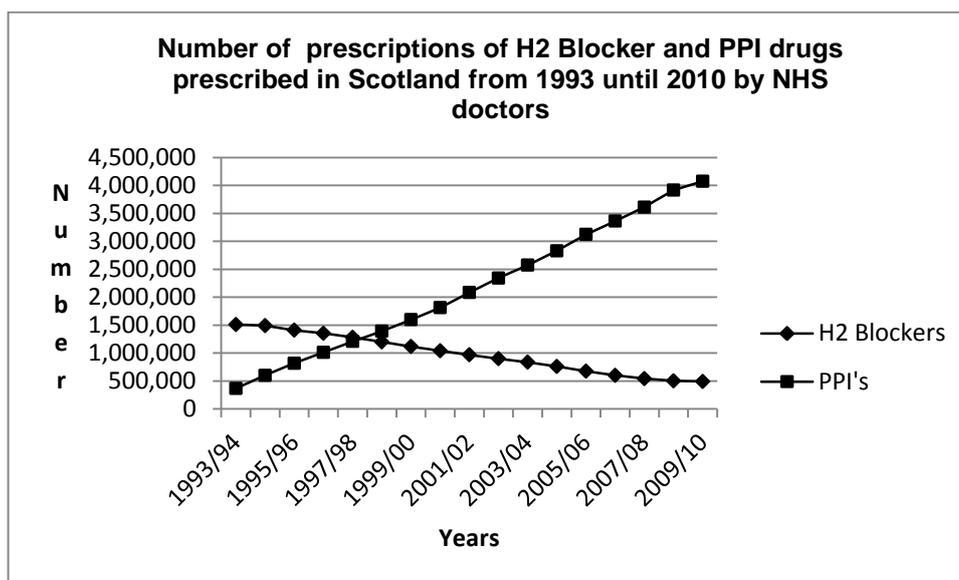


Figure 5

Prescribing of H2 blocker and PPI drugs in Scotland from 1993-2010. Data provided by the Information Services Division of the NHS in Scotland (ISD NHS Scotland)

Omeprazole was licensed for the treatment of all of the dyspeptic conditions which the H2 blockers had hitherto been used for.<sup>985</sup> There was less of a problem of establishing itself than for the H2 blockers for, by this time, doctors had considerable experience of such drugs. They quickly began to use it for all dyspeptic disorders and a study showed a ten-fold increase in its prescribing between 1991 and 1995.<sup>986</sup> In 1994, a competitor appeared, lansoprazole (Zoton) produced and marketed by Astra-Zeneca, followed in 1996 by

<sup>983</sup> Ekman L, Bolcsfoldi G, MacDonald J, 'Genotoxicity studies of gastric acid inhibiting drugs', *The Lancet*, Feb 17<sup>th</sup> 1990, 419-20

<sup>984</sup> Goodlad R, Wright R A, 'Omeprazole', *British Medical Journal*, 5<sup>th</sup> Oct 1991, 851. This edition of the *British Medical Journal* also contains letters from McCloy R, Howden C W, Holt S and Harrington R on this subject in pp850-1.

<sup>985</sup> British Medical Association and Royal Pharmaceutical Society of Great Britain, 'Cimetidine', *British National Formulary*, Sep 1998, No. 36, p36

<sup>986</sup> Bashford J N R, Norwood J, Chapman S R, 'Why are patients prescribed proton pump inhibitors? Retrospective link between morbidity and prescribing in the General Practice Research Database', *British Medical Journal*, Aug 15<sup>th</sup> 1998, 452-6

pantoprazole (Protium) marketed by Knoll Pharmaceuticals and in 1998 by rabeprazole (Pariet) marketed by Janssen-Cilag. The major issue about prescribing this new group of drugs was the high cost. However its efficacy made it very attractive for general practitioners and patients alike. At last doctors had a group of drugs which brought relief to almost every patient with a peptic ulcer disorder, also helping those with peptic oesophagitis very effectively for the first time. The graph in Figure 5 above illustrates how successful these drugs were and show the effect that they had on the prescribing of H2 blockers.

The PPI group of drugs undoubtedly allowed doctors to effectively treat the symptoms of peptic ulcer for the majority of patients but peptic ulcer remained a problem among those who had peptic ulcers and were unaware of the fact until they became suddenly ill, or those in the 'at risk' groups comprising the elderly, smokers and those who took NSAIDs.<sup>987</sup> In Chapter five it was shown that gastric and duodenal ulcers were declining as causes of death and morbidity by 1970. The trend continued and by 1990, the number of hospital admissions for elective surgery had declined by 80% and perforations of duodenal ulcers had fallen by 45%.<sup>988</sup> However duodenal perforations in women were continuing to rise and were 93% higher in 1990 than 1975. Perforations in men over 65 came second in highest incidence but had declined by 24% over the same period. Perforated duodenal ulcer was becoming a disease of the elderly and slowly declining in all other age groups.

## Conclusion to chapter eight

Modern management, investigation and treatment of peptic disorders have been discussed in this chapter. It has been seen how the introduction of the first effective oral medications for their treatment led to competition between two pharmaceutical companies to gain an increasing share of an expanding market as patients increasingly were taken off traditional remedies. The placebo effect was also discussed and offered as an explanation as to why patients with peptic ulcers under medical care 'did well' in times when no effective medications were available to doctors. The promotional tactics used by the pharmaceutical companies for newly introduced drugs and their relationship with doctors was discussed as were the resultant ethical dilemmas which continue to affect all practitioners who seek to use new drugs for their patients' benefits. As a consequence of the use of a new generation

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<sup>987</sup> 'NSAIDs' is an acronym for the drug group called 'Non-Steroidal Anti-inflammatory Drugs'. A common example is Ibuprofen. They relieve pain and reduce inflammation in rheumatic conditions and are commonly used general painkillers.

<sup>988</sup> Jibril J A, Redpath A, Macintyre M C, 'Changing pattern of admission and operation for duodenal ulcer in Scotland', *British Journal of Surgery*, Jan 1994, vol. 81, issue 1, 87-9

of anti-ulcer drugs, by the last decade of the century, most peptic ulcers could be effectively treated.

The next chapter will show how a return to an older abandoned concept of peptic ulcer aetiology led to the discovery of a bacterial cause for most peptic ulcers. The chapter will reveal the slow acceptance of the new hypothesis which offered the possibility of a cure, rather than a continuous effective treatment, for most duodenal and the majority of gastric ulcers. Background hostility from industry and healthcare professionals, whose clinical investment in peptic ulcer research was threatened, will be discussed. Eventually the bacterium *Helicobacter pylori* will be seen to be accepted as the cause of most peptic ulcers. A large body of research followed upon its discovery which has been the key to the effective treatment of a disease which was one of the most challenging of the twentieth century. The chapter will examine peptic ulcer disease in the elderly and in children and will discuss particular research in African children which would prove to be of seminal importance in the understanding of when *H. pylori* infection is acquired. Finally the chapter will conclude with a discussion of autopsy at the end of the twentieth century.

## Chapter 9. *Helicobacter pylori*: Its rôle in the aetiology of peptic ulcer disease

### Introduction to chapter nine

The final chapter of this thesis begins with the resurrection of the nineteenth century germ theory of ulcer genesis. The account is given of the discovery of *Helicobacter pylori* and of how clinicians responded to the new theory in the UK both in favour of it and against it and it is seen how it gradually became accepted as a major contribution to the understanding and eventual treatment of most gastric and duodenal ulcers. Personal accounts of physicians and surgeons supplement the history. How peptic ulcers affected the elderly, children and African children in particular is also described and an appraisal of the contribution of Robin Warren and Barry Marshall is made. The chapter concludes by showing that the practice of autopsy, which had played such an important role in the early understanding of peptic ulcers, has reverted in the minds of the public to the position of mistrust which prevailed at the end of the eighteenth century.

### 9. 1: The germ theory revisited

In 1938 James Doenges examined histological specimens from the stomachs of humans obtained at autopsy and found that 43% contained ‘spirochaetes’ in gastric glands, with a few showing ‘granules’ in the parietal cells.<sup>989 990</sup> His researches were prompted by a published report in 1936 of the incidental finding at autopsy of what were called ‘spirochaetes’, in the cytoplasm of parietal cells and in the lumens of the gastric glands of ‘Macaca’ monkeys.<sup>991</sup> Stone Freedberg and Louis Barron in 1940, repeated Doenges’ work and confirmed his findings adding that using a silver stain they could see the bacteria more easily.<sup>992</sup> In 1954, Eddy Palmer published a study to microscopically investigate these ‘spirochaetes’ found in stomach specimens by other researchers but found none in the 1180 specimens examined.<sup>993</sup> His report stated,

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<sup>989</sup> ‘Spirochaetes’ are spiral shaped micro-organisms and had been observed by Jaworski in 1889 in the stomach

<sup>990</sup> Doenges J L, ‘Spirochaetes in gastric glands of *Macacus rhesus* and humans without definite history of related disease’, *Proceedings of the Society for Experimental Biology and Medicine*, May 1938, vol. 38, issue 4, 536-8

<sup>991</sup> Cowdry E V, Scott G H, ‘Effects on monkeys of small doses of a concentrated preparation of viosterol’, *Archives of Pathology*, Jul 1936, vol. 22, issue 1, 1-23, esp p18

<sup>992</sup> Freedberg A S, Barron L E, ‘The presence of spirochaetes in human gastric mucosa’, *American Journal of Digestive Diseases*, Oct 1940, vol. 7, no. 10, 443-5

<sup>993</sup> Palmer ED, ‘Investigation of the gastric mucosa spirochaetes of the human’, *Gastroenterology*, vol. 27, no. 2, Aug 1954, 218-220

*It is concluded that spirochaetes are not part of the histologic picture of the human gastric mucosa in health or prior to the agony in illness. Simple contamination of the mucosal surface by swallowed spirochaetes appears to be encouraged by certain gastric diseases and is common at death, but actual invasion of the tubule lumina and of the tissues does not occur during life.*

The apparent conclusiveness of this piece of research, the eminence of the author and of the journal it was published in, marked an end to research into bacteria in the stomach for forty years. Had Palmer used a different stain, viz silver, it is likely that he would have found the spiral organisms.<sup>994</sup>

A generation followed with no active research of bacteria in the stomach until 1979. Robin Warren a pathologist working in Perth, Western Australia, had seen spiral shaped bacteria in stomach biopsy samples taken with endoscopes in association with gastritis, as had many other pathologists and all assumed that the bacteria were a secondary phenomenon rather than the cause of gastritis.<sup>995</sup> Warren was not satisfied with this explanation and built up an archive of cases of gastritis associated with the presence of spiral organisms. He discovered that if he stained his specimens with a silver stain (Warthin-Starry), then he could find the bacteria more easily. He studied multiple histological sections of stomach specimens over a two year period and found bacteria in association with chronic gastritis in almost half the biopsies examined. In 1981, Warren began to write up his findings intending to publish them. His colleagues in the hospital where he worked regarded him as ‘a bit eccentric’.<sup>996</sup> Barry Marshall, a young physician training in gastroenterology in the same hospital was looking for a research project for possible publication and approached Warren with a view to a collaborative project. Initially Marshall was sceptical but agreed to take endoscopic biopsy specimens from the gastric antrums of the stomachs of 20 patients which were normal-looking. To their surprise, the specimens showed both gastritis and bacteria in apparently healthy tissue and Marshall became enthusiastic about setting up a larger scale study of 100 patients. These spiral bacteria looked like *Campylobacter* bacilli and were initially called *Campylobacter-like organisms (CLO)*. Later they were renamed, three times, beginning with *Campylobacter pyloridis* until Latin

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<sup>994</sup> Kidd M, Modlin I M, ‘A century of *Helicobacter pylori*; paradigms lost-paradigms regained’, *Digestion*, vol. 59, 1998, 1-15 esp10. Also note, Palmer used haematoxylin and eosin (H+E) stains in microscopic samples. Some bacteria such as Tubercle bacilli do not stain at all with H+E stains and specialised staining techniques are required for them. Silver stains are used selectively for other histology and bacteriology purposes but not for general use.

<sup>995</sup> Marshall B J, *Helicobacter Pioneers*, ed Barry Marshall (Victoria, 2002, Blackwell Science), pxi

<sup>996</sup> This history is to be found in Warren J R, ‘Discovery of *H. Pylori* in Perth, WA’, in Marshall B.J, *Helicobacter Pioneers*, ed, Barry Marshall (Victoria, 2002, Blackwell Science), pp151-64

scholars changed ‘pyloridis’ to ‘pylori’ (being the genitive case of ‘pylorus’). Then it was decided that it was an unknown species and was reclassified as *Helicobacter pylori* by Stewart Goodwin in 1988.<sup>997</sup>

Out of 100 patients sampled, Warren and Marshall successfully cultured the organism from all 13 patients with duodenal ulcers and from 24 of 28 patients with gastric ulcers. Active gastritis was found in the stomachs and duodenum of patients with gastric and duodenal ulcers and this suggested to the researchers that both types of ulcer might have a bacterial cause. On June 4<sup>th</sup> 1983, after delays of several months, *The Lancet* published two letters from Warren and Marshall writing separately.<sup>998</sup> These letters represented the first published research on the germ theory of ulcer genesis for thirty years and opened the door to further researchers. *The Lancet’s* reluctance to publish reflected the scepticism of the time regarding the possibility of there being a bacterial cause for stomach ulcers. Warren asserted, ‘The extraordinary features of these bacteria are that they are almost unknown to clinicians and pathologists alike ... .’ He went on to describe their presence in association with gastritis. He suggested that the stomach must not be viewed as a sterile organ with no permanent flora. Marshall’s accompanying letter mentioned Doenges’ previous sightings of spiral shaped bacteria in the stomach in 1938 and concluded, ‘If these bacteria are truly associated with antral gastritis, as described by Warren, they may have a part to play in other poorly understood, gastritis associated diseases (i.e. peptic ulcer and gastric cancer).’

After the initial publication of the letters in *The Lancet*, Barry Marshall contacted Martin Skirrow, a leading authority on *Campylobacter*, and met him in Worcester in England en-route to the European Campylobacter Workshop in Brussels in September 1983 where he presented his preliminary findings to mixed reactions.<sup>999</sup> Other pathologists were beginning to be aware of the same link of gastritis and the presence of spiral organisms, including Terence Rollason and associates in Birmingham.<sup>1000</sup> Warren and Marshall’s work was replicated by Cliodna McNulty, a registrar in Martin Skirrow’s microbiology laboratory in Worcester, and a letter to this effect was published in *The Lancet* on May 12<sup>th</sup> 1984.<sup>1001</sup>

<sup>997</sup> Goodwin C S, ‘*Helicobacter pylori*: 10<sup>th</sup> anniversary of its culture in 1982’, *Gut*, Mar 1993, vol. 34, issue 3, 393-4

<sup>998</sup> Warren J R, Marshall B J, ‘Unidentified curved bacilli on gastric epithelium in active chronic gastritis,’ *The Lancet*, Jun 4<sup>th</sup> 1983, 1273-5

<sup>999</sup> This history is to be found in Marshall B J, ‘The discovery that *Helicobacter pylori*, a spiral bacterium, caused peptic ulcer disease’, in Marshall B J, *Helicobacter Pioneers*, op cit, pp165-202

<sup>1000</sup> Rollason T P, Stone J, Rhodes J M, ‘Spiral organisms in endoscopic biopsies of the human stomach’, *Journal of Clinical Pathology*, Jan 1984, vol. 37, issue 1, 23-6

<sup>1001</sup> McNulty C A M, Watson D M, ‘Spiral bacteria of the gastric antrum’, *The Lancet*, May 12<sup>th</sup> 1984, 1068-9

*The Lancet* published Warren and Marshall's 100 patient study on the 16<sup>th</sup> June 1984 in an edition which also included an editorial article about spirals and ulcers and three letters confirming further work which confirmed Warren and Marshall's initial work about this organism.<sup>1002 1003 1004</sup> Whilst all this experimental work was proceeding, Marshall sought to find a cure for the infection and with knowledge of the sensitivities of *Campylobacter* to amoxicillin, tetracycline, erythromycin and tinidazole he used them first singly. Bismuth, in the form of the proprietary medication 'De-Nol', also was used, since Marshall had read about its apparent bactericidal effects in an old textbook of medicine by William Osler.

In a dramatic attempt to show that the bacterium caused gastritis, Marshall swallowed a broth containing *Helicobacter pylori* which he had cultured from a patient who had gastritis.<sup>1005</sup> Prior to taking the bacterial broth Marshall had had a normal gastric biopsy obtained by endoscopy and a subsequent biopsy two weeks later demonstrated acute gastritis. Fortunately his subsequent self-medication cured his gastritis.<sup>1006</sup> His experiment was to establish a causal link between infection by *Helicobacter pylori* and acute gastritis. However Professor McColl, one witness, commented, 'Marshall could show that *Helicobacter pylori* could cause gastritis, but so could a contaminated burger eaten at the week-end. It was a very long step from gastritis, which no-one understood anyway, to ulcer and even further to gastric cancer, as suggested by Marshall.'<sup>1007</sup> In the next two years, Marshall was involved in setting up a double-blind prospective study of different agents for the eradication of the spiral organism.<sup>1008</sup> On its completion, he left Australia to work in the University of Virginia in August 1986, hoping to find a receptive audience. Of this time he commented; 'I was disappointed. It was to be another eight years before the bacteria was finally accepted there, following the consensus conference held by the National Institutes of Health in February 1994.'<sup>1009</sup>

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<sup>1002</sup> Marshall B J, Warren J R, 'Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration', *The Lancet*, Jun 16<sup>th</sup> 1984, 1311-4

<sup>1003</sup> Editorial, 'Spirals and ulcers', *The Lancet*, Jun 16<sup>th</sup> 1984, 1336-7

<sup>1004</sup> Langenberg M I, Tytgat G N J, Schipper M E I, et al, '*Campylobacter-like organisms* in the stomachs of patients and healthy individuals,' *The Lancet*, Jun 16<sup>th</sup> 1984, 1348; Burnett R A, Forrest J A H, Girdwood R W A, et al, '*Campylobacter-like organisms* in the stomachs of patients and healthy individuals', *The Lancet*, Jun 16<sup>th</sup> 1984, 1348-9; Pearson A D, Ireland A, Bamforth J, et al, 'Polyacrylamide gel electrophoresis of spiral bacteria from the gastric antrum', *The Lancet*, Jun 16<sup>th</sup> 1984, 1349-50

<sup>1005</sup> *Helicobacter pylori* in medical publications is customarily shortened to *H. pylori*

<sup>1006</sup> Marshall B J, Armstrong J A, McGeachie D B, et al, 'Attempt to fulfil Koch's postulates for pyloric, *Campylobacter*', *The Medical Journal of Australia*, Apr 15<sup>th</sup> 1985, vol. 142, 436-9

<sup>1007</sup> From Testimony T1

<sup>1008</sup> Marshall B J, Goodwin C S, Warren J R, et al, 'Prospective double-blind trial of duodenal ulcer relapse after eradication of *Campylobacter pylori*', *The Lancet*, Dec 24/31<sup>st</sup> 1988, 1437-41

<sup>1009</sup> Marshall B J, *Helicobacter Pioneers*, op cit, p201

Interest grew throughout the world and growing numbers of bacteriologists and gastroenterologists took an interest in the field, publishing their research in the medical journals of the time. The graph below shows the steady growth of such articles which eventually became exponential.

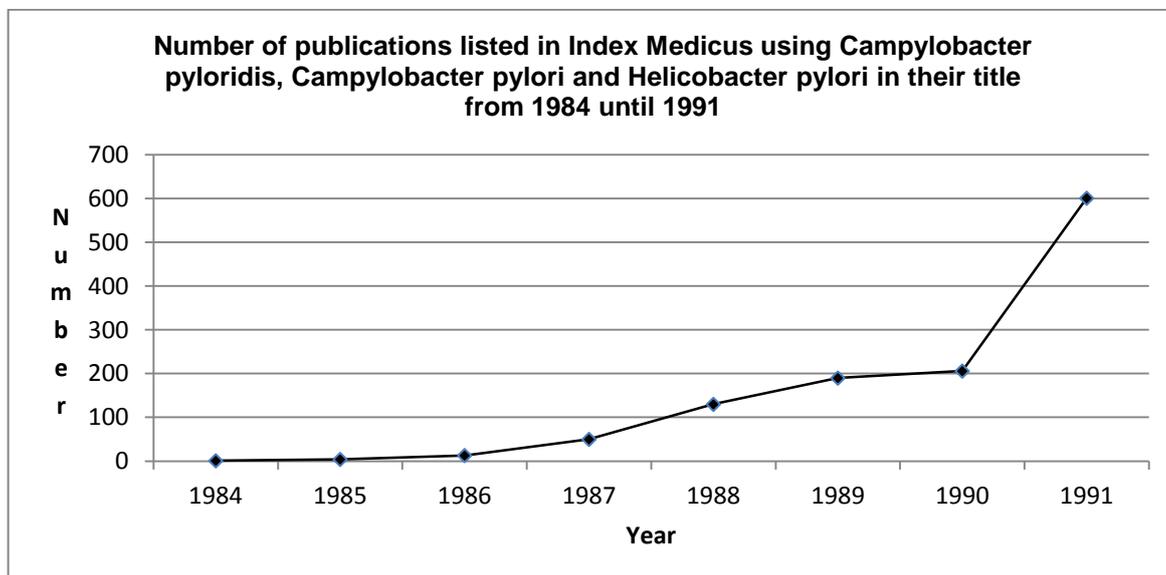


Figure 6.

Data extracted manually from Index Medicus

British gastroenterologists were cautious initially in accepting the hypothesis but in 1986, *Gut*, the journal of the British Society of Gastroenterology published a leading article on *Campylobacter pyloridis*.<sup>1010 1011</sup> It outlined most of the contemporary knowledge of the organism leaving open the question as to whether or not it was the pathogen responsible for peptic ulcer disease. Successful research of the treatment of patients with duodenal ulcers and *C. pylori* infection began to be published in the years which followed.<sup>1012 1013</sup> When Marshall's prospective double-blind treatment trial, published in 1988, was summarised by Walter Peterson in *Gastroenterology*, he was critical of the design of the study especially the small numbers involved and suggested that much more research was required before embarking on widespread use of antibiotics to treat duodenal ulcers. Marshall was allowed to respond to Peterson's commentary and argued that large therapeutic trials would not be supported by the pharmaceutical industry since the drugs

<sup>1010</sup> From Testimony T4

<sup>1011</sup> Rathbone B J, Wyatt J I, Heatley R V, 'Campylobacter pyloridis - A new factor in peptic ulcer disease?', *Gut*, Jun 1986, vol. 27, no. 6, 635-41

<sup>1012</sup> Coghlin J G, Gilligan D, Humphries H, et al, 'Campylobacter pylori and recurrence of duodenal ulcers - a 12 month follow-up study', *The Lancet*, Nov 14<sup>th</sup> 1987, 1109-11

<sup>1013</sup> Marshall B J, Goodwin C S, Warren J R, et al, 'Prospective double-blind trial', op cit, 1437-41

used were all generic and that it would take three years for such a study to come to publication.<sup>1014</sup>

In the ten years which followed Warren and Marshall's first letters in *The Lancet*, an ever decreasing number of doctors continued to support the acid-aetiology theory of ulcer genesis. In 1994, the National Institute of Health Consensus Development Panel on *Helicobacter pylori* in Peptic Ulcer Disease reported its findings in the *Journal of the American Medical Association* and concluded as follows:

*The discovery of H. pylori as a gastrointestinal pathogen has had a profound effect on current concepts of the pathogenesis of peptic ulcer disease. Evidence presented at this Consensus Development Conference has led to the following conclusions:*

*Ulcer patients with H. pylori infection require treatment with antimicrobial agents in addition to antisecretory drugs whether on first presentation of this illness or on recurrence.*

*The value of treatment with nonulcerative dyspepsia and H. pylori infection remains to be determined. The interesting relationship between H. pylori infection and gastric cancers requires further exploration.*<sup>1015</sup>

This report effectively ended most arguments about the relevance of *H. pylori* in the genesis of peptic ulcers and in March 1996, a journal called *Helicobacter* was launched devoted purely to *Helicobacter* research. In 1998, Kenneth McColl wrote, 'The rôle of *H. pylori* in the pathogenesis of duodenal ulcer disease is no longer disputed and eradication of this infection is now regarded as the first-line treatment for this common disorder.'<sup>1016</sup> The two Australians were jointly awarded the Nobel Prize in Physiology or Medicine in 2005.

There remains much to be learned about *H. pylori* including the mode of its transmission which has still not been definitively demonstrated but this is not the place to examine such research further. The question then may be asked: Where do Warren and Marshall stand in the history of duodenal and gastric ulcer? The answer may be summarised in the words of Albert Szent-Gyorgyi, the Nobel Laureate who coined the saying; 'Discovery consists of

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<sup>1014</sup> Peterson W L, 'Antimicrobial treatment of duodenal ulcer? Hold off for now!', *Gastroenterology*, Aug 1989, vol. 97, no. 2, 508-10

<sup>1015</sup> NIH Consensus Conference. (1994), '*Helicobacter pylori* in peptic ulcer disease', *Journal of the American Medical Association*, Jul 6<sup>th</sup> 1994, vol. 272, 65-9

<sup>1016</sup> McColl K E L, '*Helicobacter pylori* 1988-1998', *European Journal of Gastroenterology and Hepatology*, Jan 1999, vol. 11, issue 1, 13-6

seeing what everyone has seen and thinking what nobody has thought.’ This was their contribution. Mr Alan MacKay, one of my witnesses describes Barry Marshall thus,

*I think he is the genuine original researcher. If you think; he comes up with a mind-blowing theory to destroy 80 years’ worth of surgical physiology and is rejected by the scientific community and then finds a dramatic way of convincing them and turns around medical practice throughout the world.<sup>1017</sup>*

## 9. 2. 1: What everyone saw and nobody thought

Robin Warren was not aware that bacteria had been found in gastric samples of all types, for over a hundred years, when he began to find them in his biopsy samples. The earliest finding of bacteria in specimens from gastric ulcers in 1875 was by Professor Arthur Boettcher in Dorpat in Germany, reported in *The Lancet* in 1878 and recorded in Mark Kidd and Irvine Modlin’s comprehensive account of bacteria in the stomach since 1875.<sup>1018 1019</sup> Most pathologists around 1980 had seen bacteria in specimens sent to them by surgeons, often in cancer biopsies. However Robin Warren’s account puts it; ‘Basic medical teaching for more than a hundred years stated that bacteria do not grow in a normal stomach, probably because of the acid environment.’<sup>1020</sup> Warren was beginning to think the unthinkable that there were bacteria living in the stomach and that they might be pathogens.

Warren’s discovery occurred at a time of innovation in gastroenterology with the massive increase in the use of endoscopes due to improvements in their design, especially in the taking of biopsy samples, which provided the pathologist freshly fixed biopsy specimens.<sup>1021</sup> These endoscopically obtained gastric mucosal samples were unlike surgical excision samples which were subject to autolysis (self digestion) before they were fixed for pathological examination. Fresh endoscopy samples mostly showed bacteria in association with gastritis where there were duodenal ulcers and, in a lesser proportion, where there was a gastric ulcer. Five witnesses reported seeing bacteria on slides of stomach samples and two had seen electron micrograph photographs of them before Warren and Marshall had published their letters.<sup>1022</sup> Dr Ian Brown had himself produced a photo-electron micrograph of a *Helicobacter* microorganism within the secretory

<sup>1017</sup> From Testimony T3

<sup>1018</sup> Editorial, *The Lancet*, Apr 13th 1878, 539

<sup>1019</sup> Kidd M, Modlin I M, ‘A century of *Helicobacter pylori*, op cit, 1-15

<sup>1020</sup> Warren J R, ‘Discovery of *H. Pylori* in Perth, WA’, op cit, p151

<sup>1021</sup> ‘Fixing’ of pathological specimens consists of pickling them in chemicals which inhibit natural post mortem degradation or autolysis.

<sup>1022</sup> From Testimonies T1, T2, T8, T15, T16

canaliculus of a parietal cell but did not interpret its significance until Warren and Marshall's hypothesis became better known.<sup>1023 1024</sup> In 1987, looking for evidence of the organism in pathology specimens with colleagues in Stobhill hospital they devised a new bacteriological stain which clearly showed the bacteria with associated gastritis in a very large number of specimens.<sup>1025</sup>

## 9. 2. 2: The germ theory and the testimony of clinicians

The initial letters of Warren and Marshall to *The Lancet* seem to have largely passed unnoticed at the time by most of those clinicians I questioned. Professor Kenneth McColl at a local research meeting in 1985 heard of the possibility that a bacterium might be causing ulcers.<sup>1026</sup> He was initially hostile to the hypothesis but later, having read up about the organism, began to believe in the possibilities that this organism might be causing pathogenic effects.<sup>1027</sup> By 1987, he was actively promoting treatment of *H. pylori* and one GP witness, Dr Amanda MacKenzie remembers being at lectures given by Professor McColl and meeting Barry Marshall at a symposium in Glasgow that year.<sup>1028</sup> She clearly remembered the first time that year, when she prescribed triple therapy for a patient with a duodenal ulcer. On discussing the topic with her husband, a consultant gastroenterologist, his response was that the hypothesis was, 'complete rubbish'. He changed his mind shortly thereafter. Others of my witnesses gradually became aware of the hypothesis, including one who heard of it thanks to Barry Marshall's self inoculation with the bacterium and Glasgow gastroenterologists whom I interviewed, began to treat *H. pylori* as a cause of peptic ulcer disease after 1987.<sup>1029</sup> In his Wellcome Symposium testimony, Kenneth McColl says, 'The way in which this new treatment became adopted, was not from the profession down, it was from the patients up. And it was through the press getting hold of the story through their (television) programmes and newspapers, that the patients demanded this new treatment.'<sup>1030</sup>

There remained hostility to the hypothesis from the 'acid doctors' whose research interests were invested in research on stomach acid production and its role in peptic ulcer. One such researcher was described by one of my witnesses,

<sup>1023</sup> The secretory canaliculus of a parietal cell is the part of the cell which secretes the acid.

<sup>1024</sup> From Testimony T15

<sup>1025</sup> Burnett R A, Brown I L, Findlay J, 'Cresyl fast violet staining method for *campylobacter like organisms*', *Journal of Clinical Pathology*, Mar 1987, vol. 40, issue 3, 353

<sup>1026</sup> McColl K L, *Wellcome Witnesses*, op cit, p99

<sup>1027</sup> From Testimony T1

<sup>1028</sup> From Testimony T26

<sup>1029</sup> From Testimony T8

<sup>1030</sup> McColl K L, *Wellcome Witnesses*, op cit, p95

*Dr X was very interested in acid and was a firm believer in the acid school and acid concept ...*

*there were some people who felt this (germ theory) was nonsense, who clung vigorously to the idea. I am not sure how early on Dr X accepted it for example but I don't want to criticise him ... You've got to understand those people had a deep investment in antacids, I don't think financially but the concept of acid output and the factors there. The idea that this was just a little bug there that you treated and the whole thing was cleared up, was almost incomprehensible.* <sup>1031</sup>

Hostility to the germ theory could become quite personal as related by Kenneth McColl,

*Early on there was definite hostility to (it) ... quite understandably. These drug companies were making a small fortune out of ulcer disease and I think at that time more money was prescribed on ulcer drugs than for anything else. It was then that the companies shot up the scale with huge profits and they saw this as a threat, and we came up against this and I can remember we put up a presentation to the British Society of Gastroenterology on the effect of *Helicobacter pylori* on gastrin and saying how it might cause ulcers and it was selected for a press conference before the BSG meeting. I presented my work at this press conference and then I remember shares actually fell the next day and when I was at the BSG meeting, I got a 'phone call from the doctor who was the Secretary of BSG telling me I had not to speak to the press again about *Helicobacter pylori* infection ...* <sup>1032 1033</sup>

*I can remember the hostility didn't just come from (only) the drug companies, it came from the doctors and I can remember one of these meetings where one of the senior BSG members who was chairing the meeting where I was about to speak. He gave very, very disparaging remarks about this talk I was going to give on *H. pylori*. I remember too at that same meeting, in the canteen over breakfast, there was a group of senior consultants who didn't know I was there and they really were making very derisory remarks about this research we were doing and how it was so stupid. There was a huge amount of resistance from the drug companies. You would arrange meetings and choose speakers to be quite biased in opinion, preventing people like me getting to these meetings.* <sup>1034</sup>

<sup>1031</sup> Abridged from Testimony T13

<sup>1032</sup> Gill L, 'Catching the ulcer culprit', *The Times*, Thurs, Apr 26<sup>th</sup> 1990, p18

<sup>1033</sup> McColl K E L, Fullarton G M, El Nujumi A M, et al, 'Serum gastrin and gastric acid status, one and seven months after *Helicobacter pylori* eradication', British Gastroenterological Society Spring meeting, *Gut*, May 1990, vol. 31, A601

<sup>1034</sup> McColl K L, *Wellcome Witnesses*, op cit p95 and abridged from Testimony T1

*Davidson's Textbook of Medicine*, edited by Professor Ian Bouchier, first mentioned *H. pylori* in the sixteenth edition in 1991, and in the seventeenth included *Helicobacter* eradication for the treatment of peptic ulcers. *Muir's Textbook of Pathology* first included *H. pylori* in 1992 in a section on 'The Aetiology and Pathogenesis of Chronic Peptic Ulcer'. This chapter was written by Professor Frederick Lee, another witness, and it is noticeably tentative in its description of the rôle of *H. pylori*. These two textbooks were standard texts for British medical students and practising doctors.

As ulcers began to be treated with antisecretory drug/antibiotic combinations, there was much discussion regarding the best treatment courses for the eradication of *H. pylori*. The first mention of treatment of the organism, which was then still called *Campylobacter*, in the *British National Formulary (BNF)* was in September 1989. A year later it was listed as *Helicobacter*. In March 1995 detailed lists of treatment regimes were included and in September 1995, two suggested regimens are listed, each using two antibiotics and omeprazole for a week's course.<sup>1035</sup> These regimens involved taking three different drugs and were difficult for the patients to manage. For this reason, patient packs were produced, 'Heliclear' in April 1999 and 'Helimet' in March 2002 which contained different triple therapies for *H. pylori* eradication.

Therapeutics dominated medical discussion in the field of *H. pylori* research. Professor Ian Bouchier who was a president of the British Society of Gastroenterology in 1994-5 remembers some of the discussions,

*And of course what happened was there was a huge explosion of research and early on they realised that the organism became resistant and so that led to a whole series of trials of different sorts of medicine, an enormous number of trials. There were world conferences on H. pylori, some held in Scotland. I was invited to go and listen to these and they were all dealing with the various treatment protocols that you used.*<sup>1036</sup>

By 2000, general practitioners were treating patients with duodenal and gastric ulcers in their surgeries on the basis of endoscopic diagnosis provided by their local gastroenterologist. Barium meals were by this time rarely done for routine duodenal and gastric ulcer investigations. *H. pylori* was the main treatable cause of peptic ulcer, but for those patients who got peptic ulcers who were not *H. pylori* infected, two other issues were

<sup>1035</sup> 'Ulcer healing drugs', *British National Formulary*, Sep 1995, (30), lists; Regimen 1: Omeprazole 20mg twice daily with Metronidazole 400mg three times a day as well as Amoxicillin 500mg three times a day. Regimen 2: Omeprazole 20mg twice daily with Clarythromycin 250mg and Tinidazole 500mg twice daily.

<sup>1036</sup> Abridged from Testimony T13

seen to play a part, viz smoking and the taking of non-steroidal anti-inflammatory drugs (NSAIDs).

Aging too was seen to be increasingly important for, in the elderly, there was a higher incidence of haematemesis and perforation than for the general population. The incidence of perforation in men over 65 was slowly falling but in women over 65 it was rising.<sup>1037</sup> All thoughts of peptic ulcers having a psychological basis had largely been discarded by those in the medical profession who specialized in their treatment, except for the small numbers of practitioners who still used psychotherapy as their main means of making a living. Susan Levenstein writes of this in two articles which chronicle the decline of the psychosomatic contribution to the formation of peptic ulcers.<sup>1038</sup> In one paper she concludes that stress contributes to the aetiology of peptic ulcer formation in between 30 and 65% of cases and produces evidence to support her statement derived largely from research from psychosomatic medical writing.<sup>1039</sup> Dr Mark Hughson who spent his working life as a psychiatrist had this to say about peptic ulcer,

*The treatment of peptic ulcer disease is fascinating. I remember the days when psychological factors were thought important in helping to cause peptic ulcer disease ... There seems to be a similar story with tuberculosis, with emphasis on the psychological make-up of the consumptive, until the discovery of the mycobacterium ... I have noticed a tendency in some doctors who, if really they don't know why the patient is ill, tend to convey to the patient that there must be something psychological involved. Why? Why can't they just tell the patient that they don't know?*<sup>1040</sup>

Smoking was a common habit in the UK for much of the twentieth century but little was written about it in connection with diseases. In 1927, Charles Barnett in Boston looked at the evidence regarding smoking and peptic ulcer.<sup>1041</sup> His conclusion was that, 'There is no proof that smoking is of any importance in the etiology of peptic ulcer or gastric neurosis.' However his study did clearly show that smokers got ulcers at a younger age than non-smokers. In 1947, Arthur Douthwaite commented that, 'Experimental evidence favours

<sup>1037</sup> Jibril J A, Redpath A, Macintyre M C, 'Changing pattern of admission and operation for duodenal ulcer in Scotland', *British Journal of Surgery*, Jan 1994, vol. 81, issue 1, 87-9

<sup>1038</sup> Levenstein S, 'The very model of a modern etiology: a biopsychosocial view of peptic ulcer', *Psychosomatic Medicine*, Apr 2000, vol. 62, 176-85; Levenstein S, 'Bellyaching in these pages: Upper gastrointestinal disorders in *Psychosomatic Medicine*', *Psychosomatic Medicine*, Sept 2002, vol. 64, 767-72

<sup>1039</sup> Levenstein S, 'The very model', *ibid*, 181

<sup>1040</sup> Personal communication.

<sup>1041</sup> Barnett C W, 'Tobacco smoking as a factor in the production of peptic ulcer and gastric neurosis', *Boston Medical and Surgical Journal*, Sep 22<sup>nd</sup> 1927, vol. 197, no. 12, 457-9

harmlessness of smoking to patients with chronic ulcer.<sup>1042</sup> He added his own observation of his patients that smoking caused pain in the active phase of the disease but he stopped short of advising abstinence. At the One Hundred and Seventeenth Annual Meeting of the *British Medical Association* in 1949, Richard Doll reported that his investigations showed no difference in the incidence of peptic ulcer in smokers and in non-smokers.<sup>1043</sup> Nine years later, Doll and associates published an article in *The Lancet* to study the effects of smoking in patients with peptic ulcers.<sup>1044</sup> Again the results were inconclusive stating that, 'It appears unlikely, however, that smoking is an important and direct cause of peptic ulcer.' He included a small sample trial which demonstrated accelerated healing in patients with gastric ulcers who had been advised to stop smoking over a four week period compared with those who were not so advised. This article has been cited 264 times by other authors.<sup>1045</sup> In 1976, when hospital admissions were examined with reference to perforations of ulcers, no conclusive evidence linked smoking to perforations of ulcers.<sup>1046</sup>

A UK study on 1985 demonstrated that tobacco smoking delayed healing of gastric ulcers and influenced duodenal ulceration.<sup>1047</sup> However in 1987 a study of patients with duodenal ulcers in New South Wales failed to show any clinical effect of smoking on clinical duodenal ulcer course.<sup>1048</sup> Then in 1994 Garcia Rodriguez in a UK study of patients taking NSAIDs showed that they had a five times overall greater risk of a stomach bleed than the population as a whole rising to 13 times greater for those 60 and older.<sup>1049</sup> Smoking increased the risk by 40%. For perforation, the relative risk of taking NSAIDs was eight times greater. By 1997 the evidence of the role of tobacco smoking in peptic ulcer formation was increasingly being demonstrated to be of major importance.<sup>1050</sup> In 2003, *Gut* published a large prospective cohort study of Danish adults looking for risk factors for

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<sup>1042</sup> Douthwaite A H, 'Choice of drugs in the treatment of duodenal ulcer', *British Medical Journal*, Jul 12<sup>th</sup> 1947, 43-7

<sup>1043</sup> Doll R, 'Treatment of peptic ulcer' *British Medical Journal*, Jul 9<sup>th</sup> 1949, 79

<sup>1044</sup> Doll R, Avery-Jones F, Pygott F, 'Effect of smoking on the production and maintenance of gastric and duodenal ulcers', *The Lancet*, Mar 29<sup>th</sup> 1958, 657-62

<sup>1045</sup> A *Web of Science* database search, using 'Doll R' with a time limit '1932', showed that this paper had been cited 264 times in other articles

<sup>1046</sup> Brown R C, Langman M J S, Lambert P M, 'Hospital admissions for peptic ulcer during 1958-72', *British Medical Journal*, Jan 3<sup>rd</sup> 1976, 35-7

<sup>1047</sup> Hull D H, Beale P J, 'Cigarette smoking and duodenal ulcer', *Gut*, Dec 1985, vol. 26, 1333-7

<sup>1048</sup> Nasirey R W, McIntosh J H, Byth K, et al, 'Prognosis of chronic duodenal ulcer: A prospective study of the effects of demographic and environmental factors and ulcer healing', *Gut*, May 1987, vol. 28, issue 5, 538-9

<sup>1049</sup> Rodriguez L A G, Jick H, 'Risk of upper gastrointestinal bleeding and perforation associated with individual non-steroidal anti-inflammatory drugs', *The Lancet*, Mar 26<sup>th</sup> 1994, 769-72

<sup>1050</sup> Svanes C, Søreide J A, Skarstein A, et al, 'Smoking and ulcer perforation', *Gut*, Aug 1997, vol. 41, 177-80

peptic ulcer disease.<sup>1051</sup> Its results showed a significant correlation between *H. pylori* infection, tobacco smoking, the ingestion of tranquillisers and the risk of peptic ulcer disease. Further recent studies confirm these findings and it is now accepted that cigarette smoking is a significant factor in peptic ulcer formation.

### 9. 3. 1: Peptic ulcers and the elderly

From Rodriguez's paper it is evident that age is an important factor in the aetiology of complicated peptic ulcer.<sup>1052</sup> With this in mind, I interviewed two geriatricians to bring their perspective to the history. The presentation of patients over the age of 65 with duodenal or gastric ulcers tended to differ from the younger population. Dr Brendan Devine gives the clinical picture of this group of patients,

*It tends to present with anaemia, with G-I bleeding, not so much with severe dyspepsia. I have endoscoped many elderly patients during my years and I've learned that if they don't have dyspepsia and they're anaemic it's almost certainly going to be large bowel (pathology). I've endoscoped hundreds of elderly patients with no dyspepsia but have anaemia and almost invariably they don't have anything in their upper GI tract.*

*Symptoms matter in that group. The other thing is obviously, as you know, the people who die of GI bleeding and perforation are elderly patients. That's partly because of their multiple pathology and their general frailty but also because they are the guys that have been stuffed with non-steroidal anti-inflammatory drugs.<sup>1053</sup>*

Dr James Davie, another geriatrician reinforced the message about NSAIDs,

*We became very conscious of the fact that the prescription of large numbers of non-steroidals was certainly having an adverse affect which seemed to be to some extent may be just because they were older, female biased, and we also became conscious of a number of patients who in fact were given 75mg of aspirin, coming in with upper GI symptoms from that and sometimes haematemesis, quite often haematemesis.<sup>1054</sup>*

Dr Devine was passionate about his opposition to elderly patients being prescribed NSAIDs and in his teaching of junior doctors he expressed his thoughts forcefully,

<sup>1051</sup> Rosenstock S, Jørgenson T, Bonnevie O, et al, 'Risk factors for peptic ulcer disease: a population based prospective cohort study comprising 2416 Danish adults', *Gut*, Feb 2003, vol. 52, issue 2, 186-93

<sup>1052</sup> Rodriguez L A G, Jick H, 'Risk of upper gastrointestinal bleeding,' op cit, 769-72

<sup>1053</sup> From Testimony T23

<sup>1054</sup> From Testimony T12

*When I talk to my juniors now I tell them that non-steroidal drugs are poison and they must never give them to elderly patients unless they've got acute gout or they've got bone cancer and nothing else is helping. But as a general painkiller you should never use them and I always stop them from doing it.*<sup>1055</sup>

There are other good reasons for not giving NSAIDs to elderly patients, being a special hazard in patients with cardiac disease or renal impairment, which may again place older patients at particular risk.<sup>1056</sup> Perforations which occur in the elderly when the patient does not have the dramatic symptom of sudden severe abdominal pain accompanied by collapse, are called 'silent' and because the patients do not present with a typical picture they require a greater degree of skill and experience in making an accurate diagnosis.<sup>1057</sup> There is a received wisdom that silent perforations are commoner in the elderly but when asked, Dr Devine had little experience of them.

Elderly patients present different problems than younger ones and the job of the geriatrician is to unravel the presenting issue and return the patient to best health for them in the presence on multiple health problems. Dr Davie outlined the issue,

*I see our main function as geriatricians as dealing with an elderly person with a number of different illnesses, including possibly dementia, but not necessarily. They will often have arthritis complicating their cardiac failure and the cardiac failure is further complicated by a long standing chest condition, etc. So you're approaching it from a multi factorial point of view. We do still see people who come in with a single pathology, for example, someone who has got a pneumonia and nothing else much wrong with them but I see our function as mainly being to deal with the more complex multiple pathology.*<sup>1058</sup>

Among this pathology is a higher incidence of duodenal and gastric ulcers.

### 9. 3. 2: Children with peptic ulcer

Peptic ulcers were believed to be uncommon in children. *The Lancet* of 1858 describes the cases of two boys, one eleven and the other twelve, who had been diagnosed with gastric ulcers on the basis of epigastric pains and haematemesis.<sup>1059</sup> Their attending doctor quoted

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<sup>1055</sup> From Testimony T23

<sup>1056</sup> British Medical Association and Royal Pharmaceutical Society of Great Britain, 'Prescribing for the elderly,' *British National Formulary*, Mar 2002, vol. 43, p18

<sup>1057</sup> Kane E, Fried G, Mc Sherry C K, 'Perforated peptic ulcer in the elderly', *Journal of the American Geriatric Society*, May 1981, vol. 29, issue 5, 224-7

<sup>1058</sup> From Testimony T12

<sup>1059</sup> Sieveking E H, 'On two cases of ulceration of the stomach in boys', *The Lancet*, Oct 9<sup>th</sup> 1858, 370-1

William Brinton's remark that liability to ulcer of the stomach 'rises from what is almost a zero at the age of ten to a high rate, which it maintains through the period of middle life'.<sup>1060</sup> Both boys recovered, the first was given bismuth and the second, lime water, along with other medicaments. In 1922, Donald Paterson described two more cases of duodenal ulcer and, having reviewed the English language literature of that time, found less than 100 cases of duodenal and gastric ulcers in children, mainly American but with three British.<sup>1061</sup> Two years later, Amy Thoms added another case of a death from duodenal ulcer in a five month old infant and in 1932 Jerome Selinger reported the autopsies of three children aged two, three and eleven months with gastric ulcers.<sup>1062 1063</sup> In 1941, Clarence Bird and associates in New York reported that they had found 119 cases in the literature of children under the age of 16 who had had surgery for gastric or duodenal ulcer.<sup>1064</sup> The following year Katharine Guthrie in Glasgow Royal Hospital for Sick Children reported the autopsy results of nine children gathered between 1914 and 1941.<sup>1065</sup> The youngest was three days old, seven were under 24 weeks and the oldest was six years old having suffered severe internal injuries in an accident. This girl began to have severe melaena five days after admission which continued for three days before she died. Guthrie's account also contains a historical account of other cases going back to Cruveilhier (c1830).

*The Lancet* in 1953 included an account of a boy and a girl, each five years old, with perforated duodenal ulcers.<sup>1066</sup> Alberto Ramos and associates in 1960 published an account of 32 cases gathered from 1936-1958 in Chicago.<sup>1067</sup> Twenty six of them were over 11 years old, there was a neonate, one two and one four year old and three under seven years old. Nine patients were unsuccessfully treated medically but seven children had surgery with the remaining two having radiotherapy treatment.<sup>1068</sup> In 1987, Stephen Murphy and Edmund Eastham from Newcastle published an article on peptic disease in

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<sup>1060</sup> Brinton W, *On the Pathology, Symptoms and Treatment of Ulcers of the Stomach*, (London, 1857, John Churchill), p9

<sup>1061</sup> Paterson D, 'Duodenal ulcer in infancy', *The Lancet*, Jan 14<sup>th</sup> 1922, 63-5

<sup>1062</sup> Thoms A, 'A case of duodenal ulcer in an infant', *The Lancet*, Oct 25<sup>th</sup> 1924, 854-5

<sup>1063</sup> Selinger J, 'Peptic ulcer in infants under one year of age', *Annals of Surgery*, Aug 1932, vol. 96, issue 2, 204-9

<sup>1064</sup> Bird C E, Linper M A, Mayer J M, 'Surgery in peptic ulcer of stomach and duodenum in infants and children', *Annals of Surgery*, Oct 1941, vol. 114, issue 4, 526-42

<sup>1065</sup> Guthrie K J, 'Peptic ulcer in infancy and childhood with a review of the literature', *Archives of Disease in Childhood*, Jun 1942, vol. 17, issue 90, 82-94

<sup>1066</sup> Bell D M, 'Perforated duodenal ulcer in children', *The Lancet*, Oct 17<sup>th</sup> 1953, 810-1

<sup>1067</sup> Ramos A R, Kirsner J B, Palmer W L, 'Peptic ulcer in children', *American Medical Association Journal of Diseases of Children*, 1960, vol. 99, issue 2, 135-48

<sup>1068</sup> Chicago hospitals had a major centre which used radiotherapy for the treatment of peptic ulcers, see chapter 5.

childhood from 1960-1972 which included 19 patients, all but four of whom developed ulcers after the age of ten, the youngest being three. The course of their illnesses followed the well recognized adult pattern and nine had surgery, with six having a vagotomy and pyloroplasty and one a partial gastrectomy. In 2007, a Taiwanese study of twenty years' experience of perforated peptic ulcer in children was published.<sup>1069</sup> Fifty two patients were included, 90% of whom were adolescents. All required surgery and did well. The authors suggested that perforation of peptic ulcer should be considered as a possibility when adolescents present with acute abdominal pain.

Dr Michael Blair was one of two paediatricians interviewed with interests in gastroenterology. He had spent most of his working lifetime working in Ayrshire and he regularly saw children with peptic ulcers but not in large numbers. He investigated them using mainly barium meals because endoscopy in children requires a general anaesthetic. His main criterion for investigation was a strong clinical history,

*If the barium meal was positive then we probably did follow that up every time with an endoscopy and if it was doubtful then we might still do an endoscopy. The basic things from history would be; a positive family history would be high on the cards, the type of abdominal pain; upper abdominal pain, worse at night time, relieved by food or milk ...*<sup>1070</sup>

The peak age for peptic ulcers was ten to twelve. They were treated medically in the same way an adult would be. Dr Blair never referred a child for ulcer surgery in his working lifetime.

The second witness, Professor Lawrence Weaver learned in his training that, 'peptic ulcers were not that rare in children, it may be unusual but it was not something that you should rule out. And the chief symptoms were night-time abdominal pain.'<sup>1071</sup> Barium meals and follow-through were the main diagnostic method before endoscopy began to be used in children. Children with abdominal pain make up a large percentage of the work of the paediatric gastroenterologist and both witnesses testified to the levels on anxiety they generate in the family.

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<sup>1069</sup> Hua M-C, Kong M-S, Lai M-W, et al, 'Perforated Peptic Ulcer in children: a 20 year experience', *Journal of Pediatric Gastroenterology and Nutrition*, Jul 2007, vol. 45, no. 1, 71-4

<sup>1070</sup> From Testimony T25

<sup>1071</sup> From Testimony T18

Dr Blair describes the problem,

*A paediatrician's nightmare ... You'd have families, often middle class families, coming in with a child who had frequent severe abdominal pain. And you would sit there and look at the child who looked perfectly healthy, well nourished, happy, no problems when they were sitting in front of you. But you were getting this story of recurrent pain, usually associated with pallor and if parents were more aware, then dilated pupils. And if you came out with the most likely answer, which was that there was no organic cause for this pain, straight away, then you would usually meet a bit of disbelief and perhaps antagonism because the parents were seeing this child in genuine distress. And if we came out and said, 'Look there's nothing wrong', then they wouldn't like that. So you learnt very quickly not to say that.*

Naturally this engendered much distress to the family but paediatricians learned to help the family cope with the situation until the problem disappeared with maturity. This required a professional approach.

*You would do a full examination, you would do probably routine bloods, which again in paediatrics you've got to think about and there shouldn't ever be a routine blood test in paediatrics, you've got to have a very good reason for doing something. But you would check full blood count and ESR and probably U's and E's, LFT's and bone screen, things like that.<sup>1072</sup> And if that was all perfectly normal and your clinical examination was perfectly normal and urinalysis was perfectly normal, you would then go down the line this was non-organic abdominal pain. Genuine pain, because the child clearly was suffering, but you could reassure the family that there was nothing serious going on inside the abdomen and that this would go away. You couldn't say when it would go away, it might take several years to go away, but it would go away. And you would see then on a regular basis and support them through that time.<sup>1073</sup>*

Lawrence Weaver further put the problem in context,

*The childhood 'belly-achers' were mostly regarded as younger children, toddlers up to secondary school but the peptic ulcer children were certainly generally*

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<sup>1072</sup> These abbreviations are shorthand for the most common blood tests done by doctors generally which give an indication of whether there is anaemia or other blood disorder, the immune system's working, kidney and liver function and bone metabolism, all of which may rarely in children cause symptoms.

<sup>1073</sup> From Testimony T25

*thought to be teenagers. So the childhood peptic ulcer was seen as a continuum with adult peptic ulcer disease, not a separate phenomenon in children.*

In the past two decades, the role of *H. pylori* has become important in the understanding and treatment of duodenal and gastric ulcers and other dyspeptic conditions. In older children, it was no different; those diagnosed with the infection who had ulcers were treated as adults were with triple therapy.

### 9. 3. 3: *H. pylori* in African children

Lawrence Weaver and his colleagues' contribution to the *H. pylori* story follows a very different path from the adult research of the rest of the world. As stated earlier in this chapter, the exact mode of transmission of *H. pylori* has not been precisely discovered. It is known to be associated with overcrowding, poor sanitation and poverty but when it is acquired was not known until a research project was begun in The Gambia of which Lawrence Weaver was a part.

*I was working in a nutritional research centre that had a clinical research station in The Gambia in West Africa. And the dominant interest of the work that we did there was on infant and child malnutrition and diarrhoea, so that we had a large population of children that were failing to thrive, not growing, who had diarrhoea, who were underweight and the big area of interest in paediatric gastroenterology or overseas interest in child health was in chronic diarrhoea in children. And that was the biggest killer of children worldwide, malnutrition and growth failure. The statistic we used to trot out was that the same number of children as the number of people in a jumbo jet was dying every day of chronic malnutrition and diarrhoea and it was the big childhood disease.*

*...we did a survey of all the children who attended the clinic in The Gambia of about two hundred children, I think. Now we found that 95% of them under one had positive breath tests, which was a complete surprise. There was an enormous resistance to believing this, the journals wouldn't publish it because they had a practice of putting the words into their editors' mouths or into heads that by then, *Helicobacter* was regarded as an adult disease causing peptic ulcer and here was a group of paediatricians who had been working in Africa telling them that *Helicobacter* was a childhood disease and it caused diarrhoea. And they said 'No, no, no.'<sup>1074</sup>*

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<sup>1074</sup> From Testimony T18

On July 10<sup>th</sup> 1993, *The Lancet* published a letter out of the MRC Dunn Nutrition Unit in Cambridge which outlined the results of the research and reinforced the message about the importance of breast feeding to protect babies from the diarrhoeal illness which *H. pylori* causes in African children.<sup>1075</sup> This research seems to have been received with some reservation but in 1999, the prestigious paediatric journal *Pediatric Research* published their methods and results.<sup>1076</sup>

In Professor Weaver's own words,

*And now everyone accepts that Helicobacter is a common disease that's acquired in childhood. It's the same old story, you do something new. First, everyone shakes their heads and says, 'It can't be true' and then they grudgingly say, 'It's true,' and then they say, 'Yes of course, we all knew that.'*

Irvine Modlin and George Sachs' book, *Acid Related Diseases*, published in 2004 presents the view that the mode of transmission is still unknown summarising Thomas et al's Gambian research and other researchers' work in their section on Epidemiology; 'The evidence for fecal-oral transmission is based on a small group of children in Africa, on contaminated water supplies, and by analogy with hepatitis A.'<sup>1077</sup> Subsequent research however reinforces Professor Weaver's research and today Modlin and Sachs would have great difficulty in reinforcing their view in the light of current knowledge.

#### 9. 4: *H. pylori* and peptic ulcer

It would be naïve to assume that the discovery of *H. pylori* has led to a full understanding of the nature of duodenal and gastric ulcer. It is true that most duodenal and gastric ulcer sufferers who are infected by *H. pylori* can have their ulcers healed by its eradication from their stomachs.<sup>1078</sup> What remains unknown is the answer to the question of why do some individuals get an ulcer when so many more carry the organism without ill-effect?<sup>1079</sup> Also it is known that strains of *H. pylori* vary in virulence and this may be a part explanation of

<sup>1075</sup> Thomas J E, Austin S, Dale A, et al, 'Protection by human milk IgA against *Helicobacter pylori* infection in infancy', *The Lancet*, July 10<sup>th</sup> 1993, 121

<sup>1076</sup> Thomas J E, Dale A, Harding M, et al, 'Interpreting the urea C-13 breath test among a large population of young children in a developing country', *Pediatric Research*, Aug 1999, vol. 46, issue 2, 147-51

<sup>1077</sup> Modlin I M, Sachs G, *Acid Related Diseases; Biology and Treatment*, 2<sup>nd</sup> ed., (Philadelphia, 2004, Lippincott Williams & Wilkins) p496

<sup>1078</sup> Penston J G, 'Review article: clinical aspects of *Helicobacter pylori* eradication therapy in peptic ulcer disease', *Alimentary Pharmacology and Therapeutics*, Aug 1996, vol. 10, issue 4, 469-86

<sup>1079</sup> Cover T L, Blaser M J, '*Helicobacter pylori* and gastroduodenal disease', *Annual Review of Medicine*, Feb 1992, vol. 43, 135-45

why some individuals get gastric cancer.<sup>1080</sup> It is believed that earlier in the twentieth century, *H. pylori* colonization was virtually universal but in the second half of the century it reduced and is falling in the West. The appearance of *H. pylori* as an explanation of peptic ulcer disease gave a new opportunity for historians to take a fresh look at its history but it does not provide a complete explanation of its nature.<sup>1081</sup> It is also known that it is possible for people to develop peptic ulcers and not have *H. pylori*. Use of NSAIDs and smoking are high on the list of such ulcer aetiologies but there remain an ‘idiopathic’ group for which no cause is known.<sup>1082</sup>

From the point of view of patient safety, there is now an effective treatment for duodenal ulcer and gastric ulcer and only in the rarest of circumstances is elective surgery resorted to. Surgery still plays a most important emergency role in perforation and haematemesis to save lives. Had *H. pylori* not been discovered then researchers would still be investigating acid physiology and ulcer pathology and drug companies would still be spending vast sums trying to produce drugs to treat a chronic condition and benefit from sales of them.

To quote Professor McColl again; ‘... if you look at the sort of research that had been done into ulcers then, the high quality, highly funded, reductionist research, if it hadn’t been for Marshall, we would still be doing that today and we wouldn’t get any further ahead.’<sup>1083</sup> Professor Stewart Goodwin thinks that this is unlikely, for other histopathologists were aware of these spiral bacteria in 1981 and he mentions Terence Rollason as one, already cited above.<sup>1084</sup> Marshall’s rôle was that of the evangelist and one bacteriologist whose interest he stimulated was Martin Skirrow, whom he met in England before speaking at the 1983 *Campylobacter* conference in Brussels. Marshall’s hypothesis received a lukewarm response there. However his persistence got *The Lancet* letters published and his later series article, thanks to Martin Skirrow’s support. The story of his dramatic ingestion of the infected broth eventually was reported in the non-medical press all over the world and this also played a part in publicising the hypothesis. The *Wellcome Witnesses* symposium gives a flavour of the effect that Barry Marshall had on other medical professionals. There is a grudging admiration of his achievement but a criticism that he did not attribute any thanks or gratitude to other people who may have helped him on the way.<sup>1085</sup> This

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<sup>1080</sup> Parsonnet J, Friedman G D, Orentreich N et al, ‘Risk for gastric cancer in people with CagA positive or CagA negative *Helicobacter pylori* infection’, *Gut*, Mar 1997, vol. 40, issue 3, 297-301

<sup>1081</sup> This is more fully discussed in chapter 3 of this thesis

<sup>1082</sup> ‘Aetiology’ means ‘cause’ and ‘idiopathic’ means ‘cause unknown’.

<sup>1083</sup> From Testimony T1

<sup>1084</sup> Goodwin C S, *Wellcome Witnesses*, op cit, pp87-91

<sup>1085</sup> O’Morain C, *Wellcome Witnesses*, op cit, p93

criticism seems quite unjust when Barry Marshall's own account is read in his book called *Helicobacter Pioneers*.<sup>1086</sup> Jealousy may have played a part, for Marshall profited from his discoveries by patenting several tests, which was not commonly done in the UK at that time and he was not regarded as a 'typical clinical scientist'.<sup>1087</sup> Professor Kenneth McColl summed it up concisely,

*I think, all those working in ulcer disease at the time were too close to it, [they had] their own ideas and other folks' ideas and they basically weren't actually seeing the forest for the trees and somehow Marshall was far enough away from it that he could see this.*<sup>1088</sup>

It is not an exaggeration to say that the *H. pylori* discovery was the most significant scientific discovery in the history of peptic ulcer disease in the twentieth century and all the science which has flowed from it has brought great benefit to humankind including the possibility that gastric cancer might one day be prevented by a vaccine.

There are however those who continue to dissent as to the rôle of *H. pylori* in the genesis of duodenal ulcers. Michael Hobsley and his co-authors question the basic premise that the key element in duodenal ulcer formation is *H. pylori*.<sup>1089</sup> Their arguments include the historical ones that when *H. pylori* was at its most prevalent then there were less duodenal ulcers and also that in areas such as the developed world where *H. pylori* is very common, duodenal ulceration is not. The discussion contained in chapter five may answer these objections. These authors have invested much research into acid pathology in peptic ulcers in their working lifetimes and return to it to justify their assertion that high acid is the main agent in the cause of duodenal ulceration. They end with a plea for researchers not to assume that *H. pylori* answers all the questions regarding duodenal ulceration pointing out early in the article that it appears that modern researchers believe that, 'there is little more of interest to be discovered about the condition.' The *British Medical Journal* in 2009 published two articles on the subject, 'Does *Helicobacter pylori* really cause duodenal ulcers?' in a piece called 'Head to Head' where two groups of protagonists put the argument for and against the proposition. Alexander Ford and Nicholas Talley proposed the 'Yes' argument and Hobsley and his colleagues proposed the 'No' argument. The

<sup>1086</sup> Marshall B J, 'The discovery that *Helicobacter pylori*, a spiral bacterium, caused peptic ulcer disease', in *Helicobacter Pioneers*, op cit, pp165-202

<sup>1087</sup> O'Morain C, Pounder R, Wood J, *Wellcome Witnesses*, op cit pp93-4; Atherton J, Pounder R, *Wellcome Witnesses*, op cit, p96

<sup>1088</sup> From Testimony T1

<sup>1089</sup> Hobsley M, Tovey F I, Holton J, 'Controversies in the *Helicobacter pylori*/Duodenal ulcer story', *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2008, vol. 102, 1171-5

debate does not seem to have excited much interest, being cited in only two other articles.<sup>1090</sup>

People still suffer from dyspepsia and get ulcers of the duodenum and stomach, so that the upper gastrointestinal tract will remain a site of clinical interest for gastroenterologists for the foreseeable future. This is true also in the developing world where it is now recognized that it is much more of a problem than had hitherto been realised. The adoption of the term 'peptic ulcer disease' in recent years recognises that the oesophagus also is a locus for ulceration, both benign and malignant, in a way which was barely appreciated until recent times, and is in itself emerging as a large field of research.

## 9. 5: Autopsy full circle

This dissertation began with an account of an autopsy on a corpse 2000 years old which revealed the presence of a peptic ulcer as a cause of death.<sup>1091</sup> In 1960, seeking to discover the incidence of peptic ulcer in the community from autopsy data, Geoffrey Watkinson published the results of twenty thousand autopsies from two series. The first series from Leeds gathered all autopsies from 1930 until 1949 and the second series gathered all deaths in eleven teaching hospitals in England and Scotland in the year 1956.<sup>1092</sup> Watkinson's study looked at all the autopsy reports to find signs of peptic ulcer disease. The Leeds series was reported by one person with an interest in peptic ulcer, supervised by a similarly interested professor of pathology. This study was 'forward planned' by a group of pathologists with a specific interest in peptic ulcer. When Watkinson examined all the reports for evidence of peptic ulcers in the Leeds study he found that, when the results of autopsy of those dying from causes other than peptic ulcer were taken into account, the incidence of peptic ulcer, both active and undiagnosed, was high with one in six having had a previous peptic ulcer and one in twenty having active ulcers at the time of death. In the second study the incidence of previous ulceration was approximately half that of the Leeds study but similar for active ulcer. The inappropriateness of using autopsy evidence as a marker for whole populations is well known and recognised by Watkinson but his studies do illustrate how common lesion-producing peptic ulcer was at the time.

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<sup>1090</sup> Ford A, Talley N, 'Does *Helicobacter pylori* really cause duodenal ulcers? Yes,'; Hobsley M, Tovey F I, Bardhan K D, et al, 'Does *Helicobacter pylori* really cause duodenal ulcers? No', *British Medical Journal*, Sep 5<sup>th</sup> 2009, 542-3

<sup>1091</sup> Cheng T O, 'Glimpses of the past from the recently unearthed ancient corpses in China', *Annals of Internal Medicine*, Nov 1<sup>st</sup> 1984, vol. 101, 714-5

<sup>1092</sup> Watkinson G, 'The incidence of chronic peptic ulcer found at autopsy', *Gut*, Mar 1960, vol. 1, no. 1, 14-30

In chapter two the importance of autopsy in the understanding of pathology and of the training of doctors described how autopsy findings taken in conjunction with the clinical features of the patient began to increase the understanding of peptic ulcer. The initial antagonism of the British population to the dissection of the dead for pathological purposes slowly receded over the course of the nineteenth century and by the middle of the twentieth century the relatives of deceased persons acceded to requests for post-mortem examination in large numbers which allowed such extensive studies as were reported by Watkinson.<sup>1093</sup>

Lester King stated,

*Early in the twentieth century, medical progress depended largely on the bedside and the autopsy room. The good clinician paid careful attention to the history, the physical signs and the course of the disease. Then if the patient died the autopsy might confirm the diagnosis or, if not, show the true state of affairs so that the clinician could find out where and how he went wrong.*<sup>1094</sup>

The autopsy had the power to show that clinicians do not uncover every pathological condition of their patients before their deaths and audits have revealed that major diagnostic errors have occurred and continue to do so.<sup>1095 1096</sup> Such data challenges the assumptions of modern clinicians who are of the opinion that with modern imaging techniques and other advanced tests they can be confident of making correct diagnoses.<sup>1097</sup> Nevertheless clinicians may choose to challenge the validity of findings of autopsy, as Andrew Duncan was reported to have done in 1795 and is described in chapter two.<sup>1098</sup>

Dr Ian Brown, a consultant pathologist, was asked about the value of autopsy with reference to peptic ulcer,

**ACP:** *...how many autopsies did you do where peptic ulceration had not been diagnosed before death?*

**IB:** *A significant number in the elderly, not in young people, but in elderly patients where you would quite often find people coming from long term care, geriatric units, an eight, nine, ten centimetre ulcer in their stomach that had not been*

<sup>1093</sup> Watkinson G, 'The incidence of chronic peptic ulcer', op cit, 14-30

<sup>1094</sup> King L S, Meehan M C, 'A history of autopsy', *American Journal of Pathology*, Nov 1973, vol. 73, no. 2, 513-44

<sup>1095</sup> Biggs M J P, Brown L J R, Ruddy G N, 'Can cause of death be predicted from the pre-necropsy information provided in coroner' cases?', *Journal of Clinical Pathology*, Jan 2008, vol. 61, 124-6

<sup>1096</sup> Shojania K G, Burton E C, McDonald K M, et al, 'Changes in rates of autopsy-detected errors over time', *Journal of the American Medical Association*, Jun 4<sup>th</sup> 2003, vol. 289. no. 21, 2849-56

<sup>1097</sup> Frübeck G, 'Death of the teaching autopsy: Advances in technology have not reduced the value of the autopsy', *British Medical Journal*, Jan 17<sup>th</sup> 2004, 165-6

<sup>1098</sup> Risse G B, *Hospital Life in Enlightenment Scotland: Care and Teaching at the Royal Infirmary of Edinburgh*, (Cambridge, 1986, Cambridge University Press), pp265-6

*diagnosed, a huge big silent gastric ulcer. I would probably say that about a third of patients who came from the geriatric, psycho geriatric, I don't think that's the correct term anymore, units would have had a silent ulcer.*

When asked about a clinician's response to information about his or her deceased patient's autopsy results, Dr Brown recalled,

*ACP: Did you ever have any problem convincing a clinician that what you found was the cause of death, was the cause of death and not what he had thought it was beforehand?*

*IB: Oh regularly yes.*

*ACP: How did you handle that?*

*IB: You basically present what we find and we put together all the information in the case sheet, the morbid anatomical findings for the post mortem and put it together to make a sensible story and present it to the clinician. Sometimes they would say, 'Oh no, no, the patient most definitely didn't have that,' and you would say, 'Well actually, there it is.' But sometimes people were quite reluctant to, particularly if it was something that had been missed, for example; a silent perforation somewhere in the small intestine or maybe a bit of a leak from a gall bladder, biliary peritonitis that hadn't been picked up, just a sort of vague abdominal pain that wasn't identified.*

*ACP: They felt threatened by your information?*

*IB: I think some people probably felt that they had missed things and they shouldn't have missed things and therefore this was a bit threatening.*

*ACP: And they were a bit defensive about it?*

*IB: A bit defensive about it. But a lot of people, I would say the majority of people would use it as an educational exercise and when, we regularly in the Western and in the Royal, at the hospital meeting, there was almost always a pathology presentation of cases or a case in collaboration with the clinician and often these were 'lessons to be learned' cases that we put on.<sup>1099</sup>*

Professor Frederick Lee, also a pathologist, had similar experiences but expressed them differently,

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<sup>1099</sup> From Testimony T15

*... what happened was not that they refused to accept what we said but they were sometimes astonished at what we found because it was often at variance from the clinical diagnosis. Quite frequently, I would say in something like twenty or thirty percent of cases, we found serious illnesses that had not been found during life and peptic ulcer might be one of them although it was usually other things that were found, for example thromboembolism was quite often picked up which had not been seen and pulmonary embolism was a common thing to find.<sup>1100</sup>*

Dr Brendan Devine, a consultant geriatrician, was very candid and realistic regarding autopsies and their possible revelations,

*ACP: Do many of your patients who die have post mortems these days?*

*BD: Practically none. I can remember when I was a student and when I was a junior doctor, you would go into the mortuary and there would be four bodies on the slabs all being operated on. ...Now it's something like one percent of deaths and usually those are fiscal. The new regulations were brought in because of those heart cases.*

*ACP: Liverpool Hospital case yes.*

*BD: That has wiped the floor with pathology, we are losing so much knowledge and I remember being absolutely convinced I knew what was wrong with the patient, they'd go to post mortem and it was complete rubbish. They would turn out to have died from a pulmonary embolism or something or other.<sup>1101</sup>*

Dr Devine was referring to what has become known as The Royal Liverpool Children's Inquiry Report of 2001 where a single pathologist retained the hearts of every child who had had an autopsy in his department in Alder Hey Hospital, without the knowledge or consent of the deceased childrens' relatives, during his tenure as a consultant.<sup>1102</sup> It emerged that, while this was an extreme case, other pathologists were acting similarly, retaining organs and tissues without consent. Parents' outrage led to a major Inquiry whose effect was to greatly reduce public willingness to allow post mortem examinations. Sadly the Inquiry Report found that Professor Dick van Velzen, the pathologist responsible for most of the retentions of childrens' organs, was dishonest and deceitful in trying to

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<sup>1100</sup> From Testimony T16

<sup>1101</sup> From Testimony T23

<sup>1102</sup> *The Royal Liverpool Childrens' Inquiry; Summary and Recommendations*, (London, Jan 30<sup>th</sup> 2001, House of Commons), Summary (3)

cover up his activities.<sup>1103</sup> The growing public unease about autopsy as a learning exercise grew, and in the UK public attitudes towards autopsy had reverted to those which had prevailed at the end of the eighteenth century.

While it is likely that the Alder Hey scandal ended the previous trust that the British population as a whole had in doctors to perform autopsies for ethical reasons, this was not the whole reason for the virtual demise of its routine practice, for autopsy rates had fallen for the last forty years of the twentieth century in the UK.<sup>1104</sup> Mohomad Dada and Naseem Ansari in an article in the *Journal of Clinical Pathology* discussed the reasons,

*Sadly the number of PM's being done is declining. This can be attributed to: religious and cultural differences, spiraling autopsy costs; loss of prestige of the autopsy with resultant decrease in pathologists' morale and loss of confidence of clinicians; prevailing belief that newer high-tech diagnostic tools are more sensitive and specific in making diagnosis; adverse public view of the PM procedure; and the erroneous belief among some clinicians that by requesting autopsy examination of their patients that they would be exposing themselves to malpractice suits.*<sup>1105</sup>

In the foreseeable future it is unlikely that routine autopsy will recover its previous important rôle in medical teaching and learning however it does continue to enjoy considerable public interest in its forensic form as witnessed by its popularity in current popular fiction and television programmes.

## Conclusion to chapter nine

The final chapter of this thesis has shown how *Helicobacter pylori* came to be accepted as the cause of most peptic ulcers. Despite initial opposition, the discovery of *Helicobacter pylori* has set in motion a vast amount of research as investigators attempt to understand the organism more clearly and its effect on human health. Its eradication from the human stomach by appropriate safe therapy has virtually removed elective surgical treatments of chronic ulcers from medical practice. It has also given an insight into the ways in which peptic ulcer affects the lives of the elderly and of children. The manner in which *Helicobacter pylori* affects children in Africa, in particular, is discussed because of the insight it gives as to the mode of transmission of the organism and of its importance as a

<sup>1103</sup> *The Royal Liverpool Childrens' Inquiry*, ibid, Summary (28)

<sup>1104</sup> O'Grady G, 'The death of the teaching autopsy', *British Medical Journal*, Oct 4<sup>th</sup> 2002, 802-2

<sup>1105</sup> Dada M A, Ansari N A, 'The post-mortem examination in diagnosis', *Journal of Clinical Pathology*, 1996. vol. 49, 965-6

major public health issue. Finally the chapter returns to the autopsy to where the modern clinical understanding of the nature of peptic ulcer began.

## Thesis Conclusion

In the first chapter of this thesis I asked the questions, ‘What were the significant ideas and discoveries which played a part in the evolution of the understanding of this disease over the two hundred year period covered by the thesis?’, and, ‘To what extent does analysis of these changes challenge received understanding of the history of peptic ulcer disease?’ In these concluding remarks I outline what which I consider to be important issues in the history of peptic ulcer disease which I have uncovered and have not been written about by other authors or which have been interpreted differently. I have based the narrative of this thesis mainly on primary sourced material, much of it unquoted by other contemporary authors and throughout the thesis I have attempted to situate the history of peptic ulcer disease within its contemporaneous societal history.

In the first chapter, the reader is introduced to the diagnostic term, ‘dyspepsia’, which has continued to be used since the eighteenth century. It is seen that the word underwent changes in meaning to include a broad collection of almost every type of symptom which could be attributed to a disturbance of the upper gastrointestinal tract, as well as being accorded the status of a disease in its own right. In the nineteenth century, those who tried to explain such disorders made much of different specific symptoms, collecting them in what they perceived to be related groups, in order to describe the different disease processes which they thought were linked to these. At first, diagnosis was based upon what could be inferred from the patient’s symptoms and the experience of his medical attendant, in the absence of diagnostic tools which allowed doctors to directly observe disease processes. At the end of the chapter, it is shown that when modern diagnostic techniques have been applied to the clinical problem of dyspepsia, then many of the symptoms which have been associated with it are found not to be specific to any particular part of the upper gastrointestinal tract. Patients with diseases of the oesophagus, stomach, duodenum, gallbladder or pancreas may have very similar dyspeptic symptoms.

The significance of this important point is that those who write about the history of peptic ulcer disease should now have to find a way of understanding the diagnoses used at any particular time other than accepting them to be true in terms of modern diagnoses. It also challenges the results and conclusions of publications which have accepted available diagnostic data. No recent author has raised this issue in any detail.

In chapter two I have shown how medical understanding of disease began to be overturned at the end of the eighteenth century as a consequence of the practice of autopsy and the

adoption of the clinico-anatomical method which demonstrated that diseases were caused by visible pathological lesions and not by humoral influences as was previously believed. First extensively practiced in Paris after the Revolution, the clinico-anatomical method related the histories of diseases with autopsy findings, and increasingly employed new physical examination techniques which appeared in the nineteenth century. I show in this chapter that it was John Abercrombie, an Edinburgh physician, who was the first doctor to describe the clinical picture of gastric and duodenal ulcer sufferers and link it to autopsy findings.

I uncovered one significant finding in the writings of Thomas Hodgkin, an influential physician and anatomist of the 1840s where he makes a comment about the duodenum that, 'It does not appear from the results either of my own inspections or of those of others, that this portion of the alimentary canal is often the seat of morbid appearances'. This statement, I suggest, may have had an effect on post-mortem practices for several decades. Coming from so eminent a person, it may have led to subsequent under-reporting of findings of duodenal ulcer, until autopsy examinations were performed within agreed protocols.

I have shown that elective surgery on the stomach began tentatively after 1849, initially with very high mortalities, and that by the end of the century, death rates following gastric surgery were of the order of ten per cent. However death rates after emergency surgery of perforated ulcers was one hundred per cent until 1892 when the first patient survived. After this, more emergency surgery for perforation was performed and at the beginning of the new century, post-operative death rates were of the order of 50 per cent. I suggest reasons for the low rates of hospital admissions of patients with perforated peptic ulcers, which may have had an effect on the statistics for peptic ulcers at this time.

In chapter three I have shown that three methods were devised to 'look into the body' in an attempt to make diagnoses of stomach ailments. Test meals were shown to have some utility but their results were indicative rather than diagnostic. Opaque meal X-rays fared better and for eighty years, they were reckoned to be 80% diagnostically accurate. The endoscope allowed investigation of the upper gastrointestinal tract and I describe the development of fully flexible endoscopes from rigid tubes over a period of one hundred years.

I also show how medical practitioners utilised the germ theory, initially as an explanation for the occurrence of peptic ulcers, and later as a theoretical construct to attack putative

foci of infection, both surgically and by the use of vaccines. I show that gastric acid was seen to represent a conceptual problem in the part it played in ulcer genesis which was not resolved until the 1950s. I also trace the history of psychological effects on the stomach over more than two hundred years, from 'sympathy' in the eighteenth century and through the nineteenth century when the influence of the mind upon the stomach was acknowledged. In the twentieth century, I show that the neurobiological link between peptic ulcer disease and brain disease as suggested by Harvey Cushing played an important part in the development of psychosomatic theory in upper gastrointestinal disorders.

In chapter four, I discuss the potentially life-threatening complications of peptic ulcer disease; perforation, haematemesis and pyloric stenosis. I show that hospital admissions increased rapidly for their treatment over the first half of the twentieth century although with high mortality rates by today's standards. These increases in admissions were driven by a growing confidence in the new ability of hospitals to treat these serious problems. I also show in the thesis that many suggested treatments for peptic ulcer were contested by some colleagues, even in the face of apparently better published results, with many clinicians adhering to their own perceived view and remedies. I reveal that at least one reason for this was that no treatment for the complications of peptic ulcer disease was completely safe with all having potential problems. The chapter ends with a brief section about peptic ulcer in soldiers at the beginning of WWII which for a time seemed to be a new war-related disease but I have shown that this was quickly disproved when it was found that the majority of soldiers so affected had taken pre-existing asymptomatic peptic ulcers into the war zone with them which became symptomatic under field conditions.

In chapter five I give an outline of how the current received history has evolved. I begin by showing that several writers of peptic ulcer history have based it upon two *Lancet* articles by Denys Jennings in 1940 which used inherently unreliable sources. I then address the subject of cohort theory which has played a part in the current historical view and make the point that cohort theory is reliant upon death certification data from published data from RGO annual returns of births, marriages and deaths. I show that diagnoses within these data are inherently unreliable and offer several explanations as to why they are inaccurate. I examine the detail of two articles written by Baron and Sonnenberg, who attempt to prove that peptic ulcer was an uncommon disease in the early nineteenth century which became increasingly common, as the century progressed and show how their conclusions are not supported by the statistical sources which they have used. In addition, I criticise their historical method which suggests that numbers of articles

written on the subject of peptic ulcer can be used as a surrogate measure of disease incidence. In an examination of the social history of the period, I refute Blaser and Graham's explanations of how duodenal ulcer became the dominant form of peptic ulcer disease in Britain at the end of the nineteenth century and show that their understanding of life and living conditions in the UK at the time, is not based upon a historically sustainable position.

In this chapter, I also argue that autopsies, which have been much used to support statements about peptic ulcer disease prevalence, are not reliable sources for this purpose. I show too that the clinical presentations of gastric and duodenal ulcers are sufficiently different to influence the rates of hospitalisation of their sufferers which had an effect upon recorded data. I draw attention to the opinions of three prominent clinicians of the time who disagreed that there was any change in the relative disease prevalences of the two types of ulcers, a point also made by Ian Miller. In my examination of the 'rise' in peptic ulcer disease I provide a graph extracted from the RGO published data of crude death rates of the two types of ulcers from 1911 until 1969, which demonstrates how the current historical view has been reached. I then compare the death rates outwith England and Wales and demonstrate that there was no similar rise in peptic ulcer rates in the first half of the twentieth century in France or in Japan. I conclude the chapter by considering the effect on the history of peptic ulcer disease of the arrival of *Helicobacter pylori* as an explanation of the cause of gastric and duodenal ulcer and show that this bacterium has commonly produced duodenal ulcers in most other countries of the world. The arguments made in this chapter have not been made by other authors with the exception of the point made by Miller. This represents new knowledge arising out of my researches.

In the next four chapters, I incorporate the use of oral history as a reference framework to illustrate the history of peptic ulcer disease in the second half of the twentieth century. In chapter six, I describe the social history of Britain before and after the inception of the NHS and provide a description of how people with peptic ulcers were treated. I provide new data concerning drug prescribing, extracted from contemporaneous sources, and show how this changed over a period of two decades, partly influenced by the results of drug trials which began to be used in the UK after 1950 to assess the worth of treatments for this disease. In research from primary sources, I uncover the wide range of treatments used to try to help peptic ulcer sufferers, from drug regimens to physical treatments involving radiotherapy, gastric freezing and brain surgery. At the end of the chapter I show from

witness testimonies that the evidence for the decline in peptic ulcer disease went largely unnoticed by those most closely involved in its treatment.

In chapter seven, I record the testimonies of those who worked in hospitals, local pharmacies and general practitioners' surgeries to provide an insight of how each place of work presented differing challenges. Gastroenterology is seen to have widely developed as a specialty in the NHS from the early 1970s, partly but not solely, as a response to the need for diagnosis and treatment of peptic ulcer disease. I show that for almost three decades from the start of the NHS, surgical intervention led to unacceptable adverse side effects and I describe the measures taken to treat these. I then turn to the development of a new surgical operation designed to avoid these problems and show that its introduction was contested by surgeons who believed that existing surgical results were acceptable and that the problems caused by gastric surgery were relatively small inconveniences acceptable in the bigger picture. I close the chapter with a discussion of the topic of 'collegialty' which shows how it became possible for many of those working in different parts of the health-care professions to cooperate in managing peptic ulcer patient care.

In chapter eight, which covers the last three decades of the twentieth century, I describe the patient pathway from initial presentation of dyspeptic symptoms to the general practitioner to the specialist. The novel approach to the management of the complication of haematemesis, first introduced in the Western Infirmary in Glasgow in the early 1970s, is described and I show that it took more than ten years for this beneficial practice to be universally adopted in the UK. This was a time when endoscopy was developing as a routine technique for upper gastrointestinal investigation and I describe initial experiences and how it eventually displaced barium meal X-ray examinations in the investigation of peptic ulcers.

I then describe the development and introduction of two types of drugs, the H<sub>2</sub> blockers and later the proton pump inhibitors, which completely changed the face of peptic ulcer disease by providing good oral medications which, after approximately ten years, made most elective surgery for peptic ulcer patients unnecessary. The success of these drugs was the consequence of directed pharmaceutical company research which needed the cooperation of doctors to complete their marketability. I show that this led to potential conflicts of interests between doctors and drug companies and discuss the ethical dilemmas which can arise from some of these relationships.

In the final chapter, I relate how *Helicobacter pylori* was discovered to be the cause of most cases of gastric and duodenal ulcers and how this was initially contested by doctors and others with vested interests in research directed towards the stomach's production of acid. I use the testimonies of some of those involved to illustrate how the concept of the new theory began to be accepted by clinicians and I record the nature of the disputes which arose. From an examination of successive editions of *The British National Formulary*, I show that it was not until 1995 that a regimen for the eradication of *Helicobacter pylori* was first proposed in it.

I also asked questions about how peptic ulcer disease was manifested in the elderly and childhood populations. The outcome of these enquiries showed that in the elderly, while dyspepsia was common, the main presenting symptom of peptic ulceration was gastrointestinal bleeding, usually with accompanying anaemia. NSAID drugs were seen to be a particular precipitating cause of this gastrointestinal bleeding. In the case of children, peptic ulceration was seen to be relatively uncommon, tending to occur in older children who were medically managed along the same lines as adults. When *Helicobacter pylori* and its effects on children is discussed, the important work of Lawrence Weaver and his colleagues in the Gambia emerged to show that the bacterium was acquired shortly after birth and was a major cause of African babies having diarrhoea and failing to thrive, many dying as a consequence. Finally, I show at the end of this chapter how the practice of autopsy, which had played such an important part in the understanding of peptic ulcer disease, had been declining as the century neared its end and was dealt a serious blow by the publicised misdemeanours of a Liverpool pathologist in 2001.

I began the thesis with dyspepsia and I will close with it. In the eighteenth century, it was a descriptive term for a nervous condition which affected the stomach and in the nineteenth century it became a diagnosis in its own right. At the end of the twentieth century, dyspepsia still affected 40 per cent of the British population but medical specialists have shown that 40 per cent have gastro-oesophageal reflux disease, 13 per cent have duodenal or gastric ulcer and the remainder were suffering from 'functional' or 'non-ulcer' dyspepsia.<sup>1106</sup> As a diagnostic term it remains useful for doctors as a clinical challenge and for the public it represents an easily understood word for a common complaint.

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<sup>1106</sup> <http://www.nice.org.uk/CG017fullguideline>, p46

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## Appendix 1 The Testimony Database

### Background

The testimonies contained in this archive were gathered from witnesses over two periods as parts of research for two theses. The first 5 testimonies, (T1-T5), were recorded and transcribed in 2003 for background history for an MPhil thesis on which the author was engaged. The results of the work done may be seen in the document, 'A history of peptic ulcer disease from 1800 until 2003' which is to be found in the library of the Royal College of Physicians and Surgeons of Glasgow. In 2008 a further 23 witnesses were interviewed over a period of 18 months or thereby and their testimonies are numbered T6 – T28 as a research resource for this MD thesis. The final aggregated collection of testimonies is to be found in the Library of the Royal College of Physicians and Surgeons of Glasgow. Its title is 'A History of Peptic Ulcer Disease in the Second Half of the Twentieth Century'. Those seeking access to the archive must be bona fide academic researchers in History or medical practitioners with a genuine research interest in the subject and all who wish to may access it under conditions of confidentiality which will be explained to them by the librarian.

The interviewees (witnesses) came from community practice and from hospital practice. From community practice there came four general practitioners, two pharmacists, and two drug company representatives. From hospital practice there came five surgeons, six gastroenterologists, two paediatricians, two geriatricians, two pathologists, one radiologist and two senior nurses. The most senior of the witnesses began training in 1942 and several of them give histories of the early days of the NHS which may be unimaginable to today's medical and nursing professions. The testimonies are a rich source of data and give a picture which is not to be found in scientific journals although some may be gleaned from autobiographies. They tell of how things happened rather than reporting some of the end-points as achievements in the development of a particular subject. This is one of the strengths of oral history. These testimonies cover the end of the period when the stomach and duodenum were the main anatomical sites affected by peptic ulcer disease.

The transcription costs were assisted by a grant from the Gartnavel Gastroenterology and Medical Trust.

## Appendix 2 List of witnesses

- T1 Prof K McColl, Gastroenterologist
- T2 Sir D Carter, Surgeon
- T3 Mr A McKay, Surgeon
- T4 Prof R Russell, Gastroenterologist
- T5 Mr M Browne, Surgeon
- T6 Mr J Linn, Pharmacist
- T7 Mr C McKay, Surgeon
- T8 Dr A Beattie, Gastroenterologist
- T9 Dr J Allan, Gastroenterologist
- T10 Dr D Ramsay, General Practitioner
- T11 Dr R Vallance, Radiologist
- T12 Dr J Davie, Geriatrician
- T13 Prof I Bouchier, Gastroenterologist
- T14 Dr J Allan, General Practitioner
- T15 Dr I Brown, Pathologist
- T16 Prof F Lee, Pathologist
- T17 Mr I Davidson, Drug company representative
- T18 Prof L Weaver, Paediatrician
- T19 Mrs M Haggart, Nurse
- T20 Mr D Dunn, Drug company representative
- T21 Prof D Johnston, Surgeon
- T22 Miss I Duncan, Nurse
- T23 Dr B Devine, Geriatrician
- T24 Dr M Devine, General Practitioner
- T25 Dr M Blair, Paediatrician
- T26 Dr A MacKenzie, General Practitioner
- T27 Mr J Smith, Pharmacist
- T28 Dr J MacKenzie, Gastroenterologist

## Appendix 3 About the author

The author of this thesis is a retired General Practitioner with thirty seven years' service in the NHS, thirty one of which were spent in practice in the Scottish Borders' village of West Linton. He is married to a doctor and has three adult children with so far, four grandchildren.

In 2002 he spent a year studying in the History of Medicine department of the University of Glasgow and graduated with the degree of M Phil (distinction) in 2003.

In the course of preparation for this degree, he has had two articles published in peer-reviewed journals (*Emergency Medical Journal* and *Vesalius*) and two other original articles in the Association of Clinical Pathologist News journal (*ACP News*). He is currently preparing a chapter for a book on the subject of the history of ambulance services at the request of its editors.