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The ETIOLOGY, PATHOLOGY and TREATMENT of DUODENAL ULCER IN SOUTH INDIA

by

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THE ETIOLOGY, PATHOLOGY AND TREATMENT OF DUODENAL ULCER IN SOUTH INDIA.

PART I.

Introduction.

The visitor to South Indian Hospitals is at once struck by the large number of cases of Peptic Ulcer which fill the surgical wards, and in Travancore the work of the Surgeon is largely that of a specialist in gastro-intestinal diseases. The writer of this thesis and his colleague performed 2,500 operations in ten years for duodenal ulcer alone.

In contrast to this, it will be found that peptic ulcer is exceedingly rare in North India. Sir Robert McCarrison estimates that duodenal ulcer is sixty times more common in South India than in North India. Such a striking variation as this cannot be explained by racial tendency or any of the existing theories of vascular, inflammatory or nervous etiology. There must be some profound and decisive factor operating in South India and absent in North India tending to produce peptic ulcer.

What this factor is, and how it opens the way to ulcer formation, is the main burden of this thesis. At the same time a worker in a clinic such as the Neyyoor Hospital in South Travancore, with its records of over 2,500 operations for duodenal ulcer in the past ten years, is entitled to express his views on treatment, operative and non-operative, both in relation to the ulcer problem peculiar to South India, and to the problem of peptic ulcer as a whole.

Here, in one of the Native States of South India, bounded by the sea on the west and by a long range of mountains, the Western Ghats, on the east, exists a natural laboratory with human beings as the subjects. In it is being carried out by nature an experiment in peptic ulcer production, the correct interpretation of which should throw light on the thorny problem of ulcer production and provide data which may bring divergent opinions into line, and supply a link in the chain of evidence forged by workers in the west.

The possible etiological factors are: - Race, Climate, Habits of the people, and Diet.

Race is unlikely to play an important part as the races of India are mixed, and the sufferers from peptic ulcer are Aryan and Dravidian, Hindu, Muslim and Christian.

Climate also can play but a minor part, as ulcer is common all over the Madras Presidency, parts of which are humid and parts are dry and hot.

Certain factors in habits and diet are common to the people of South India as a whole and not found in the North, and it is these factors which we must examine, not only to establish them as primary or contributory causes, but to reveal the manner in which they act, and the pathological changes which they produce. Considerable prominence, therefore, will be given to pre-ulcerous changes commonly found in the population as a whole, even in those who do not complain of ulcer symptoms, and records of animal feeding experiments which demonstrate the earliest manifestations of ulcer pathology, will be introduced.

Opportunities for study.

(1) The writer has been from 1927 to the end of 1936, second surgeon in the Neyyoor Hospital of the South Travancore Medical Mission, which treats annually, on the average, 150,000 of the people of Travancore and the neighbouring parts of British India. During this period, he and his colleague, Mr. T. Howard Somervell, F.R.C.S,, and his assistants, have operared on 2,500 cases of peptic ulcer. The chief Government Hospital of the State has had an experience only slightly smaller and their records have been

made available for study. In addition, the writer has acted as consulting surgeon to thirteen small hospitals throughout Travancore and has, through the mediun of medical men in charge, been able to study the habits of life and diet of the common people, as it varies from place to place.

(2) The Government of India through the Indian Research Fund Association have made available money to institute a Peptic Ulcer Enquiry of which the writer is Officer-in-Charge. This enquiry has had its headquarters at Neyyoor, Travancore, and has established and maintained a laboratory for the study of the pathology of the condition.

(3) By the courtesy of the Director of the Institute for Nutritional Research, S. India, field surveys have been carried out and facilities provided for animal feeding experiments.

Mode of Enquiry.

(1) A survey by the questionaire method was made of India and information collected as to the incidence of peptic ulcer in different areas, and details concerning the diets used in the various provinces collected.

(2) A study of the records of 2,500 peptic ulcer operation cases in the Neyyoor Hospital was made. The age, incidence, sex, domicile, social condition, operative

findings and test meal and barium meal records were examined. The symptomatology of the Travancore ulcers is reviewed with special reference to the points at variance with the western text book description. The use of radiography and test meals determining the line of treatment, is also considered.

The clinical course of the ulcers, their tendency to atenosis and the rarity of perforation and haemorrhage is compared and contrasted with the common experience in western countries.

(3) A follow-up enquiry was carried out to estimate the success or failure of the different operative techniques in relieving symptoms and preventing recurrence of the ulcer.

(4) Pathological examinations were made of portions from stomachs exposed at operation, to determine if any constant pathological changes could be found in the stomach walls at a distance from the ulcer. Also examinations were made of stomachs removed at autopsies on persons dying suddenly from trauma. These examinations were made both in persons living in the area where peptic ulcer is endemic, and in North India where it is rare, in order to demonstrate any commonly found pre-ulcerous conditions in the stomach

and duodenum in the "Ulcer Country". In cases where ulcer was suspected after clinical and X-Ray examination, but was not demonstrated at operation, a small portion was excised from the stomach or duodenum for histological examination.

(5) A series of test meals were carried out on normal people in Travancore and other parts of India, with a view to noting any variation from the British normal.

(6) A series of barium meals in normal persons in Travancore was also carried out, and variation from the accepted normal behaviour of the stomach noted, particularly the existence of pylorospasm and hyperperistalsis and a control series were examined in North India.

(7) Feeding experiments, using the Travancore diet, and as a control, a suitable stock diet, were carried out on rats, in the attempt to produce ulcer or pre-ulcer pathology, and special note has been made of the changes of ganglion cells in the stomach walls of rats fed on the Travancore diet.

(8) Feeding experiments were also carried out with dogs, and test meals and barium meal examinations made during the experiment to demonstrate whether or not the diet of the Travancore people affected the motility, chemistry and functioning of the stomach.

As this is a surgical thesis, medical treatment is not discussed except to show how difficult it is to make medical treatment effective among the poorer class Indians, but as the writer considers peptic ulcer to be primarily a medical disease and only suitable for surgery when medical measures have been tried and found wanting, some reference is made to the prophylactic measures which might be adopted in South India to lessen the incidence of the disease.

The surgical treatment is a subject which has interested the writer for the past ten years and while a large series of posterior gastro-enterostomy operations have been performed, the results of follow-up work have caused some disquiet. Satisfactory results have been found in many cases, extremely bad results in few and the remainder justifying the operation but being far from perfect. This review has stimulated the writer to explore the possibilities of other operative measures and to attempt to devise operations suitable for different types of cases. The relative merits of the gastrectomy proceedures are discussed and the results of a follow-up of gastrectomy operations compared with gastro-enterostomy follow-up. As all the cases under review are the writers (or his colleagues using similar technique) the comparison may be accepted as a fair estimate of the relative merits of radical as opposed

to conservative surgery of the stomach.

Current literature abounds with comparisons in operative results in gastric surgery. Different operators using widely varying techniques and possessed of varying degrees of skill, uphold the merits of their favourite operation. The writer of this thesis ventures to suggest that the comparisons here made may have some special value, being as they are free from personal factors, the different operations being performed by the same operators on the same type of case under the same conditions within a comparatively short space of time, namely ten years.

The incidence of gastro-jejunal ulcer is also discussed. Theories as to its cause are compared and reviewed in the light of the writer's personal experience and technical suggestions are made, which in the writer's opinion tend to decrease the risk of gastro-jejunal ulcer. Methods of permanently reducing the gastric acidity are discussed and post-operative test meal results in varying operations are contrasted and commented upon.

The treatment of gastro-jejunal ulcers by surgical measures is reviewed. A series of 85 operations for this condition carried out by the author and his colleague is studied and the advantages and dangers of the different operative methods discussed.

The underlying object of this paper is not so much to make a compilation and review of the work of others but it is an attempt to bring to the notice of Western Surgeons a very interesting aspect of the peptic ulcer problem. Factors located in certain areas in India seem to play a dominant part in its etiology, and while many of the accepted Western ideas of etiology have little bearing on the problem in India, others take on a new significance.

The results of the enquiry, the discussion and conclusions will be grouped under the following heads:-

Historical review of the literature bearing on the problem.

Review of modern work on the anatomy, physiology and pathology.

Review of experimental work related to the Theories of ulcer Etiology.

Original observations of a clinical and experimental character made in India.

Pathological and experimental observations on the histology of peptic ulcer in South India.

The surgical treatment of peptic ulcer.

Discussion and Conclusions.

PART II.

The early writers on medical subjects such as Galen and Celcus commented upon the occasional observation of an ulcer in the stomach and throughout the literature there appear from time to time descriptions of a clinical condition which though not diagnosed as such, was in all probability a gastric or duodenal ulcer. In 1586 Marcellus Donatus described ulcer with pyloric stenosis and it is recorded that Princess Henrietta Ann, daughter of Charles I of England died of what appears to have been a perforated duodenal ulcer. She had suffered for some time from digestive disorders and abdominal discomfort. One day she was seized with a sudden pain, her face became a ghastly leaden colour and it was evident that she was suffering extreme agony. She speedily expired.

In 1737 Morgagni described gastric ulcer. In 1793 Matthew Baillie[1] of London, in describing a case of gastric ulcer gave the first accurate anatomical account and remarked on the feature which differentiates it from ulcer elsewhere in the body: "its clean cut edges and lack of inflammation in the surrounding tissues". He also gave a very accurate account of the symptomatology which accords closely with our modern conception of the condition, and in the Transactions of the London Medico-Chirurgical

Society of 1817 a Mr. Travers[3] described two cases of duodenal ulcer.

In 1829 Cruveilhier[4] distinguished between cancer, gastritis, and simple ulcer of the stomach but he failed to make any mention of duodenal ulcer. It is surprising to find how few observers in the middle of the nineteenth century do mention duodenal ulcer, though reports of gastric ulcer are quite common. If it is true that duodenal ulcer is on the increase and modern statistics suggest that it is, it is possible that conditions of life a hundred years ago failed to provide the factors necessary for duodenal ulcer formation and that duodenal ulcer is in some way associated with the modern hurry and rush of life and gastric ulcer depends on some other factor.

In 1830 John Abercrombie[5] of Edinburgh published a classical description of five cases of duodenal ulcer in the second edition of "Pathological and Practical Research on Diseases of the Stomach". He makes the following interesting statement:- "The leading peculiarity of disease of the duodenum, so far as we are at present acquainted with it, seems to be that the food is taken with relish and the first stage of digestion is not impeded, but the pain begins about the time when the food is passing out of

the stomach, or from two to four hours after a meal."

In 1842 Curling[4] reported the first case of duodenal ulcer associated with burns and laid the foundation of a toxic theory of ulcer formation. This theory prompted experiments, attended with some success, to produce ulcer by the injection of toxic substances. Curling also noted the tendency to periodicity and made mention of a farinaceous diet, milk and alkalies in the treatment.

Brinton[5] in 1856 reported that he found ulcer in 5% of all autopsies, and after describing gastric ulcer at length referred to duodenal ulcer as being essentially different in cause and appearance. The writings of this period testify to the rarity if duodenal ulcer as opposed to gastric ulcer and to the fact that when found it was in men.

In 1861 there appeared a paper by Klinger dealing especially with duodenal ulcer. Only perforating ulcer was mentioned and notes were given of three cases of the author's and of ten from the literature. In January 1864 the British and Foreign Med-Chirurgical Review reported an epitome of a Swedish account of duodenal ulcer by Trier[6], and also reported all the cases described up to this time, including details of twenty-six cases mostly from Copenhagen.

No advance beyond the recording of additional cases was made till 1887 when Bucquoy contributed an impor-

tant article in which he claimed like Abercrombie that symptoms were sufficient to make a diagnosis.

In 1893 Perry and Shaw[9] commenting on the records of 1765 autopsies in Guy's Hospital Reports, noted only seventy cases of peptic ulcer and ten of these were associated with burns.

Theories as to the Etiology of Peptic Ulcer.

By the middle of the nineteenth century when peptic ulcer had been recorded sufficiently often to arouse widespread interest, its etiology became a matter of speculation and investigation. Cruvielhier expressed the opinion that it was secondary to gastritis, and in 1837 Lebert, by injecting pus into the veins of animals, produced erosions in the gastric mucosa. In 1874 Bottcher first demonstrated bacteria in the marginal tissue and in 1907 Turck[10] produced acute and chronic ulcers by feeding B.Coli from the faeces of ulcer patients. So the inflammatory conception of ulcer formation was well established before Rosenow[11] in 1913 expounded his theory of selective affinity of certain strains of bacteria for the duodenum.

In 1916 Steinharter[12] caused ulcer by the injection of staphylococcus from an acute appendix and in 1925 Hoffman[13] isolated a comma shaped Bacillus from an ulcer and injected it into the peritoneal cavity of a guinea pig and

caused ulcer, and in the same year Haden and Bohan[14] isolated streptococci from ulcers and injected them into rabbits and induced ulcer in 53%, while streptococci from patients not having ulcer only produced ulcer in 7%.

A defect in the blood supply to the part has been advocated from time to time as an important etiological factor ever since Rokinansky[15] in 1849 showed that haemorrhagic erosions were the precursors of ulcer. In 1853 Virchow[16] suggested vascular infarction due to embolism as the cause and in 1890 Klebs[16] explained the defective supply of blood and consequent anaemia as due to spastic contraction of the muscles occluding the vessels. This has been re-emphasised by Gurnsburg[8] and von Bergman.[21]

Conheim,[17] with the idea of producing embolism injected wax into the central end of the femoral artery of dogs and ulcers resulted. Also lead chromate was injected into the splenic artery but though ulcers resulted they tended to heal. These experiments have been repeated by many workers using different substances and different vessels but their results have varied.

In 1909 Litthenar[17] ligated one-third of the gastric vessels with impunity, but when he excised a portion of the mucosa and fed dilute HCl ulcers resulted. In 1911 W. J. Mayo[20] called attention to the anaemic spot on the duo-

denum and suggested a relation between that and ulcer.

The chemical factor in ulcer formation was appreciated as early as 1869 when stomach lavage was first carried out. Leube performed gastric analysis in 1871 and Ewald introduced test meals in 1874. In 1890 Conheim[7] gave it as his opinion that ulcer depends on chemical factors, and that "there must be in addition an unknown something which prevents the healing process", but he could not say whether the gastric acidity was the vital factor or not.

It was about this time that Pavlov commenced his experiments with gastric fistulas in dogs and the study of the digestive juices became more accurate.

Reigel and others drew attention to hyperchlorhydria as the etiological factor but it was Bolton's work in 1916 that led to the modern conception of the rôle of acid in the etiology of peptic ulcer. Bolton found that feeding HCl 0.7% strength and under had no effect on the healthy mucus membrane but 0.25% HCl was capable of increasing the size of an artificial lesion. Apparently from Bolton's work one must conclude that high acidity of itself is not conducive to the formation of an ulcer, but given a devitalising factor even normal acidity can bring about and maintain a chronic ulcer.

Various workers have observed the effect of toxic substances in ulcer production since 1842 when Curling[6]

first described ulcer following burns. In 1907 Rosenau and Anderson[43] caused necrosed patches and haemorrhages by injecting diphtheria toxin. An interesting point in this experiment was the fact that there was also congestion of the suprarenal. This connection between lesions of the suprarenal and ulcer formation has been observed repeatedly by other workers, and is not a coincidence but occurs with some frequency in some forms of experimental ulcer. Almost every toxic agent has been used at some time or another in the production of ulcer. In 1893 Vassale and Sacclef[44] by burning and also by injecting burned tissues, produced congestion of the mucus membrane and enlargement of lymph follicles. Rehfuss, Hayden, Gicini[45] and others injected pilocarpine, atropine, epinephrin, and industrial poisons. Apomorphine by producing hypermotility of the stomach brought about acute ulcers and these tended to become chronic if associated with delayed emptying of the stomach.

In 1913 Bolton[46] succeeded in making a gastrotoxic serum by injecting a suspension of gastric mucosa into the peritoneal cavity of a rabbit and when immunity had developed an injection of serum from the rabbit into a guinea pig resulted in ulcer.

The rôle of the nervous system in ulcer etiology is scarcely a matter of history and will be dealt with in

a detailed manner in another section but a few classic experiments stand out and are worthy of note. The influence of the vagi in ulcer etiology was first studied by Ophuls[46] who noted in 1906 that if both vagi were cut ulcer resulted, probably by innervation of the stomach wall rendering it more liable to attack by acid. Durant[47] divided the splanchnic nerves and produced haemorrhagic necrosis. Exterpation of the coelic plexus led to varying results at the hands of different workers. The relation of the suprarenal gland to ulcer formation (as noted in connection with the production of ulcer by injection of toxins) was further studied in the years 1913-16 by Latzel, Mann[48], Elliot[49] and others. Ulcer was produced by the removal of the suprarenal capsule and after the removal of both glands. Acid appeared to be a factor in the causation in these experiments, as was alkali in the prevention.

History of Treatment.

As early as 1786 Odier recommended sub-nitrate of bismuth and rest in the treatment of dyspepsia but the earliest reference to anything approaching the modern conception of treatment by diet and medication is found in the British Medical Journal of February 21, 1891 in an article by Dreschfeld[50] who recommended a nitrogenous diet

with limited fats abd carbohydrates and the exhibition of bismuth and alkalies by mouth.

Pope[31] the following year advocated resorcine grs.5 as an antiseptic, analgesic and haemostatic.

The path was opened for surgical attack on ulcer by Wolfler[32] of Vienna who performed a gastro-enterostomy for carcinoma in 1881, but Courvoisier made an unsuccessful attempt to employ this operation for ulcer. In 1885 von Hacker[13] suggested the posterior route and in 1881 Bilroth[15] made his first attempt at resection by his first method.

In 1893 the Annals of Surgery published a review of the resections performed up to date with the discouraging mortality of 41%.

Jaboulay[36] in 1894 suggested a gastro-duodenostomy and carried out the modern operation as early as 1900. Doyen[17] reported favourably on the gastro-enterostomy operation for ulcer and two years later Roux[18] described his anterior method in Y.

The complications of the gastro-enterostomy operation soon presented themselves. Chlumsky[4] described the formation of a spur which caused regurgitant vomiting and in 1898 Stendal[39] reported a case in which the transverse mesocolon had narrowed down and caused kinking. Evidently regurgitant vomiting was the main cause of failure with

the earlier operators and several methods were described to prevent it. In 1890 Lauenstein[40] made an entero-anastomosis and the following year Hadra[41] suggested the suspension of the gut by suspending it well above and below the stoma, and in 1907 Kocher[42] attempted to form a valve by making his incision curved convex upward. The description of gastro-jejunal ulcer was first made by Braun[43] in 1899 and in 1905 Mayo-Robson in discussing the problem stated that it was very rare following gastro-enterostomy. Later Paterson, Van Roogen and Wilkie all blamed the use of unabsorbable suture material.

The technique of gastro-enterostomy gradually improved. Unabsorbable sutures were replaced by chromic catgut and as the posterior route and the importance of a no-loop anastomosis, became better understood, regurgitant vomiting became an exceptional occurrence and the operation became straight forward and simple with the result that many indifferent surgeons were tempted to employ it and because their technique was bad, or, as frequently happened, they carried out the operation for unsuitable cases, the operation fell into disrepute, and during the past ten years various forms of gastrectomy pyloroplasty and gastro-duodenostomy have been introduced but without entirely replacing the gastro-enterostomy operation.

The most marked advance of recent years, however,

has been the recognition that peptic ulcer is a medical disease and until a thorough course of medical treatment has been carried out one is not justified in operating at all. The treatment by the Histidine group of drugs has not found as wide-spread favour as was at first anticipated, but modern conceptions of the treatment of ulcer will receive consideration in a later section.

The History of Methods of Diagnosis.

This subject is sufficiently interesting to justify a closing paragraph.

Bucquoy contributed an important work in 1887. He was the first to diagnose ulcer from the symptoms alone which he did in five cases, in one of which his diagnosis was proved by post-mortem. Bucquoy was, like Abercrombie, of the opinion that the symptoms were sufficient for a diagnosis to be made with accuracy. Several ingenious devices precede our modern methods of investigation of the stomach. In 1896 Plank[44] in the Therapeutic Gazette described Turks gyrometer. This was a sponge covered by a spiral spring attached to a flexible tube and cable capable of being revolved within the stomach. It could be palpated and thereby the size and position of the stomach detected. It was used to sponge off the mucus adhering to the stomach

wall and the contents of the sponge could be examined microscopically.

In 1895 Rosenheim[45] described a straight gastroscope, which he maintained could be passed in 80% of persons without anaesthesia.

Radiography of the stomach was first suggested by Cameron as early as 1897 by using a bag filled with lead. The following year Boas[46] introduced the examination by the use of gelatine capsules filled with bismuth.

While sympathising with the sufferings of the patient undergoing a thorough gastric investigation by the gyrometer the bag of lead and the straight gastroscope, we cannot but admire the ingenuity of these early workers who paved the way for the gastric analysis, the follow-through meal and the flexible gastroscope.

Though the history of the peptic ulcer has shewn the most remarkable advance, it has been an advance interrupted by many backslidings. New developments have been proved with the passage of years to be of doubtful utility and in some cases definitely harmful. Avenues have been opened up, timidly explored and forgotten till some later explorer has trodden the way with confidence wondering at the obtuseness of his predecessors in failing to take hold upon the knowledge that awaited them.

One thing is clear from a study of these early reports, viz. gastric ulcer has been known and described for nearly two hundred years. Duodenal ulcer is a comparative newcomer and statistics shew that it is on the increase, both among the professional classes and among the poor. While in essentials of etiology the two are closely akin there is some factor as yet unknown but associated with the modern mode of life which appears to predispose to the formation of duodenal ulcer as opposed to gastric ulcer.

PART III.

Review of Modern Work.

From the vast literature daily accumulating concerning peptic ulcer it is impossible to undertake an exhaustive review within the scope of this Thesis. It is essential, however, to review the more important experimental work and theories in so far as they have a bearing on the problem under discussion.

Epidemiology.

References in the literature commenting on the frequency of peptic ulcer in primitive and uncivilized peoples are common. Thus Hartman[47] discussing the neurogenic factor in peptic ulcer formation states that peptic ulcer is almost entirely a disease of civilized peoples. Such a statement is of course completely false as a perusal of the Introduction to this paper will shew. Robinson[48], however, provides strong statistical evidence to shew that ulcer is much less common among the American Negros than among the white population, except, according to Boland[49], where the Negro adopts Western habits and diet.

Chang and Chang[50], reporting a statistical survey in North China record that three hundred and fifty five

cases of peptic ulcer or .65% of all cases treated in the Union Medical College, Peiping, were suffering from peptic ulcer and it is their view, though figures are not available, that the disease is common in North China. Robertson[51] of Mukden made the same observation.

Bergsman[52] reported a high incidence of gastric and duodenal ulcer among the natives of Abyssinia. Their diet consists of sour bread, sauce containing 50% Cayenne pepper and occasionally beans, peas and some meat.

Several interesting papers from Malay and Dutch East Indies point to a peculiar racial difference in the tendency of the natives of these parts to develop peptic ulcer. Stoel[53] reports that in the Dutch East Indies the disease is much more common among the Chinese and British Indian sections of the community than among the Javanese and he points out that the ratio of duodenal ulcer to gastric ulcer is much higher in the British Indians in Java. He attributes this to the monotomous diet and poor nutrition. Kouwenaar[54] makes a similar observation and points out that ulcer is more common in the proto-Malayan races such as the Balaks who inhabit Northern Sumatra than in the deutero-malays such as the Javanese and this difference he believes to be due to diet. He found peptic ulcer in 10% of autopsies on Chinese and in 5% of autopsies on British Indians and

only in 0.95% of Javanese. This is in spite of the fact that the Javanese eat a highly spiced diet.

Vine[56], writing from British Malay, points out the fact that the disease is common among the British Indians (mostly emigrants from South India) and the Chinese, while it is rare among the Malays themselves. He lays much stress on the ulcer diathesis of the Chiness who, he says, are vagotonic in type and having a high pain threshold insult their stomachs with hot and unsuitable food.

Bonne[57] at al noted, notwithstanding the high incidence of ulcer in the Chinese compared with the Malays, the acid values were not higher in the Chinese and there was no difference in biliary regurgitation but the tendency to chronic gastritis was greater in the Chinese.

Eagle and Gillman[58] reported the disease to be seven times more common in the white population of South Africa than in the Bantu.

Muller[59] reports a high incidence in Denmark and a low incidence in Russia.

In European countries the incidence varies. The type of ulcer also is not the same in all. Walters and Church[60] report that gastritis is not commonly associated with the ulcers seen at the Mayo Clinic, but it is known to be very common in Germany.

The epidemiology in India will be discussed in a subsequent section but there is no doubt that peptic ulcer is by no means confined to the so-called civilised races. There is clear evidence, however, to show that some races are more or less immune and the frequency and type of ulcer is not the same all the world over.

Anatomy and Physiology.

Certain anatomical facts bear directly on the theories about to be discussed and had better be numerated at the outset.

Vascular arrangement.

Reeves[40], in a study of the arteries supplying the stomach and duodenum points out that the vessels of the lesser curvature are longer and more tortuous than those of the fundus and greater curvature, and are therefore more liable to thrombosis. The vessels of the duodenum do not anastomose and are few in number and Wilkie[41] describes the vessel supplying the anterior surface of the first part of the duodenum as an end-artery, and adduces this as a reason for the frequency of ulcer in this situation.

This paper will go on to shew that it is possible to ligate all the main vessels of the stomach in a human being without devitalisation of the organ and this is being

carried out regularly by the writer as a treatment for gastric and duodenal ulcer with success. Apparently the blood supply to the stomach is so profuse and the anastomosis so free that such blood as comes from the oesophagus and duodenum is sufficient to maintain the nutrition.

Nervous Control.

Two nervous systems operate to control the secretions and movements of the stomach; the sympathetic and and parasympathetic. The end fibres from these two sets of nerves meet in the plexus of Auerbach situated between the muscle coats and the plexus of Meissner situated in the muscularis mucosae. Alvarez[52] believes that the movements of the stomach and the secretions are directly under the control of these two plexuses which conduct stimuli and co-ordinate movement keeping the muscles and secretion from being too active, and that it is on the health and efficiency of these two plexuses that the normal functioning of the bowel depends.

The cells comprising these ganglia are large pear-shaped or oblong with one end of the oblong rounded. They have a large clear refractile nucleus with a well marked nucleolus and nuclear membrane. In a normal ganglion three or four ganglion cells are seen in one group with a

few endothelial cells. Holsti[45] calls them glial cells. The ganglion is not enclosed in a capsule and the cells appear to lie in direct contact with the muscle. The ganglion is difficult to demonstrate in a completely normal specimen, and sometimes a well cut and stained section may fail to show any ganglion at all. In abnormal sections, as will be described later, the picture is quite different and the ganglia are easily seen.

The rôle played by the vagus and sympathetic in relation to gastric motility and secretion is a debated point and the experimental frequently tend to produce entirely different effects and thus the work of one worker appears to contradict the work of another. Recent experimental work in this subject falls under four main heads:

a) Section of the vagus or sympathetic nerves at different levels.

b) Stimulation of the vagus and sympathetic nerves by stimuli of varying degree.

c) Stimulation of different areas in the cortex.

d) The effect of drugs on the action of the vagus and sympathetic.

a) Barron, Curtis & Hauerfield[44] divided both splanchnic nerves and the result was hypermotility, increased tonus and contraction of the stomach and no symptoms. Alvarez[46] noted a

tendency to the formation of gastric ulcers after bilateral sympathetic section while other observers had negative results.

Thoracic vagotomy in the dog has lengthened the final emptying time but Meek and Herrin[66] shewed that vagotomy shortened the initial emptying time for a diet of milk but not of solid food. Farrel[67] shewed that section of both vagi resulted in a failure in the psychic phase of gastric secretion, as tested by sham feeding experiments. An unprecedented result occurred in the work of Bollman and Mann[68] who found that peptic ulcer resulted. This is not borne out by other workers and the result is probably due to a lowering in resistance of the part.

An interesting observation on a man confirms the experimental evidence that the vagus, acting in excess of the sympathetic, leads to hyperperistalsis and pylorospasm. The patient suffered from gastric symptoms and X-ray examination shewed that the emptying time was six hours and forty-five minutes, in spite of active peristalsis. No ulcer was detected. With heavy atropin medication the gastric tonus and motility was less and the emptying time became five hours twelve minutes. Barron and Curtis studied this patient by inserting balloons into the stomach and making kynographic tracings. They came to the conclusion

that the patient's symptoms were due to over action of the vagus leading to hyperperistalsis hypertonus and pylorospasm. They prevailed upon the patient to undergo operation and divided the left vagus nerve in the anterior wall of the oesophagus under the diaphragm. The tonus and motiligy decreased and the emptying time became two hours fifty minutes; and five months later it was two hours. The symptoms disappeared. Apparently pylorospasm had been replaced by a patulous pylorous. They quote other observers most of whom made similar findings in experimental animals but the few exceptions to the usual result of vagotomy are explained by the fact that there are both motor and inhibitory fibres in the vagus. That is, it is not a pure parasympathetic nerve. The motor fibres respond to stimuli of a low intensity and the inhibitory fibres to stimuli of a high intensity. Heslop[9] also found that the splanchnic and vagus are mixed nerves and for a pure sympathetic or pure vagal response the posterior and anterior parts of the hypothalamus must be stimulated.

While the part played by the vagus and sympathetic in the control of the emptying time and motility is not altogether clear and different observers obtain somewhat conflicting results, the consensus of opinion appears to be that stimulation of the vagus increases gastric secre-

tion and that the psychic phase of secretion is entirely of vagal origin. Hartzel[70] quotes Pavlov who showed that the vagus supplied secreting fibres to the gastric glands and he also quotes Exner and Schwarzmann who in 1914 treated twenty cases of gastric crisis by vagotomy with beneficial results in 50%. He comments on the divergent results of vagotomy in the hands of different workers and points out the following fallacies in assessing the results.

1) Pre-operative normal state has not been determined with sufficient accuracy in some experiments.

2) The animals used have been subjected to previous operations for the formation of pouches of fistule, etc.

3) The period of post-operative observation has been too brief.

In his own experiments he trained his animals for several weeks till he could obtain a uniform acidity curve from each. In those animals in which the vagus nerve was cut in the thorax there was a marked reduction in both free and total acidity. Pauchet[71], Mayo[72] and others have reported successful results from the division of the pyloro-duodenal nerves for pylorospasm and found the pylorus patulous thereafter.

Moll and Flint[73] found that bilateral division of the sympathetic caused hyperchlorhydria and in particular increases the fasting juice.

b) Stimulation of the nerves.

Beattie[74] found that stimulation of the vagus

nerve in the resting stomach gave rise to increased intragastric pressure while McCrea, McSwiney and Stopford[75] concluded that the main effect of vagal stimulation was the initiation of the gastric contraction and McSwiney and Wage showed that stimulation of the vagus while the tonus is low produces contraction, but if the tonus is high inhibition results. This again suggests that the vagus is a mixed nerve. Laughton[76] made a similar observation.

c) Stimulation of the cortical centres.

In 1876 Bochefontain pointed out that faradic stimulation of the region of the sigmoid gyrus in the dog caused peristaltic contraction of the pyloric region of the stomach followed by inhibition of the pylorus itself and that sometimes such stimulation produced movements of the stomach and large bowel.

Modern work on cortical stimulation goes to show that the hypothalamus is the area from which sympathetic and para-sympathetic impulses originate. Beattie showed that stimulation of the anterior part of the hypothalamus resulted in a vagal response and stimulation of the posterior part led to a splanchnic response. Heslop confirmed this and added the interesting observation that posterior hypothalamic stimulation led to a decrease in the amount of acid and an increase in the outflow of mucus. This fact is of importance and will be commented upon in the later section dealing with the control of gastric acidity.

d). The effect of drugs on the action of the vagus and sympathetic.

Herrin, Rubin and Backhuber[77] found that atropine increased the initial and final emptying time in normal dogs, but atropine did not act on denervated dogs, which shows that its action is through the vagus and not on Auerbachs plexus, but pilocarpine shortened the initial and final emptying time in denervated dogs. Moll and Flint[73] experimenting on the function of the sympathetic tried the effect of various drugs. Their results may be summarised as follows:-

1) Thyroid feeding produced subnormal acidity.
2) Adrenalin also lowered acidity.
3) Nicotine by paralysing the sympathetic gave rise to hyperchlorhydria.
4) Atropine diminished secretion.

Review.

While some of the results recorded appear at first sight contradictory and confusing certain important physiological principles stand out.

1) The cortical centres associated with gastric motility, tone and secretion are in the hypothalamus. Stimulation of the anterior part gives rise to hyperchlorhydria, hyperperistalsis and pyloro-spasm. Stimulation of the posterior part inhibits the above.

2) The vagus nerve is a mixed nerve and conveys in-

hibitory fibres as well as stimulating fibres. Its stimulating effect is produced by stimuli of mild intensity or when the stomach is atonic. Inhibition takes place when the stimulation is of high intensity or the gastric tone is high.

3) The splanchnic is always inhibitory in its action and stimulation of the splanchnic not only decreases the flow of acid but increases the outflow of mucus.

4) Auerbachs plexus appears to be the co-ordinating centre for impulses from the brain and in itself enjoys a certain amount of autonomy.

Other Anatomical and Physiological factors which may have a bearing on the formation of Ulcer.

The anatomical arrangement of the vessels along the lesser curvature and duodenum have been described and their relation to ulcer etiology discussed but it must be recognised that the mucosa also differs to some extent in these areas from that found elsewhere. It is not thrown into folds and is not freely moveable in the duodenum and lesser curvature and this may render it more liable to trauma than the mucosa of other parts of the stomach.

Lymphoid elements in the form of microscopic follicles are found all over the stomach deeply in the mucosa but these are more numerous in the region of the pyloric antrum and duodenum and reference will be made

later to the part they play in pre-ulcer pathology.

The movements of the stomach according to Alvarez, Mann and others are normally orderly and change the injesta into a suitable state for its reception by the duodenum and pass it on when ready. The duodenum itself has a peristaltic action and is capable of sweeping the contents rapidly on into the jejunum or if it is not properly prepared, returning it to the stomach.

The passage of food appears to depend on three factors according to Crider and Thomas[79]:-

1) The tone of the duodenum. Thus if duodenal tone is high and the pylorus relaxed regurgitation of bile may take place into the stomach. Reffuss and Eads[80] showed by experiments with balloons that in hunger definite contractions of the duodenum occur and these may be more powerful than the stomach contractions. The introduction of food into the stomach, however, led to a cessation of these contractions.

2) The relaxation of the pylorus.

3) The tone of the stomach.

This regurgitation and consequent mixing of bile and acid in the stomach has been held by Spira[81] to be responsible for ulcer formation.

Mann[82], Broster[83] and others have pointed out that

the ulcer bearing region of the stomach is where the interchange of acid and alkali occurs and some writers go so far as to suggest that in those persons in whom regurgitation is habitual by reason of a patulous pylorus and a high duodenal tone, gastric ulcer is more likely to form and those in whom a highly acid gastric juice is ejected into the duodenum through a semi-relaxed pylorus are more liable to suffer from duodenal ulcer.

The effect of fat upon the stomach emptying time has been studied by Quigliey, Zellelman and Ivy.[54] They found in common with others that the administration of fats by the mouth tended to delay emptying of the stomach and to encourage regurgitation of bile. They found, however, that fat injected intravenously had no effect nor did fat applied directly to the stomach, but if applied to the duodenum or jejunum the characteristic result was obtained showing that a hormonal effect was at work.

Neutralisation of the gastric acidity.

This is still in the stage of experimental investigation, and while it would be out of place to describe all the modern work in this sphere the main lines of investigation and the salient points might be reviewed.

The secretion of acid in the stomach appears to respond to four stimuli. First, there is a constant se-

cretion into the stomach under vagal or cephalic control. This is estimated by Hollander[15] to be in the region of 170. This is damaging to the tissues and the acidity of the mixed gastric secretions seldom reaches this level. Secondly, there is an increase due to psychic stimulation when food is seen, smelt or tasted. The third phase is known as the hormonal phase and is due to the stimulation of the gastric glands when peptones and amino-acids are absorbed from the pyloric antrum. This phase can be abolished by complete removal of the antrum, but McCann[86] found that if even a small portion of the antrum remained the hormonal phase of secretion took place. The fourth phase which Wilhelmj Finegan and Hill[87] describe and call the intestinal phase is really hormonal and is due to absorption from the intestine. Fauly and Ivy[88] found that ligation of the pancreatic ducts in Pavlov pouch dogs produced hypernormal secretion in the intestinal phase. The relative intensity of these four phases of secretion vary in different people and may account for the variation in results in certain experiments and operations.

Though it is fairly well established that gastric secretion is stimulated by the above mentioned factors the manner of its neutralisation is by no means so clear.

Boldyrief[89] in 1907 first pointed out that duodenal or biliary regurgitation was the factor responsible for the

reduction of acidity. Bolton[90] taught that when the acidity rose to a certain level relaxation of the pylorus took place and bile was regurgitated thereby lowering the acidity. This view is called in question by many and Reynolds found that feeding acid till the acidity was far above normal failed to bring about a relaxation in the pylorus and regurgitation of bile.

The most convincing experiment to prove that duodenal secretions are of great importance in the control of gastric acidity was carried out by Elman and Eckert.[91] They passed a ligature round the pylorus and instead of tying it, led the two ends through a tube to the surface. By pulling on the two ends of the ligature the pylorus could be closed and when the ends were relaxed the pylorus opened. The experiment showed that pyloric stenosis led to high acidity and acid introduced into the stomach could not be neutralised as rapidly as normal. When the pylorus was opened during a neutralisation test, neutralisation went on normally but when it was closed by the tightening of the ligature neutralisation ceased. This was also borne out by Senn (quoted by Elman and Eckert) who demonstrated high acidity in infants with pyloric stenosis and a marked lowering of the acidity after an operation to relieve stenosis.

Hollander, McLean and Griffith,[92] and others adduce

evidence to shew that duodenal regurgitation, if it occurs at all, is not the prime factor in lowering acidity and that there is some intragastric factor capable of lowering the acidity or bringing about neutralisation of acids introduced by the mouth. Their evidence is built up on experiments with whole stomach pouches in which bile is not admitted but in which a neutralising factor appears to be at work. Morton[97] found with dogs in which Exalto duodenal drainage had been carried out that acidity remained under control. MacLean and Griffith shewed that in the normal stomach, secretion the chloride ion is about the concentration in which it is present in the blood. Some of the chloride is secreted as HCl while the remainder is secreted as neutral chloride, the relative proportions of the two being different at different stages of digestion. Finegan and Hill also demonstrated by the whole pouch technique that there was an intragastric inhibitory mechanism which came into play when the gastric acidity rose to a certain level, but they also found that where duodenal regurgitation was allowed to occur there was a great inrush of duodenal fluid which lowered the acidity by dilution. They draw, what is probably the correct conclusion, that duodenal regurgitation plays the major part in the lowering of acidity but that should regurgitation fail to keep pace with acidity the intragastric inhibitory mechanism comes into play. It is possible that the two factors work in different people to varying

extents. In one it may be that inhibition is the main factor and in another it may be regurgitation. Alvarez, Vanyant and Osterberg[93] examined three persons daily for four months and found extreme variations in their gastric acidity. This was the more marked in nervous and highly strung persons.

The rôle of mucus in buffering gastric acidity has been studied by Webster[94] with a dog with a Heidenhain pouch. Injestion of different foods produced a flow of acid gastric juice and finally a scanty secretion of slightly acid fluid rich in mucin. McCann found that injection of histamine caused a rise in the free HCl in fifteen minutes with a change from a mucoid type of secretion to one of a more watery type. Later as the acidity fell the secretion became more mucoid. He concludes that a constant secretion of .5%-.6% HCl is secreted which, in the presence of pepsin, combines with mucus to form an acid mucus and neutral chloride. Due to the stimulation of the pyloric segment by the food acid is increased, hence not all is combined with mucus and so acidity rises, to be diluted with mucus later as the stimulation diminishes by food pouring out of the stomach.

Hollander was not impressed by the value of mucus as a buffer substance as in a sham feeding experiment the volume increased 45 times before the acid fell. Wilhelmj

Henrich and Hill[95] estimated the acid secretion of the stomach at 578-604 mgm. per 100 cc. and the non-acid secretions at 335 mgm. per 100 cc. The average alkalinity of the non-acid secretions was found to be 0.04% normal which cannot make it a very important factor in the neutralisation of acid, and they come to the conclusion that the most important intragastric factor is the regulation of gastric acidity by the intensity of the stimulation.

In spite of what appears to be conflicting evidence a few important points appear to be established.

1) Stimulation is partly cephalic by way of the vagus and partly hormonal by way of food absorbed from the pyloric antrum and jejunum.

2) Regurgitation of duodenal contents plays an important though not all important part in lowering acidity.

3) An intragastric mechanism exists by which a lowering of acidity may be brought about in the absence of duodenal regurgitation.

4) How this intragastric mechanism acts is still subject of debate but there is some evidence that it is brought about by a lessening of the hormonal phase of secretion as the food passes out of the stomach and the mucus and non-acid secretions are capable of buffering or at least diluting such acid as continues to be secreted.

PART IV.

Review of Experimental Work related to Theories of Ulcer Causation.

The multiplicity of processes by which acute ulcer has been produced is a tribute to the ingenuity of the investigators but not particularly enlightening to those who would seek to read the story of chronic peptic ulcer in man. Lesions of the stomach and duodenum have been produced by an immense variety of procedures such as:-

1) Experimental lesions of the central nervous system.

2) Experimental lesions of the gastric and duodenal nerves.

3) Circulatory disturbances by ligature or experimental embolism of various vessels.

4) Removal of adrenal glands.

5) Trauma of stomach and duodenum.

6) Ingestion of bacteria.

7) Intravenous injection of bacteria.

8) Intravenous injection of toxic substances.

9) Intravenous injection of mineral poisons.

10) Cutaneous burns.

11) Diatetic deficiency.

12) Disturbance of the anatomy of the stomach and duodenum by operation.

13) Ingestion of hydrochloric acid or measures to increase the acidity of the stomach.

All these methods produce acute ulcers but few of them give rise to chronic ulcers akin to the ulcers found in human beings.

The experimental work has fallen into five main groups, each of which attempts to explain the etiology of ulcer by a particular theory. The five main theories are:-

1) Vascular. 2) Infective. 3) Chemical. 4) Diatetic deficiency, 5) Neurogenic.

These theories will now be considered separately and the evidence assessed for each.

The Vascular theory.

Virchow[96] in 1853 suggested that ulcers were produced by infarction of a terminal blood vessel, resulting in necrosis or loss of vitality and this devitalised spot became the starting point for digestion by the gastric juice. Von Bergman[97] in 1918 suggested that the condition was a spasm of the vessels and Eppinger and Hess suggested that vagotonia produced spasm of the muscularis mucossae and gastric muscles, leading to areas of ischaemia which eventually became ulcerated. Wilkie injected the vessels of the stomach and duodenum and shewed that the vessels of the lesser curvature are longer and more tortuous than those of the fundus and therefore more liable to blockage

by thrombosis or emboli. He also demonstrated the end artery which supplies the anterior surface of the first part of the duodenum. His embolic theory, however, seems to have been largely conjectural and Konjetzney[104] was not able to find any microscopic evidence of change in the blood vessels in the resected stomachs which he examined.

Morton[98] transplanted portions of the jejunum with the blood supply intact into the greater curvature and lesser curvature of the stomach and found that the transplanted patches in the lesser curvature became ulcerated while those in the greater curvature remained healthy. This has been cited as an example of effect of the better blood supply in maintaining the nutrition of the transplant and protecting it from ulceration. This scarcely seems to be a tenable conclusion, as the transplants all had an adequate blood supply from their mesenteric attachments and if it was not sufficient to protect the transplant from the digestive juices, it is hardly conceivable that the blood supply of the greater curvature could permeate a patch of jejunum sufficiently rapidly to protect it from erosion in the first few days.

Ligature of the vessels can be carried out with impunity in the stomach and the anastomosis is so free in the sub-mucosa that it is scarcely conceivable that a chance occlusion of a long and tortuous vessel on the lesser

curvature would make much difference to the vitality of the part. It seems much more likely that some mechanical factor such as the fixity of the mucus membrane in the first part of the duodenum and lesser curvature rendering it more liable to injury, or the impingement of highly acid secretions on the anterior wall of the first part of the duodenum determines the localisation of the ulcer rather than any localised defect in blood supply.

The Infective Theory.

Gastritis and duodenitis have always been associated with the etiology of peptic ulcer, but with the introduction of the vascular and nervous explanations for ulcer, infection has tended to fall into the background but is again being brought into prominence by Continental writers. In 1921 Rosenow[99] demonstrated the elective localisation of bacteria. He produced the same strain of streptococcus from a peptic ulcer as was found in the gall-bladder and appendix and his theory was that a focus of infection could harbour an organism which was capable of developing an affinity for the duodenum. Nickel and Hufford[100] found foci of infection in 79 out of 80 cases of peptic ulcer. From these they isolated a streptococcus which, if injected intravenously into rabbits produced haemorrhagic erosion of the stomach. They also injected

it into the pulp chamber of dogs teeth, causing foci of infection. These dogs developed haemorrhagic lesions of the stomach and those which lived a year or more developed ulcer. Hayden[101] injected streptococci from ulcer cases into rabbits, 53% of which developed ulcer. He also inject- streptococci from non-ulcer patients and only 7% developed ulcer.

Intriguing as these experiments are, they do not explain why ulcer so often recurs when foci of infection have been cleared up and they do not explain why certain races of North India, in whom oral sepsis is exceedingly common, are almost free from ulcer; while other races in South India whose teeth are on the whole better, suffer from ulcer in large numbers.

It is scarcely to be expected that men are three times more liable to oral sepsis than women though they are three times more liable to ulcer.

The relationship between chronic gastritis and duodenitis and ulcer has been commented upon again and again. In 1902 Smith[102] described cases of suspected ulcer where only pin point erosions were found in the mucosa and and in 1906 Miller[103] described the histopathology of gastric ulcer in four stages.— 1) An enlarged lymph follicle bursts and exposes the basement membrane. 2) The defect

is not made good owing to the stiffening of the mucus membrane by inflammation. 3) The basement membrane is digested. 4) The vessels become thrombosed or eroded.

Konjetzney[104] gave the classic description of gastritis and duodenitis. He examined twenty-two cases of duodenal ulcer and examined the stomach at a distance from the ulcer. He found all stages of superficial ulceration from tiny abrasions to fissures and ulcers of appreciable size. Microscopically, inflammatory changes were seen in the mucosa. Infiltration with lymphocytes and leucocytes and sometimes inflammatory erosions of the mucosa were seen without epithelial defect. These changes were limited to the pyloric antrum and the first part of the duodenum. Similar changes have been described by Judd and Nagel[105], Wellbrock[106], Kellog[107], Faber[108], Johnston[109] and Fitzgerald[110]. Their description does not vary much and the points common to all are the infiltration of the round cells, oedema and the formation of lymph follicles, which may be seen rupturing on to the surface causing minute erosions, and at times the replacement of the mucosal glands by inflammatory tissue. Hurst[111], however, attaches but little importance to follicular ulcers as the precursors of chronic peptic ulcers.

Fitzgerald[112], Hale-White and others have described haemorrhage from the stomach in the absence of macroscopic

ulcer and this condition is so common in some European countries that surgeons such as Finsterer recommend gastric resection to cure the tendency to repeated massive haemorrhages in chronic gastritis.

The symptomatology of chronic gastritis and duodenitis has been commented upon by Garry[1], who says that the signs and symptoms may simulate duodenal ulcer, chronic pancreatitis, cholecystitis, or appendicitis. The X-Ray shows an abnormal irritability of the duodenum with increased spasticity and hypermotility. The duodenal bulb is deformed and the outline hazy. Friedenwald and Feldman[3] describe a condition which they call irritable duodenum, which is characterised by rapid emptying, fibrillar movements and irregularities and a tender duodenal bulb. Faber[10] believes that the symptoms of this condition simulate ulcer and are due to the spastic contraction of the stomach and duodenal muscle on the enlarged lymph follicles and microscopic ulcers.

The most recent contribution to this subject has been made by Simmonds[14], who produced experimentally, gastric ulcers in rats by injecting cinchophen. His description of the process is particularly interesting as it shows the close relationship between the inflammatory condition just described and peptic ulcer. The following developments

were noted in the process of his experiment.

1) Oedema of single or several villi.

2) Diffuse infiltration of villi with plasma cells and lymphocytes.

3) Superficial erosions.

4) Focal accumulation of polymorphs in villi just above the muscularis mucosae, often accompanied by liquifactive necrosis.

5) Narrow fistula like channels extending from such foci to the surface.

6) Large deep ulcers.

The above description will be found particularly interesting when compared with the description of rat feeding experiments carried out by the writer and described in the next section of this Thesis.

Summary and Conclusions.

Infection appears to play a part in peptic ulcer etiology though other factors must be at work as well.

A pre-ulcerous condition, known as irritable duodenum or follicular gastritis is described, in which the symptoms may simulate peptic ulcer and this condition is believed by many writers to be the precursor of ulcer.

The outstanding pathological finding is the presence of large numbers of lymph follicles, some of which

display liquifactive necrosis and others which have ruptured on to the surface causing fissures or minute pin-point ulcers.

THE CHEMICAL THEORY OF ULCER FORMATION.

The chemical substances cited as of major importance in ulcer formation are:-

1) Irritants in the food such as spices and condiments, high game and over-ripe fruit.

2) Irritants introduced in the course of an experiment.

3) Toxins such as those liberated in the body in severe burns.

4) Hyperacidity.

1) Irritants.

There is no doubt that peptic ulcer is common in races whose diet contains large quantities of pepper, spices or curry. Examples have been quoted already from South India, Abyssinia, etc., but it is not at all clear that these irritants of themselves cause ulcer, as most of the diets quoted above are markedly deficient in important food factors. There are other races, such as the Japanese, whose diet is highly spiced who develop no tendency to ulcer formation. Examples will be quoted later to shew that women in South India rarely develop ulcer though they partake of the same hot curries as the men.

2) Experimental Irritation. Injection of chemical substances such as silver nitrate into the mucosa of the stomach has been a favourite method of producing ulcer for

experimental purposes. But Mathews and Dragstardt[115] shewed that such ulcers heal rapidly provided the chemistry of the gastric secretions is unaltered. Such ulcers, can, however, be prevented from healing and may become chronic, if by deviation of the alkaline juices of the duodenum or by feeding acid by mouth, the stomach acidity is raised. This is probably true of erosions induced by the irritant diets mentioned above. Unless there is something to upset the chemistry and motility of the stomach these lesions tend to heal rapidly, and do not become chronic.

3) Toxins.

Bolton[22] succeeded in producing a gastrotoxic substance but though the injection of this toxin resulted in ulcer, this ulcer tended to heal, unless dysfunction of the pylorus was produced to prevent duodenal regurgitation.

Toxins absorbed from burns have, however, been known for long to be a cause of acute perforating ulcer. What these toxins are, is a matter of doubt, but Levin[118] describes them as substances akin to histamine which result in a devitalisation of the mucus membrane and a raising of the acidity. Judging by the rapidity with which such ulcers perforate it is likely that serious devitalisation results.

Toxaemia can play but a small part in the etio-

logy of chronic ulcer and apart from the condition mentioned in relation to burns,probably does not enter into the problem at all.

4) Hyperacidity.

The rôle of acid in ulcer etiology, however, is one which deserves close inspection. Countless experiments on animals have been carried out and clinical data accumulated, which has convinced Deaver and Burden[11] that hyperacidity is the primary factor, or at any rate a factor of major importance.

Venables[12] has shewn that the tendency to hyperchlorhydria in ulcer is not, as was formerly taught, due to the ulcer itself but that it is constitutional, being a congenital and often familial variation from the average normal, which predisposes to the development of ulcer.

The following are the main experiments and observations which lend weight to this conception:-

1) Experimental dysfunction of the pylorus.

2) Diversion of the pancreatic and biliary secretions.

3) Complete duodenal drainage operations.

4) Feeding HCl.

5) Implanting gastric mucosa into the small bowel.

6) Implanting bowel with blood and nerve supply intact into the stomach.

7) Sham feeding of dogs with duodenal fistulas.

8) Injection of drugs calculated to raise the gastric acidity.

Experimental Dysfunction of the Pylorus.

Matthews and Dragstadt[37] inserted a valve into the pylorus in order to prevent the regurgitation of bile and thereby raised the acidity of the stomach and prevented the healing of artificially produced ulcers. Hugleson produced the reverse effect by causing experimental ulcers in dogs and in one group splinted the pylorus to keep it open and in the other group left the pylorus unsplinted and subject to a certain amount of spasm, due to reflex irritation, resulting from the experimentally produced ulcer. In the group with the splinted pylorus there was free regurgitation of the duodenal juices and the ulcer healed in half the time taken by the other group. The inference being that higher acidity resulted in delayed healing. Bolton[22] found also that ulcers produced by injection of foreign protein persisted for a much longer period if the pylorus was completely closed.

Deviation of Pancreatic and Biliary Secretion.

Blanck[10] experimented with methods of complete external drainage of bile and found that though actual ulceration did not occur, gastritis, duodenitis and jejunitis were frequently observed. Kapsinow[42] frequently met with ulcer by this method. Graves[43] studied the combined and

separate effects of deviation of bile and pancreatic secretions and came to the conclusion that the deviation of bile alone does not cause ulcer, but deviation of pancreatic juice was more liable to be followed by ulcer, while a large proportion of experimental animals developed ulcer when both bile and pancreatic juiceswere deviated. He quotes Kehrer who obtained 100% of successes by this method and Mann and Williamson[23] who obtained fourteen successes out of sixteen attempts.

An interesting pathological finding is reported by Morton and Graham[24] and bears out the experimental findings reported above. They report the death of a man, due to haemorrhage, from a duodenal ulcer following an operation for gall stones. At post-mortem a large calculus was found blocking the common duct and a pancreatic calculus was found partially obstructing the pancreatic duct. They offer this as evidence in support of the theory that ulcer formation is due to the failure of bile and pancreatic juice to neutralise gastric acidity. Berg and Jobling[25] and also Mann[26] cast doubts on the idea that the above findings are due to the raising of the gastric acidity and suggest that the ulcer results from the devitalisation of the mucus membrane or the removal of some specific protective factor in the duodenal secretions.

Complete Duodenal Drainage.

Believing that bile and pancreatic juice were but two of the neutralising factors in the duodenum, Mann and Williamson[43] adapted the duodenal drainage operation of Exalto by dividing the pylorus and duodeno-jejunal junction and suturing the jejunum to the pylorus and diverting the entire duodenal contents into the terminal ileum. The result of the operation was the production of ulcer in the jejunum, just distal to the anastomosis with the pylorus in 100% of the operations. Modifications of this operation resulted in a lowering of the incidence. For example an end to side anastomosis of the pylorus into jejunum whereby narrowing of the stoma was avoided, resulted in ulcer in only 43% of attempts. If the pyloric antrum was resected and an end to side anastomosis made, the ulcer incidence was 12%, and if a high gastrectomy was performed the incidence was nil. The last two operative procedures of course lower the acidity to a considerable extent.

Implanting the duodenum into the jejunum near the anastomosis, instead of into the terminal ileum resulted in 5% of ulcer, as regurgitation of duodenal contents occurred to some extent, but if a valve were placed between the pyloro-jejunal anastomosis and the deviated duodenal contents, thereby preventing regurgitation, the incidence rose to 30%. (Matthews and Dragstadt).[27]

This duodenal drainage technique is so constant in its results that it has become the standard method of producing experimental ulcer in order to test the efficiency of various methods of preventing ulcer formation. One interesting observation of this type was made by McCann[127] who carried the duodenal drainage into the fundus instead of into the ileum. The point of the experiment being, "Could these alkaline juices control gastric secretions to such an extent that ulcer would not develop?" However, typical ulcers developed in 80% of the experiments in the jejunum just beyond the suture line. Evidently, the reaction of the duodenal juices in the normal physiological relationship is to act as a buffer terminating the peptic activity of the gastric secretions. McCann[115] showed that in the duodenal drainage into the terminal ileum there was no marked rise in the gastric acidity and concluded that the normal unbuffered gastric juice was capable of producing ulcer and that the stomach has a mechanism for controlling gastric acidity quite apart from duodenal regurgitation. Weiss and Hubster[120] repeated the duodenal drainage experiments, producing ulcer but without any rise in acidity. They believe that the secretions have a protective function and not an anti-acid function. Weiss and Aron[130] interpreted the duodenal drainage experiment as a failure of the splitting of proteins into amino-acids on account of the

deviation of pancreatic secretion. They hold the opinion that the proper absorption of amino-acids from the upper intestine is essential to the resisting power of the mucosa, and they attribute the value of histidine injections in the treatment of peptic ulcer to the amino-acid content.

Feeding Hydrochloric Acid.

Attempts have been made to produce peptic ulcer by increasing the gastric acidity by feeding hydrochloric acid. Mann and Bollman[131] found that the most effective method of increasing the peptic activity and producing ulcer was by feeding .4% HCl continuously, 1 c.c. every minute through a gastric fistula. Howes,[132] Flood and Mullins[133] tested the effect of HCl in retarding the healing of artificially produced mucosal defects by feeding .9% hydrochloric acid. Healing was not delayed by this concentration but if pepsin was added, healing was delayed but chronic ulcer did not develop. In order to determine whether there might or might not be some specific factor in the juice of a patient suffering from peptic ulcer they fed such juice to dogs but no harmful effect was noted. Various combinations of pepsin and HCl were fed to rats and the effect of feeding the acid pepsin on a fasting stomach was tried out by Matzner and Windmer.[134] They found that a combination of

acid and pepsin coupled with forty-eight hour fasts resulted in ulcer formation in 96% of experimental rats. The fasting appeared to enhance the effect of the acid-pepsin very considerably.

Implanting portions of the Stomach into the Jejunum.

Since Meckels observation in 1815 that ectopic gastric mucosa in a Meckels diverticulum could ulcerate the tissues around, attempts have been made to implant gastric tissue into the jejunum. Matthews and Dragstadt[115] carried out this operation successfully and produced ulcer in 85% of attempts where the implant was into the jejunum and 100% of attempts where the implant was into the ileum.

Implanting bowel with blood and nerve supply intact into the Stomach.

Morton[28] implanted jejunal patches with blood and nerve supply intact into the stonach wall and nothing happened, but when the chemistry of the stomach was upset by duodenal drainage the patches in the lesser curvature developed ulcer while those in the greater curvature did not. This interesting observation could only be accounted for by increased liability of the lesser curvature to trauma and could scarcely be due to a difference in the chemistry

of the two parts of the stomach. Preventing duodenal regurgitation by placing a valve in the pylorus also had the effect of producing ulceration of jejunal implants into the stomach wall.

Sham Feeding of Dogs with Duodenal Fistulas.

Schmidt and Fogelson[135] submitted dogs to sham feeding for ten or twelve hours daily. No ulcers resulted but duodenitis developed. Silberman carried out the same experiments and the stomach secreted an acid of concentration and digestive power five times greater than the normal. When the dogs were examined from fourteen to forty-nine days later, all showed ulceration in varying degrees of development. Matthews and Dragstedt also found that ulcer developed in totally isolated stomachs in presence of high acid-pepsin.

Injection of Drugs calculated to raise the gastric acidity.

Various workers have reported the effect of histamine injections in delaying the healing of ulcers and in inducing ulcers and erosions. Stalker, Bollman and Mann[136] studied the effects of injecting cinchophen. They treated twelve dogs, in eleven the acidity was not raised but the quantity of the acid was increased and they all developed

ulcer, save one, in which the quantity and acidity was not affected.

SUMMARY AND CONCLUSIONS.

Significant points suggesting acid as a factor in ulcer Etiology.

Ulcer resulted after sham feeding experiments in which the acidity was raised to five times that normally found in the stomach. It also resulted from the continuous drip method of feeding HCl of high concentration. In both these experiments, however, conditions were present which are never approached in any condition of the humen stomach. In the sham feeding experiments gross distortion of the anatomical relationships existed, but in the second experiment the continuous drip of acid was the only factor which could be blamed for the ulcer.

Experiments in which other factors apart from acid come into play.

Duodenal drainage operations and intestinal implants resulted in ulceration of the intestinal mucosa which is not strictly comparable to ulcer forming in the stomach or duodenum. It was significant, however, that artificially produced defects healed more slowly if the

acid was kept at an artificially high level. It was even more significant, however, that duodenal drainage operations in which the duodenal secretions were drained into the fundus resulted in 80% of ulcers of the jejunum just beyond the anastomosis. In this experiment there must have been a lowering of the acidity of the stomach by the inrush of all the alkaline contents of the duodenum but the buffering action did not take place at the time and place that nature intended it to operate and the result was ulcer. Furthermore, the duodenal drainage operation, in which the shunt was made low down in the ileum, did not materially raise the acidity but again the buffering action failed to take place, with the inevitable result.

The only conclusion we can draw regarding the rôle of acid in the etiology of ulcer is, that provided the buffering action of the duodenal juices proceeds normally, an acidity within the range of the human stomach to secrete, is not sufficient to cause ulcer in itself, though it may delay the healing of an ulcer produced by some other cause. On the other hand any serious upset in the acid-alkali interchange taking place in the duodenum and pyloric antrum appears to deprive the tissues of an effective protective mechanism and ulcer may result from an acidity by no means excessive.

For practical purposes then we cannot ascribe to the acid juices of the stomach the prime rôle in ulcer etiology. It only plays a part when other factors lowering the resistance of the mucosa are present.

The Theory of Intestinal Implants in the Gastric Mucosa.

A most interesting speculation was made by Clar[158] as a result of his observations of patches of mucosa of the intestinal type in the stomachs of foetuses and in adult stomachs, subject to chronic gastritis. He described the cell structure of such islets, in which he found goblet cells, Paneth cells, and chromaffin cells. He found such islets very frequently in foetuses but after birth the incidence became much reduced and no such islets were found in adult stomachs. In stomachs the seat of ulcer, however, 50% shewed such islets clearly defined and situated at considerable distances from the ulcer, although the mucosa was otherwise normal. The interpretation he put upon his finding was that they were rests of intestinal tissue, analogous to the rests of gastric tissue sometimes found in Meckels diverticulum. He went on to suggest that these rests became ulcerated by the gastric juice and thereby formed chronic ulcers.

Attractive as this theory sounds, it is not borne out by the work of other observers such as Maquire[159] who showed that the so-called intestinal rests were really the result of chronic gastritis and represented a metaplastic condition resulting from the repair of the mucus membrane after inflammatory changes.

The fact that intestinal rests have never been demonstrated in normal adult stomachs and have only been seen in stomachs the seat of gastritis or ulcer puts the balance of evidence in favour of the "metaplasia" as against the "congenital rest" explanation of their existence.

The Theory of Dietetic Deficiency.

Exhaustive enquiries into the diet of the peptic ulcer patient in England and America has shewn that there is no difference between the diet of those who develop ulcer and those who do not. Harris[M], however, attributes the great increase in duodenal ulcer in America to the increasing prevalence of sweet carbohydrate foods and soft drinks in the present generation. He is convinced that there is a lack of vitamin A in the diet of the average town dwelling American and his treatment of ulcer is by tomato juice, green vegetables and food stuffs which supply abundance of the deficient elements.

References have been made in the paragraph on epidemiology to the frequency of peptic ulcer in Malaya, Abyssinia and South India, on account of the diet of the people. This subject will be dealt with in detail in the next section of this Thesis, but it might be of interest

at this stage to examine the result of experimental work on animals in the attempt to produce ulcer by deficient diets.

In 1931 Sir Robert McCarrison[xi] published the results of his experiments on rats with the South Indian diets. Albino rats were used for the experiment. A control group was fed on the diet of the Punjab (a district in which ulcer is not common) consisting of wheat, flour, butter, sprouted gram, fresh cabbage and carrots, milk and a small ration of meat. 600 rats fed in this manner displayed no tendency to ulcer and gastro-intestinal lesions were never found on post-mortem examination. Eighteen of the rats were fed on the diet of Travancore (a Native State in South India where duodenal ulcer is very common) and a similar number were fed on the diet of the Madras Presidency where the natives are also prone to suffer from peptic ulcer.

Travancore Diet.	
Tapioca Root	10 oz.
Rice	10 oz.
Chillies	1/8 oz.
Tamarind	1/8 oz.
Fish	2 oz.
Rice Water ad lib.	

Madras Diet.	
Rice	20 oz.
Chillies	1/8 oz.
Tamarind	1/8 oz.
Fish	2 oz.
Rice Water ad lib.	

These two diets are obviously very deficient in protein, and in vitamins A. and B.

The mortality rate in the Travancore group was 94% and in the Madras group 84%.

In both groups, one rat was discarded as it lived less than six months on the diet.

Eight out of the seventeen rats on the Travancore diet developed lesions of the stomach or duodenum such as gastritis and duodenitis and five had actual ulcer of 0.1 to 0.5 cm. in diameter. That is 47% were affected.

Six out of the Madras series had lesions, but only two had definite ulcer. That is 35% were affected. Magee and Anderson[42] reported congestion haemorrhage and degenerative changes in and around the pyloric region, both on the duodenal and on the gastric side, in cavies fed on a diet deficient in Vitamin A. and D. They also noted that intussusception occurred frequently, and they came to the conclusion that the adrenal gland was affected by the diet and the balance of the sympathetic upset. They pointed out that patients with severe burns who developed duodenal ulcer also had congestion and haemorrhage of the adrenal gland. Hoelzel and Da Costa[41] produced ulcer in rats on a diet wholly deficient in protein and noted that periods of starvation increased the tendency to ulcer formation. They also experimented with diets deficient in vitamins A and B but found that it took longer to produce ulcer than with protein deficiency. Weech and Paige[44] commenting on the above experiment suggest that the ulcer forms, not as the result of an increase in acidity but due to the amino-acid deficiency.

Windmer and Sobel[45] deny this explanation of the results, while agreeing with the facts. To lend weight to the above experiment, Weech and Paige fed dogs on a diet in which the vitamins were well represented but in which proteins were deficient. Twenty-two dogs were fed. Eight developed true peptic ulcer. Five exhibited superficial erosions of the gastric and duodenal mucosa and in nine no ulcer or erosions were found.

Dallidorf, Gilbert, and Kellog[46] also succeeded in producing ulcer in 73% of albino rats fed on a diet deficient in vitamin B and protein. Pappenheimer and Larrymore[47] made similar observations on rats and Cheney[48] on chicks. The most interesting and convincing series of experiments along this line have been made by Holzel and Da Costa.[49] They implanted pieces of metal in the mucosa of rats and found that erosion of the metal was increased and gastric retention prolonged if a diet high in carbohydrate and low in protein was provided. The retention could be cleared up by giving adequate quantities of protein and again induced by restricting protein. They found that prolonged deprivation of protein increased the irritability of the pyloric region in man and rats.

SUMMARY AND CONCLUSIONS.

The dietetic experiments herein reviewed have one refreshing feature in contrast to chemical and other experiments. There is more or less uniformity of result. The conclusion that all observers come to is, that certain dietetic deficiencies, of which protein is the most outstanding and Vitamins A. B. & C. come next in importance, are capable of inducing a condition of congestion and erosion and even ulceration in the stomach and duodenum of rats, chicks, and dogs. As to how this arises we are left in some doubt but there is strong evidence to support the view that the deficiency brings about an inbalance of the neuro-muscular mechanism of the stomach and pylorus, which leads to gastric retention and congestion. The theory that a failure of absorption of amino-acids is responsible for all this is an interesting speculation but so far, there is not enough evidence to make the argument convincing.

While the deficiency view of ulcer etiology may have little to do with the problem in European countries it certainly helps to explain the amazing freedom from peptic ulcer of certain races and the liability of others,

While the causal factor may differ in different parts of the world the same chain of events seems to lead to ulcer and this chain of events may be brought about by different means.

NEUROGENIC THEORY OF ULCER FORMATION.

This subject was not considered in detail in the historical section of this Thesis as nearly all the important work on the neurological aspect of peptic ulcer is of recent date and but a few historic records are worthy of note.

As early as 1846 Rokitansky[5] noted gastric changes caused by nerve lesions and in 1875 Brown Sequard[119] reported gastric erosions associated with injury to the base of the brain.

Virchow[96] in 1853 suggested that spasm of vessels might be responsible for ulcer formation and von Bergman[97] suggested as an alternative to this, that muscular spasm might compress the vessels and thereby lead to devitalisation of the part and ulcer formation.

Beyond these somewhat unconvincing expressions of opinion, little has been written of the relationship between peptic ulcer and a neurogenic upset till Harvey Cushing[156] laid the foundation of our modern knowledge by his observation that acute ulcers tended to form after operative interference with the mid-brain, due to parasympathetic stimulation or possibly sympathetic paralysis. He found that stimulation of certain parts of the mid-

brain led to the syndrom of hypersecretion, hyperacidity, hypermotility and hypertonicity of the pyloric segment. This spasm led to small areas of ischaemia and haemorrhagic infarction. This is borne out by the experimental work of Beattie[71] and Heslop,[69] and McCrea McSwiney and Stopford[75] already described in the section on Physiology in this Thesis.

Cushing's work on this subject led to the almost general acceptance of the view that if one could bring about a state of hypersecretion, hyperperistalsis and pylorospeam one would create the soil in which peptic ulcer would flourish.

Ulcer Diathesis.

The fact that there is a certain type of person liable to peptic ulcer and that this type is the lean, active, alert, dynamic individual has been stressed by Hurst,[111] Hartman,[67] Hertzler,[151] and Robinson[66] and Russ.[152] Such people have hyperactive stomachs, in which the vagal influence proponderates over the sympathetic. They are subject to anxiety states and Davis and Wilson[63] in a study of 205 cases of ulcer and recurrences of ulcer found that there was a history of financial difficulty, marital disharmony and overstrain associated with almost every recurrence. A few years ago the strike among the London 'bus drivers

led to an enquiry into their conditions of work related to their health and the report showed that the 'bus drivers suffered from an excess of gastric illness over other transport workers, though the general health of the 'bus drivers was above that of other groups. This has been attributed to the increased strain and anxiety imposed upon these men by modern traffic conditions in London.

Robinson points out that the conditions of modern life are leading to an increase in peptic ulcer and contrasts the low incidence among American Negros, with the ever-rising incidence among the white population. It has been noted, however, that when the American Negro competes in the battle of life with the white man he also, is liable to peptic ulcer. Statistics shew that the highest incidence of peptic ulcer in Great Britain is among those classes living under unusl strain, such as financiers, medical men, etc.

Hurst describes the typical duodenal ulcer type as having a high transverse stomach of good tone and with active peristalsis. Such stomachs empty rapidly and are devoid of food for many hours each day, while the normal stomach has a residue of food in it when the next meal is taken.

Muller and Heimberger[5] made the interesting observation that certain individuals have a vaso-neurotic diathesis and the vessels of their lips, if examined by the

capillary microscope, show a spastic irregularity. They found the same irregularity in thirty stomechs resected for ulcer, the observation being made on the fresh warm specimen in the operation room. Von Bergman explains the condition by stating that worry and over work act by enhancing the vagus impulses in a person with the ulcer diathesis. Certain families appear to be more affected in this way than others and instances occur in the literature where both parents had undergone operation for ulcer and ulcers developed in the children.

Granted that certain persons have an ulcer diathesis and that this diathesis is vagotonic in type and leads to hypersecretion, hypertonicity and pylorospasm, have we any indication as to how these conditions are directly associated with ulcer formation?

Relationship of Pylorospasm to Hyperperistalsis.

Hughes[166] noted that the peristaltic waves of the stomach cannot be increased in frequency and amplitude without a corresponding hyperactivity of the pylorus and vice versa and the same observation was made by Bastianelli[167] who recognused pylorospasm as a clinical entity, causing dyspeptic symptoms and treated it by an operation of the Ramstedt type. Morton[167] and others have noted that in

cases of duodenal ulcer, the pylorus appears to be hypertrophied and spastic and this can be relieved by atropine. Morton experimentally produced pyloric dysfunction in several dogs by encircling the pylorus with a ring of jejunal muscle, this led to superficial erosions and infiltration of the mucosa with lymphocytes and plasma cells and hypertrophy of the lymph follicles, in other words, a preulcerous duodenitis.

The varied clinical and experimental studies indicate that a hyperactive pylorus, associated with hyperperistalsis, is a common accompaniment of duodenal ulcer, and that spasm of the pylorus, leads to pre-ulcer like pathology in the antrum and duodenum. The question to decide is, is the spasm the result of the ulcer or is the sequence of events, spasm first then ulcer. The following experimental evidence suggests but does not prove that the latter is the case.

Bolton noted that if ulcers were caused experimentally and the pylorus partially closed so that relaxation and regurgitation of duodenal contents could not take place there was considerable delay in the healing of the ulcer, while Hugheson found that if ulcer was caused and the pylorus was splinted and kept open the ulcer healed more rapidly than if the pylorus were untouched. The

factor of spasm was further studied by Steinberg and Starr[157] who carried out a duodenal drainage operation, but eliminated spasm of the first ten centimeters of the anastomosed jejunum (the part where ulcer occurs in these experiments) by denuding it of its muscle coat, leaving only the mucosa and sub-mucosa. The result was that instead of ulcer forming just beyond the anastomosis in 100% of the experiments, ulcer was only found in 30% and then the ulcer was 11 to 12 cms. distal to the anastomosis and on the part of the bowel not denuded of its muscle coat. They believe that the ulcer formed at this part, as this would be the first part of the jejunum to go into spasm. Fauley and Ivy[77] repeated this experiment but failed to obtain the same result and are sceptical about the part played by spasm in the etiology of peptic ulcer.

It is evident from the foregoing experimental work that spasm and hyperperistalsis are closely associated with ulcer and further evidence concerning this will be led in a later section of this thesis, dealing with original observations.

No further survey of the literature or comment on the rôle of the nervous system in ulcer etiology, need be made at this stage and the thesis will go on to present the evidence drawn from clinical and experimental observations by the writer in India, to support the theory that

the earliest manifestation of pre-ulcer pathology is to be found in the nervous changes of the stomach and pylorus.

PART V.

ORIGINAL OBSERVATIONS IN SOUTH INDIA.

As indicated in the Introduction to this Thesis, the writer has been engaged during the past ten years in surgical practice in Travancore, a large Native State in South India. During this period he and his colleagues and their assistants performed 2,500 operations for peptic ulcer, as this disease is extremely common in South India.

It was not until 1914 that Pugh diagnosed duodenal ulcer as the cause of the dyspepsia so frequently found in South India and he developed the surgical technique of treatment by gastro-enterostomy. In 1927[161] Bradfield gave the first scientific account of the condition as he met it in the wards of the General Hospital in Madras and called forth the comment of Surgeons in other parts of India. Somervell[162] pointed out the frequency with which the disease was met with in Travancore and expressed the view that the condition was due to the tendency to constipation, so common in South India. In 1927 also Hingston[163] reported that ulcer was common in Bengal, while surgeons in North India commented upon the rarity of the disease in that area. Stimulated by the varied comments from all over India, McCarrison[164] made a survey of the statistics available in the leading Government Hospitals and came to the conclusion that ulcer was

found in 1.765 per thousand of the population in the South and in 0.030 per thousand in the Punjab. PLATE II

The writer of this Thesis was stimulated to commence this investigation by the observation that in Travancore the incidence of peptic ulcer was decidedly higher than in other parts of South India and that within the State of Travancore itself the distribution was not uniform. In the Neyyoor Hospital in South Travancore where most of the clinical work of this Thesis was carried out, 85% of the cases of peptic ulcer came from the central and northern parts of the State, though the hospital is in the South. PLATE I &

Accurate statistical tables are difficult to compile, as the standard of diagnosis and classification is not uniform throughout India, and while in some districts all dyspeptic cases report for treatment to the recognised hospitals, there are other and more backward areas, where the common people have infinite faith in their own native systems of medicine for the treatment of dyspepsia and shun the European Hospitals.

The observations about to be described might be classified as follows:-

1) Survey of 2,500 peptic ulcer cases operated upon in the Neyyoor Hospital in the period under review.
2) Survey of the incidence in India as a whole.

3) Study of the diets of India in relation to ulcer etiology.

4) Comparison between South and Central India in the type of ulcer found.

5) Comparison between a series of test meals in normals in Travancore and a series in the Deccan.

6) Study of the tone activity and emptying time of stomachs in South Central and North India as evidenced by the barium meals.

7) Histological study.

1) Survey of 2500 cases of peptic ulcer operated upon in the Neyyoor Hospital, Travancore, in the ten year period.

95% of the cases were males.

85% came from the areas of North and Central Travancore, the remaining 15% came from South Travancore and the neighbouring parts of British India.

The history of all cases seen, was at least one and a half years and many gave histories of twenty-five years and longer. 35% had small ulcers of the duodenum with little deformity, no stenosis and rapid emptying with hyperperistalsis and high acidity. 58.3% had chronic stenosed duodenal ulcers associated with chronic gastritis and the acidity varying between high-normal and normal.

2.5% had gastric ulcers.

2.2% had gastric and duodenal ulcers.

2% had gastro-jejunal ulcers.

Only four in the series were operated upon for perforation.

Certain interesting points stand out in this classification:-

1) The marked preponderance of male over female.

2) The marked preponderance of duodenal over gastric ulcer.

3) The fact that 58.3% of the ulcers were of the stenosed duodenal type. In many, the ulcer was palpable as a hard mass the size of a plum and the duodenum was fixed by adhesions.

4) Only 0.16% of the operations were for perforation.

Some comment must be made on these figures. The very low incidence of perforation is remarkable when one remembers that 15% of operations for ulcer in Great Britain are for perforation. It must be allowed, however, that a certain number of these cases probably die without being brought to hospital. But even with all due allowance, the perforation incidence is small.

The percentage of women patients also may appear lower than is actually the case, because women in India find it more difficult to leave home for hospital treatment than do men, but there is no doubt that the number of women suffering from duodenal ulcer is extremely small.

A study of the social status of the patients

showed that the aboriginal and the rich were seldom affected but that the highest incidence was in the poorer classes, particularly the agricultural labourers.

2) Survey of the incidence in India as a whole.

Sir Robert McCarrison made his estimate of the incidence of peptic ulcer in India from statistics of Government Hospitals. Certain fallacies are apt to arise, as pointed out above and the writer made an attempt to repeat the survey, using as material the work of some of the large and well-known mission hospitals, as being more in touch with the life of the common people to whom they minister.

The classification was made, not in thousands of the population but in percentage of peptic ulcer admissions, in the total admissions of each hospital for one year.

In six leading hospitals in different parts of India in which the writer had opportunity for personal study, the percentage of peptic ulcer admissions to total admissions was as follows:-

South India	Travancore	10%
	East Madras	2%
	Bangalore	1.88%
Central India	Miraj (Deccan) . . .	1.52%
West Coast	Vengurla	0.46%
North India	Delhi	0.20%

The contrasts are marked and correspond roughly to McCarrison's findings. It can be seen that of all the districts in South India the incidence in Travancore is much the highest. The incidence in the Punjab Hospitals is less than Delhi, but it was not possible in the work for this Thesis to visit the Punjab in person. PLATE I.

Observations of a similar type have been made by N. M. Rao[4] in Vizagapatam in the north-east of the Madras Presidency and by Ramachandra Rao[5] in Bangalore.

N. Rao compared the statistics of admissions for peptic ulcer in different parts of India during the years 1923-26.

Years	Madras	Calcutta	Rangoon	Lahore
1923	306	25	14	0
1924	328	20	12	0
1925	429	43	16	14
1926	414	67	23	0
	1477	155	65	14

This table displays the marked disparity of ulcer incidence in India. Why fourteen cases should have been found in Lahore in the Punjab in 1925 and none in the preceding or succeeding years is not explained, but possibly some influx of South Indian troops may have accounted

for the unusual appearance of peptic ulcer in Lahore.

Rao found in Vizagapatam that 6.38% of surgical admissions were for this disease. 86.8% of these were duodenal, 6.5% pyloric and 6.7% gastric ulcers. 6.2% were found in females. Haemorrhage was very rare and the highest incidence of peptic ulcer was in the labouring classes.

The diet in this area is rich in carbohydrate, poor in fat and protein and deficient in vitamins A & B. Oral sepsis is common, as it is throughout India and the labourers have irregular meals with long fasts, as they do in Travancore.

Granted this marked discrepancy in incidence, it follows that the discovery of some common etiological factor would mark a decided advance in our knowledge of the subject, not only in India but in general.

The possible etiological factors are:-

Race,
Climate,
Habits of the people.
Diet.

Race is unlikely to play an important part, as the inhabitants of South India are of mixed origin and the sufferers from peptic ulcer are Aryan, Dravidian, Hindu and Muslim, educated and illiterate.

Climate also can play but a minor part, as ulcer is common all over the Madras Presidency, parts of which

are humid and parts dry and hot with a cold season.

Certain features of the diet of the South Indian are peculiar and not found in the North, and it is these factors which we must examine, not only to establish them as primary or contributory causes, but to study the manner in which they affect the human organism and the pathological changes they produce.

3) Study of the diets of the South Indian People.

Sir Robert McCarrison has said that the diet of the people of the Punjab is the best balanced diet in the world. It consists of wheat, and cereal grains, abundance of milk and milk products, green vegetables and small quantities of meat. All the vitamins are well represented and the balance of protein, carbohydrate and fat is in correct proportion for maximum physiological efficiency.

The races of the north are the virile races, and the fighting men of India, while the Bengali and the South Indian are of poorer physique.

Aykroyd and Krishnan[10] carried out a diet survey in one of the villages of South India. They found that 31 out of 44 families had no milk at all. The remainder averaged five ounces of milk per day. Food, other than cereals was consumed in very small quantities, and the diet

of the poorer people consisted almost exclusively of home-pounded parboiled rice. Small quantities of fish, mutton or chicken were eaten if available, but were looked upon as luxuries except by the prosperous. Pulses formed an important ingredient being in many cases, the main source of protein, and the green leafy vegetables were absent from many diets, but non-leafy vegetables were in common use. Fresh fruit was included in the diet of seventeen out of the forty-four families. The fruit was ripe or green plantain.

Only four families in the forty-four consumed 3,000 colories per adult male. In one family the caloric intake averaged 1664 in another 2026, and in a third 1184 per day. Speaking generally the protein and fat intake was low and there was almost a complete absence of protein of animal origin. 39 families derived 80% of their protein from vegetable sources and in eight families the proportion was as high as 95%. Vitamin A was almost absent in 39.

The above survey is fairly representative of the whole of South India but in some districts certain cereals such as ragi, with a high protein and vitamin content are used.

The same observers made a survey of the nutrition

of groups of South Indian children and found the standard of development low. The effect of adding milk in the form of dried milk powder was observed in certain schools and the result was an acceleration of growth and a marked improvement in general condition.

Stimulated by the striking findings of Aykroyd and Krishnan, the writer undertook a similar dietetic survey of families in Travancore. The method was the same as that adopted in the South Indian survey. Picked workers visited daily six families and weighed and measured every article of food coming into the house for two weeks. The number, age and sex of all the inmates was recorded and an adult man was given the value of one consumption unit and a woman .8% consumption unit and children smaller values according to age. The total consumption units in each family was ascertained, and the total food intake divided by the number of consumption units and the proportion of protein fat, carbohydrate, minerals and total calorie intake worked out for one consumption unit.

Certain interesting facts emerged. The poorer class diet in central and north Travancore consisted in almost equal proportions of Tapioca and Rice with the addition of a little cocoanut, fish, tamarind, and brinjal. This diet averaged in grammes per consump-

tion unit:-

Protein (g)	Fat (g)	Carbohydrates (g)	Calories.	Ca. (g)	Ph. (g)	Fe. (mg)
48.45	13	614.78	2769.54	.32	1.9	16.77

Compared with Akyrod and Krishnan's South Indian survey this shows an adequate caloric intake but even greater excess of carbohydrate. 98% of the calories were derived from vegetable sources, and these vegetable sources were very poor in vegetable protein.

There was marked deficiency in vitamins A and B1, and to some extent C, but vitamin D was probably accounted for by the habit of oil baths and subsequent irradiation by the sun. Now a further interesting point arose. It was found that the use of Tapioca root was confined to Central and North Travancore and was never used in the south of the State where the diet conformed closely to the rest of South India, the staple diet being rice. The tapioca is a crude plant imported from South America at a time of rice famine fifty years ago.

Its composition is:-

Moisture 59%. Protein .68%. Fat .20%. Carbohydrate 38% and its caloric value per 100 grms. is 159.6 and it contains, as far as can be estimated at present, little or no vitamin A B C or D.

Deficient as is the diet of South India in general, including South Travancore, we see that the diet of

TABLE No. 1.

A typical poor Travancore diet.

Family No. IV. Inteke in grammes per consumption Unit.

Food	No. of Persons.	No. of Consumption Units	Protein (g)	Fat (g)	Carbohydrate (g)	Calories	Calcium (g)	Phosphorus (g)	Iron (FE) (mg)
Rice	-	-	41.0	1.76	376	1680	0336	.801	10.56
Tapioca	-	-	4.1	1.2	232.6	957.6	27	.234	5.52
Coconut	5	-	1.12	10.4	3.29	111.2	003	.61	.42
Fish	-	4.4	1.28	.098	"	6	0033	.248	.137
Chillies	-	-	.953	.394	1.89	14.74	.0098	.0223	.135
TOTAL			48.45	13.84	614.78	2769.54	32	1.92	16.77

TABLE No. II.

A Typical better middle class Travancore family diet.

Family No. XIII.

Food	No. of Persons.	No. of Consumption Units	Protein (g)	Fat (g)	Carbohydrate. (g)	Calories	Calcium (g)	Phosphorus (g)	Iron (mg)
Rice	-	-	31.837	1.312	293.51	1306.5	.03	.315	12.48
Ragiflan	-	-	2.13	.387	23.625	105.06	.1002	.0816	1.64
Milk	-	-	7.92	8.64	11.52	254.64	.328	2.23	.574
Coconut	-	-	6.7	62.4	19.78	667.05	.0195	.364	2.55
Chillies	-	-	2.38	.936	4.726	36.86	.024	.056	.338
Fish	-	-	32.23	2.45	"	150.9	.083	.619	3.42
Meat	10	7.3	13.56	1.55	"	68.22	.0024	.114	.482
Brinjal	-	-	.197	.038	.966	8.85	.0068	.0083	.2415
Tapioca	-	-	.204	.006	11.63	47.88	.0135	.0117	.276
Green leaves	-	-	.635	.075	.865	7.08	.075	.017	3.21
Banana	-	-	.399	.045	10.92	44.28	.0006	.0135	.126
TOTAL			98.19	77.85	377.54	2697.32	.68	3.83	25.34

Central and North Travancore is even worse. The lack being protein, especially animal protein and fat and vitamins A and B1.

Krishnan[67] carried out a diet survey in Travancore and reported a condition similar to the above, but made the interesting observation from a study of 278 boys and 197 girls between the ages of 6 and 15, that in height and weight the children of Travancore were below the standard of other parts of South India.

During the course of this survey, certain striking facts were noted. It has been pointed out that it is in Central and North Travancore that the ulcer incidence is highest, yet the writer found in one hospital on the sea coast in Central Travancore that peptic ulcer was very rare among the fisher folk living by the sea, while the incidence was high among the field workers coming from inland. The local doctor was emphatic that while he continually had to give medical treatment to the inland villagers for peptic ulcer, he rarely saw a case among the fisher folk and only one case of duodenal ulcer among fishermen, proved by operation, is on the records. The fisher folk eat large quantities of small fish of the sardine type which they swallow whole. Thus they supply themselves with adequate amounts of protein, fat and vitamin A and D.

Another interesting contrast was found on the West coast south of Bombay, in a large surgical clinic at Vengurla where a wide range of surgical work is carried on by American surgeons, the percentage of peptic ulcer admissions was only 0.46% though the local diet was not unlike that found in some parts of South India. However, a study of the records showed that though the hospital was situated among Marathi Hindu villages 75% of the patients came from Goa in Portuguese territory. The incidence of peptic ulcer among the Goans was 0.16% while among the local Hindus, who consume a diet similar to that used in some parts of the Madras Presidency, the incidence was 1.4% of admissions. The Goans are a well-to-do community and can afford an expensive diet and furthermore being Roman Catholics, they are not restricted, as are the Hindus, from eating animal foods. They eat rice, meat, fish and eggs, milk and vegetables, both local and imported.

The small proportion of women patients in the Travancore figures for peptic ulcer (five per cent.), is not so surprising when one remembers that in most European clinics the ratio is eight-five men to fifteen women. The reason for this disparity of incidence among the sexes has been attributed to various factors. Much attention has been focused recently on the influence of the female sex

hormons on the control or prevention of peptic ulcer. Sanders noted that injections of Antuitrin S had a marked protective effect in resisting attempts to produce experimental ulcer and in speeding up the healing of ulcer. If there is anything in this point of view, the Indian women are protected by the same factors as keep the incidence low among European women. There are certain factors operating in India, however, which may help to reduce the susceptibility of the female to peptic ulcer. The woman of the coolie class spends much of her time in the home where she is preparing food and can eat small quantities of food at any time, while the man is out in the field all day working on a fasting stomach and then partakes of a large meal at night. Also in poor homes the women are reduced to eating the bran of the rice millings and drinking the rice water, while the men eat the milled or pounded rice. The women thereby derive a source of nutrition which is scorned by the men.

An interesting personal letter from Brazil reached the author from a surgeon who had read an account of peptic ulcer in South India by Somervell and Orr. He commented on the fact that in his district the incidence of ulcer was much higher than in other parts of Brazil. He commented on the close similarity between the diet of

Travancore and the diet of the country folk among whom he worked, which consisted in rice, tapioca, chillies, pepper, a very little meat and no fish. He said the ratio of duodenal to gastric ulcer was 6-1.

Rao[17] who has been quoted already in relation to his work on acidity curves in South India and the frequency of ulcer in Vizagapatam made two interesting studies. One was in relation to the deficiency of vitamin B in the etiology of peptic ulcer. He found that the bisulphite binding substances in the blood of peptic ulcer patients was increased in a large proportion of the cases showing a deficiency of vitamin B.

Secondly,[71] he made a study of vitamin C deficiency but came to the conclusion that it was not concerned in the etiology of the South Indian peptic ulcers.

Portnoy and Wilkinson[72] found a deficiency in vitamin C in ulcer cases which had lot blood but there was no evidence to show that the deficiency was the cause of the ulcer.

4) Comparison between Central and South India.

During the last year of his service in India the writer had an opportunity to observe the incidence of peptic ulcer from a new angle. He was stationed in the Deccan in a large hospital south of Poona. Here the incidence was 1.52% of admissions. The people were mostly Hindus

and agriculturists, as were the majority of the South Indians, but the staple articles of diet were a cereal grain called Bajra and another grain called Cholam. Both of these cereals have a high protein and fat content. Vitamin A is well represented in both and vitamin B1 in the Bajra. Meat was not used by the Hindus for religious reasons, milk and eggs were scarce but everyone had some source of animal protein and fat and green vegetables were available.

A comparison of the food values of the Travancorean staple diet and the grain used on the Deccan makes an interesting comparison. It may be said in general that on the Deccan the poorer people had a deficient diet but it was decidedly better than that available in Travancore. Ulcer is moderately common but is by no means as common as in Travancore.

REVIEW OF THE DECCAN ULCER.

176 cases were admitted for operation in a three year period 1936-8, 80% of the ulcers were duodenal.

The age and sex ratio were the same as in Travancore. 37.14% were in the farmer class and 23% were in the coolie class. The frequency was as already stated 1.52% of admissions as against 10% in Travancore.

Whereas in Travancore 0.16% were operated on for perforation, in the Deccan 14.3% had perforated before ad-

mission. The dense sclerosis and stenosis so often observed in Travancore was not seen. The ulcers were more acute looking and punched out, with no tendency to stenosis. Why there should be such difference in type between the two areas, is difficult to explain, but when the test-meal findings are discussed some light may be thrown on this aspect of the problem.

DISCUSSION.

This survey has made it abundantly clear that peptic ulcer is common in South India and rare in North India and that in South India the highest incidence is to be found in Central and North Travancore. Yet, in certain places peculiar local phenomena are to be found, in which two communities living side by side show entirely different degrees of peptic ulcer incidence, but these discrepancies can be accounted for by some marked difference in diet.

It has also been shown that the type of ulcer seen in South India differs to some extent from that seen in Western countries. It is more liable to stenosis and the formation of massive scar tissue which makes perforation an uncommon event. This peculiarity is only true of South India. The ulcers found in Central India conform

to the European standard.

McCARRISON'S RAT FEEDING EXPERIMENT.

One most illuminating experiment was carried out in 1927 by Sir Robert McCarrison in an endeavour to demonstrate the relationship between diet and ulcer incidence. Two groups of Albino rats were employed, eighteen in each group and the experiment continued 675 days. One group was fed on a diet similar to that used by the poorer class Travancorean and the other group was fed on the cheap Madrasi diet. The diets were cooked and prepared in the same way as by the people who use them. Stock rats fed on a diet similar to that used in the Punjab remained perfectly well throughout the period of the experiment and some hundreds were examined post-mortem: in none was ulcer or ulcer-like pathology found.

In the experimental groups, however, the rats rapidly lost weight and 35% of the Madras group developed lesions of the stomach and duodenum and 11.1% developed ulcer. 47% of the Travancore fed group developed gastric and duodenal lesions and 27.7% developed ulcers. In no case was ulcer found in the duodenum, they were all gastric ulcers, and in all the records of attempts to produce ulcer by experimental methods there is no mention of duodenal ulcer being produced in a rat, though they have been pro-

duced frequently in mice. This, it is said, is due to the fact that rats have no gall-bladder while mice have one. In the rats there is a continuous drip of bile into the duodenum, tending to buffer the action of the gastric juice, while in the mouse the bile is ejected at intervals. This may have some bearing on the explanation but the evidence is not very strong.

This experiment is not without support in the findings of other workers such as Magee and Anderson[142] who found that cavies fed on a diet deficient in vitamins A & D developed congestion, haemorrhage and degenerative changes in and around the pyloric region both on the duodenal and on the gastric side and Hoelzel and Da Costa[143] produced peptic ulcers in rats fed on a diet deficient in proteins and they found that ulcer did not appear so readily following vitamin A & B deficiency only, as when protein was withheld in addition.

Weech and Paige,[144] while experimenting on the production of edema by protein deficient diets, noted the tendency to ulcer formation in the experimental dogs. Pappenheimer and Larrimore also found that 86% of rate fed on a diet deficient in vitamin A and protein, developed ulcers but only 55% if vitamin only where deficient and protein adequate.

Other references to work along this line are given in the earlier section, dealing with modern work on peptic ulcer etiology and all go to show that there is a substantial amount of experimental evidence to support the conclusions of this clinical study that the underlying cause of the South Indian ulcers is the excess of carbohydrate and the deficiency of protein and fat in the diet, associated also with a vitamin deficiency.

INVESTIGATION OF THE EFFECTS OF THE SOUTH INDIA DIET ON THE HUMAN STOMACH.

The evidence being farily convincing that a diet deficient in protein and fat and containing an excess of carbohydrate is capable of producing peptic ulcer, the next step in the investigation was to discover the effect of this type of diet on the stomachs of those who habitually used it.

This part of the investigation was carried out by a study of :

1) Acidity curves found in so-called normal Travancoreans.
2) The movements of the stomach as seen by a Barium Meal examination.
3) The histological appearances.

1) Fractional Test Meals.

In order to ascertain whether the increased tendency to ulcer in the Travancorean was associated with an increased acidity curve, a series of fractional test meals were carried out on twenty-six apparently normal persons.

The test meals were carried out on young men who appeared to be healthy in every way. The subjects were asked to fast over night and the fasting juice drawn off early in the morning. A meal of rice gruel was then

given and samples were drawn off every fifteen minutes. Special note being made of excess of mucus, presence of bile and the time of emptying.

Six of the twenty-six persons showed hyperacidity curves. Nine had excess of mucus, indicating chronic gastritis. A composite curve of all the test meals was plotted on one chart, with normal European limits marked for comparison. The average Travancorean curve was well above the European standard of acidity, but no doubt the presence of mucus prevented the free acidity curve from being as high as might have been expected. A point of interest was that eighteen out of the twenty-six had no bile in the fasting juice and no bile in any of the succeeding samples. This suggested a failure of biliary regurgitation. PLATE III.

Later on, an opportunity presented itself to examine the natives of the Deccan in the same manner. As the incidence of ulcer is lower in this area than in South India it might have been expected that the acidity curves would have been lower. A series of twenty-seven persons were examined with the somewhat surprising finding that the average acidity was much higher than in Travancore. A free acidity peak of over a hundred was quite common. One perfectly comfortable man had a fasting juice of 64, a free acidity curve which rose to 135 and never came

below 57. A composite curve was plotted alongside the European range. PLATE III.

In no case was excess of mucus found in any sample, indicating that chronic gastritis is not common in the people of the Deccan who use cereal grains of high vitamin A content. It is interesting to note that chronic high acidity is not of itself synonymous with a high incidence of peptic ulcer. But if the stomach is free from chronic inflammatory change and an ulcer does develop its course will be more rapid and its tendency to perforate greater, than will be the case as in Travancore, where chronic gastritis and duodenitis accompany or precede the formation of an ulcer. The latter condition seems to give rise to an ulcer of the chronic stenosing type.

Other workers in other parts of India, have from time to time produced reports on test meal findings. In Vizagapatam in the north east of the Madras Presidency, M. N. Rao[73] made an examination of one hundred persons of the coolie class. He found that the fasting juice was on the average considerably higher than the European normal and average maximum acidity was 61 c.c.s. against the European standard of 47 c.c.s. These figures will be seen to compare closely to the Travancore figures and as this area is one in which ulcer is common, the similarity in test meal findings is interesting.

In Bengal Gupta carried out a similar study on forty-three persons, male and female. He found that achlorhydria was rare and that the average acidity is higher than in European countries. In Bengal the incidence of ulcer is moderately high though not so high as in South India. The people have a diet in which rice preponderates but other grains are available also.

made a study in the Punjab where, as has been pointed out, the ulcer incidence is extremely low. He found that the acidity levels corresponded to the European standards of normality.

DISCUSSION.

In the areas in India where the incidence of ulcer is high, the general tendency among the population is towards a higher acidity curve than is usually thought to be normal in European countries. In South India and Travancore the factor of chronic gastritis tends to prevent the excessive acidity curves seen in the Deccan. In the areas in which ulcer is not common acidity curves are within normal European limits.

5) Barium Meal Examinations.

Having examined the effect of diet on the secretions of the stomach, the next step was to investigate the effect on its motility, tonicity and sphincter control.

This was carried out by a series of Barium meals on normal subjects, living in Travancore, South India, the Deccan and Delhi in North India.

a) In the Travancore group twenty-four normal persons of the type likely to develop peptic ulcer and living in the district where the diet is tapioca and rice were examined by the flouroscope after partaking of a Barium meal. Though these people were supposed to be healthy individuals several admitted on careful questioning, that they were subject to a certain amount of abdominal discomfort and some were tender over the duodenum. They may, however, be taken as typical specimens of the Central Travancore agriculturist. Fourteen showed normal peristalsis and tone with normal relaxation of the pylorus and normal emptying time. Eleven showed spasm of the pylorus and pyloric antrum and hyperperistalsis.

Another group in South Travancore were examined on my behalf by the Radiologist of the Government Headquarters Hospital, Trivendrum. In this series of twenty-six patients, six had hypertonic stomachs and four of these had hyperperistalsis with pyloro-spasm and spasm of the pyloric antrum. In these six also there was evidence of duodenal hurry and the cap could not be visualised and there was slight tenderness over the duodenum.

b) Thirty-seven persons living on the rice diet of South India were examined. All but seven had stomachs of good tone placed high in the abdomen and all except three had normal peristalsis. These three had peristaltic waves of 5-6 per minute associated with pyloro-spasm and antral spasm.

c) A series of twenty-four normal persons were examined in the Deccan to compare the normal stomach of the Deccan with South India. It was found that the peristalsis rate and strength and muscle tone and sphincter activity corresponded closely to the European standard of normality. In one case only was there found to be antral spasm and irregular and overactive peristalsis.

d) An opportunity was provided by the Civil Surgeon, Delhi, to examine seventeen normal young men, mostly Punjabies in Delhi, where the incidence of ulcer is low. (0.2% of admissions.) The subjects were healthy ward boys and their diet consisted of milk, butter, ghee, cereal grain, meat and vegetables and was on the whole adequate and well balanced. No case of antral or pyloro-spasm was detected and while in nine the peristalsis was well marked, it was regular and slow, with never more than three waves per minute. Emptying was more rapid than in Travancore and South Indian stomachs, but the rate of emptying had no relation to the strength of the peristaltic movement. In some stomachs in which the

peristalsis was very shallow there was immediate passage of fluid barium through the pylorus indicating a relaxed condition.

DISCUSSION.

Of the eighty-six persons examined in Travancore and South India where the incidence of ulcer is high, it is significant that eighteen showed variation from the normal in the way of hyperperistalsis and pyloro-spasm. As the evidence of the test meal pointed to a condition of hypersecretion and failure of biliary regurgitation, it is not unreasonable to assume that a considerable proportion of the people of South India live in a state simulating Vagotonia. It is interesting to note that this state was more common among tapioca and rice eaters than among rice eaters. It is also noteworthy that in all cases women fell in the atonic group.

It is significant also, that a very high acidity curve was found in the Deccan, though the Barium meal did not indicate a condition of hypertonus. It suggests that high acidity of itself is not the prime factor in the pathogenesis of ulcer, but if a spastic and hypertonic condition is associated with high acidity the soil is prepared for the development of an ulcer.

PART VI.

PATHOLOGICAL STUDY.

The pathological changes occurring in the stomach and duodenum of individuals suffering from peptic ulcer and normal individuals have been studied in detail. Similar investigations have been carried out on animals fed on various types of deficient diet.

MATERIAL AND METHOD OF INVESTIGATION.

The clinical material for investigation was obtained from various Government and Mission Hospitals in South India. Much of this was obtained during laparotomy for peptic ulcer. Through the co-operation of Civil Surgeons in Travancore, Malabar, and North India, autopsy material for study was collected. The clinical and autopsy material may be divided into the following groups:-

A. Clinical material. - (i) During operations of gastrectomy for duodenal ulcer, a small piece of the stomach, at a distance from the ulcer, was removed in order to discover whether any variations from the normal were present in the mucosa and muscle of the stomach as a whole.

(ii) A portion of the stomach or duodenum proximal or distal to the pylorus was excised for histological investigation from patients subjected to laparotomy for suspected ulcer, but in whom no ulcer was found on operation.

B. Post-mortem material. - In order to provide a standard of comparison for changes found in the stomach at a distance from ulcers, an effort was made to collect post-mortem material from persons in South India dying a violent death, e.g. as a result of accident, hanging, or post-operative shock. Similar autopsy material was also collected in North India.

C. Experiments with rats. - Groups of young albino rats obtained from the healthy and well-fed stock of the Coonoor Laboratories were fed on the following diets:-

(i) A diet based largely on raw milled rice resembling in composition that consumed by human beings in certain parts of South India. - The composition of the diet, which is known in the Laboratories as the 'cheap Madrassi diet', was as follows:-

	Oz.	G.
Raw milled rice	21.00	596
Dhal arhar (Cajanus indicus)	0.70	20
Black gram (Phaseolus mungo)	0.70	20
Gingelly oil (Sesamum indicum)	0.10	3
Brinjal (Solanum melongena)	1.00	28
Amaranth (Amaranthus gangeticus)	0.50	14
Raw plantain (Musa paradisiaca)	0.50	14
Meat (Mutton)	0.06	1.7
Coco-nut	0.05	1.4

(ii) A diet consisting mainly of tapioca and rice, with various additions. - This diet in general resembles that consumed in the tapioca-producing areas of South India.

	Oz.	G.
Tapioca root (Manihot utilissima)	10.000	284.
Parboiled rice	10.000	284
Chillies (Capsicum annum)	0.125	3.5
Tamarind (Tamarindus indicus)	0.125	3.5
Raw Plantain	0.500	14
Brinjal	0.500	14
Coco-nut oil	0.250	7

The animals were killed after different periods of feeding on the above diets and pathological investigation of the stomach and duodenum carried out. The period of feeding before the animals were killed and examined varied from 8 to 18 months. Albino rats of roughly the same age from the stock served as controls. The latter received a good ration consisting of 'atta (whole wheat) chapatties' smeared with butter, fresh raw cabbage, fresh raw carrots, sprouted Bengal gram, cow's fresh raw milk, and meat, twice a week.

D. Experiments with dogs. - Seven dogs were kept in moderate confinement with regulated exercise and given a fairly well-balanced diet based on rice, meat, bread ad lib., and milk two ounces daily. These experiments were carried out in Miraj (S. India). Each dog was anaesthetized and, under suitable aseptic conditions, portions of the duodenum

and pyloric end of the stomach were removed to study the normal histology of these organs, and the gap closed by suturing. After a suitable interval to permit of recovery from the operation, the dogs were fed on an extremely deficient diet consisting mainly of tapioca. At the end of two and four months' feeding on this diet, the animals were subjected to laparotomy and biopsy as before. Pieces of stomach and duodenum were removed for pathological examination, the scars left by the previous sections being avoided.

The tissues so obtained were fixed in formol saline. Preparations for histological study were made in the usual manner, employing paraffin embedding and staining by Ehrich's acid haematoxylin and eosin. The rats were killed by air embolism and the organs removed and fixed immediately after death. The biopsy material from dogs and most of the human material was similarly fixed immediately after removal. During the later part of the investigation, preparations were made both from the animal and human specimens using a modified Nissl staining technique, in order to study the cytological changes in the ganglion cells of Auerbach's plexus.

DESCRIPTION OF FINDINGS.

A. (i) Sections obtained by biopsy from cases of peptic ulcer. Of the 39 stomachs re-sected, only four showed a normal mucosa. The mucous membrane in the remaining 35 specimens showed varying degrees of infiltration with plasma cells and lymphocytes. In the more advanced degrees of invasion, the normal mucosal glands were widely separated and reduced in number, the intervening spaces being crammed with round cells. In the deeper part of the mucosa, aggregation of lymphoid elements occurred to form follicles and, in some instances, the whole of the sub-mucosal space was one lymphoid area with aggregation into follicles at intervals.

The lymph follicles frequently showed abscess formation with spaces in the centre filled with necrotic cells. In some sections the follicles were seen to have ruptured and a cleft or erosion in the mucosa extended down to the crater of the follicle. PLATE VII

Round-celled infiltration of the muscle layers was present in some cases, but never to a severe degree.

Changes in Auerbach's plexus. The following description of the normal Auerbach's plexus is based on the author's observations and data contained in various text-books. The plexus is found in the fibrous septum between the longitudinal and circular layers of the muscular coat of

the gastro-intestinal tract and consists of numerous small ganglia, united by small bundles of nerve fibres, most of which are non-medullated. The nerve cells of the plexus vary much in size and shape and are grouped to form the ganglia. These ganglia are not easy to find in normal tissue. Each ganglion consists of three or four, or sometimes more, nerve cells surrounded by some endothelial cells or glial cells (Holsti, 1931). The nerve cells are larger than any other cells in the preparation; they are pear-shaped or oblong with one end of the oblong rounded. They contain a large, clear, spherical nucleus with well-formed nucleoli, usually solitary, and a 'pattern' of chromatin rods and dots. The nucleus is refractile and is generally centrally placed and surrounded by a well-marked membrane. PLATE IX FIG 9. PLATE XIII FIG 21 PLATE XIV FIG 25 PLATE XV

In sections stained by Nissl's method, finely dispersed Nissl granules are seen in the cell cytoplasm.

Some of the tissues received during the early part of the investigation could not be used for a study of the plexus, as these were not fixed and prepared in a manner suitable for the demonstration of changes in ganglion cells. Changes in the ganglion cells occur very early after death and only tissues which have been fixed immediately post-mortem provide reliable material for study. For satisfac-

tory examination, it is necessary to have tissues taken at operation or from animals killed by air embolism, and fixed immediately.

In 25 suitable specimens studied, the following points were noted:-

(1) In no case was a normal plexus observed, though isolated groups of normal cells were seen in several specimens.

(2) In most cases the plexus was enlarged, oedematous, and infiltrated with round cells and fibroblasts. The normal glial cells of the plexus were increased. Cellular infiltration of the plexus was, however, not a constant feature and was absent in some cases showing considerable degeneration of the ganglion cells. A thick capsule was sometimes observed around the degenerated plexus.

The ganglia of Auerbach's plexus were easily recognised in the sections, due to the general swelling of the plexus or atrophy of the ganglion cells. In the normal section recognition was more difficult.

Varying degrees of degenerative changes were found in the ganglion cells. Such differences in degree were often present on the same specimen or sometimes in the same ganglion. The changes varied from cloudy swelling (chromatolysis) to complete degeneration of the cell.

The cells were often swollen, the cell outlines

indistinct or uneven, and the cytoplasm homogeneous. In sections stained by Nissl's method, the cytoplasm was stained an even blue colour devoid of granules. The nuclei were swollen and did not stain well; in some instances, they were distorted and showed a defective nuclear membrane. In some cells the nuclei were shrunken, eccentric in position, and granular in appearance; the nucleoli were indistinct with the Nissl granules collected round the nucleus. In others the nucleoli were fragmented or absent.

A more advanced degree of degeneration was present in some cells. The cells were smaller than normal, vacuolated, and shrunken; the nuclei were pyknotic, pushed to one side of the cell or partly extruded, and appeared elongated and flattened. Some cells showed complete disintegration of chromatin and disappearance of the nucleus and only skeletons of dead or degenerated cells were observed. In the more advanced cases, the ganglion cells had completely disappeared, leaving empty spaces in the ganglion which appeared as a large syncytial mass infiltrated with round cells and fibroblasts.

The number of ganglion cells involved in the degenerative process and their distribution in the plexus varied considerably in the several specimens. In some ganglia, normal cells were seen alongside degenerated cells,

showing that the changes observed were not due to defects in histological technique. Groups of ganglion cells have disappeared in some specimens, while in some advanced cases marked changes were found in a large number of cells of the plexus. PLATES X. XI.

(ii) Biopsy material from cases with symptoms of ulcer, but no demonstrable ulcer at operation. - Cases have been encountered from time to time which give a history very like that of peptic ulcer, in which no ulcer is demonstrated by X-ray examination. The duodenal cap, however, is found to fill with difficulty as a result of pyloro-spasm preventing the stomach contents from passing freely into the duodenum. When the duodenal cap does fill, it presents an irregular outline and empties rapidly and is tender on pressure. This condition is labelled as 'irritable duodenum' by the radiologist and is frequently associated with powerful and rapid peristalsis of the antrum. It has been described by Garry[12] (1937) and Friedenwald and Feldman[13] (1934).

In spite of an indefinite X-ray report, the symptoms and signs simulated ulcer so closely in 10 patients that finally a laparotomy was undertaken. No ulcer was found but a small portion of the duodenum or the antrum proximal to the pylorus was removed for histological study.

In all 10 specimens, the mucosa, particularly the superficial part, was infiltrated with lymphocytes. In six cases, aggregations of lymphoid elements to form follicles were found and some of the follicles showed evidence of bursting on to the surface of the mucosa. Occasionally, an erosion of the surface mucosa led down to an erupted follicle. PLATE VII FIGS. 5 & 6.

Changes in Auerbach's plexus identical with those described in the previous section were also found in this group. In only one specimen in this series were there found normal ganglion cells in large numbers; even in this specimen, groups of cells in the earlier stages of degeneration were found and the invasion by round cells and swelling of the ganglia betrayed commencing degenerative changes. PLATE IX FIG 16.

B. Post-mortem material from persons in South and North India with no history of ulcer. - Fresh post-mortem material is exceedingly difficult to obtain in India owing to the religious and social customs of the people. Eight good specimens (stomach and duodenum) were obtained, however, in South India, the subjects being criminals after execution or persons dying in hospitals from the effects of violence or post-operative shock.

As none of the above material was especially collected and preserved with a view to showing the nerve plexus in good condition, changes in the ganglion cells could not be studied in six cases, as the possibility of post-mortem degeneration could not be excluded. In two cases, however, in which a post-mortem examination was carried out very soon after death, specimens suitable for this purpose were obtained.

As in the previous groups, all the sections showed round-celled infiltration of the mucosa and one showed hyperplasia of lymphoid follicles similar to that seen in the definitely pathological cases. PLATE VIII

The two specimens in which Auerbach's plexus was investigated are of special interest. Both were taken from the stomachs of persons who died under an anaesthetic from an operation for a condition in no way related to the gastro-intestinal tract. Both showed early degeneration of the ganglion cells of Auerbach's plexus. Only one showed any marked degree of lymphocytic infiltration of the mucosa. PLATE XII

Seven specimens were collected from post-mortem examinations made shortly after death in North India. These showed a normal healthy mucosa. No lymphoid follicles were observed and no evidences of inflammation were present in the mucous membrane. In two specimens in which Auerbach's plexus was demonstrated it appeared to be normal.

C. The stomach and duodenum of rats fed on the 'cheap Madrassi diet' and the 'tapioca diet'. - The rats were weighed at weekly intervals. The animals failed to grow satisfactorily and lost weight in the later part of the experiment. Those that had any coincident disease were rejected as not being suitable for a study of the nerve cells.

The following observations were made:-

1. None of the animals showed ulcer of the stomach or duodenum.

2. Inflammatory changes in the mucosa of the stomach or duodenum were slight or absent in the rats fed on the deficient diets for less than six months. Mild inflammatory changes such as round-celled infiltration of the mucosa were found occasionally in the animals fed on the diets for a year or more. Aggregation of the lymphoid cells to form follicles were present only in rare instances.

3. Degenerative changes in Auerbach's plexus were progressive and could be definitely demonstrated even in rats fed on the deficient diets for a few months only. In general, rats, fed on the 'tapioca diet', showed the changes earlier than the animals fed on the 'cheap Madrassi diet'. In both groups the degenerative changes in the plexus were roughly proportional to the period of deficient feeding. These changes are similar to those found in human cases of ulcer. Hyperplasia of glial cells and infiltration of the

ganglia by round cells and fibroblasts were, however, rarely present.

In well-fed stock animals the nerve cells of the plexus appeared in groups of three to five cells, with large clear nuclei and well-marked nucleoli and nuclear membrane. Pyknosis of the nucleus or other evidences of degeneration were, however, occasionally found. The cell bodies could be demonstrated in most instances even by the ordinary staining methods. Few glial cells were present in the ganglia, but no fibroblasts were seen. On the whole the differences in the appearance of the plexus in the well-fed and deficiently fed groups were striking. PLATES XV, XVI, XVII & XVIII.

D. Experimental material from dogs fed on a fairly well-balanced diet followed by a 'tapioca diet'. -

In the specimens of the stomach and duodenum removed before the tapioca diet was given, a healthy mucosa was seen. In one case, however, slight round-cell infiltration of the gastric mucosa, suggestive of early gastritis, was present. Auerbach's plexus appeared normal and closely resembled the plexus in the normal human stomach and duodenum. The ganglion cells were accompanied by few glial cells and there was little or no infiltration by lymphocytes, plasma cells, or fibroblasts. In the normal plexus, an occasional pyknotic or degenerative form was

seen but the great majority of the cells conformed to the normal as described in the preceding sections.

All the dogs fed on the tapioca diet lost weight and appetite. Two animals developed ascites and two finally died of intussusception. At the end of four months of deficient feeding, the animals which survived were emaciated and ill and hence allowed to die under the anaesthesia after biopsy.

None of the dogs developed ulcer of the stomach or duodenum.

Examination of the specimens removed at the end of two and four months respectively, showed definite changes in the plexus. The ganglion cells were pyknotic or degenerative; there was a great increase in the fibrous tissue and the plexus was surrounded by a capsule. Marked infiltration of the ganglia by round cells was observed and the condition of the plexus became similar to that found in human cases of ulcer. PLATE XII FIG 20 PLATE XIII & XIV

While the plexus changes were definite and constant, the changes in the mucosa were varied in degree. A tendency to increased round-celled infiltration and hyperplasia of lymph follicles was noted but the marked gastritis and duodenitis of the human ulcer cases were not observed. PLATE XII FIG 19

The changes in the plexus and the mucosa lesions were not parallel as regards time of appearance and intensity. The former, in general, appeared earlier; in some specimens, which showed marked plexus degeneration, no noteworthy changes in the mucosa could be discovered. In one case, already referred to, the first or 'healthy' section showed early gastritis but the ganglion cells were normal. The plexus changes are thus not the direct result of a gastritis or duodenitis, but may precede such conditions.

Plates II to VII illustrate the changes described in the preceding sections. Figs. 1 to 14 show changes in the mucous membrane and plexus in human cases. Figs. 17, and 21 to 23 illustrate the normal appearance of the plexus in dogs and rats respectively.

DISCUSSION.

Definite pathological changes were found in the mucosa and the intra-mural nerve plexus of the stomach and duodenum at a considerable distance from the peptic ulcer. The lesions of the mucosa - round-celled infiltration and an increase in the size and frequency of lymphoid follicles — are characteristic of chronic gastritis or duodenitis and may be either the precursor, the accompaniment, or the result of ulcer formation. The presence of similar changes in specimens from individuals complaining of symptoms sug-

gestive of ulcer, but in whom no ulcer crater could be demonstrated by X-rays or at operation, suggests that the chronic inflammatory condition precedes ulcer. This view is supported by the fact that many persons who suffer from typical ulcer symptoms and are operated on without any ulcer being found, undergo a second operation a year or more later, a typical ulcer having developed in the interval.

It is, however, important to note that similar appearances were observed in post-mortem material obtained from individuals in South India not complaining of symptoms referable to gastro-duodenal lesions. This suggests that such changes occur widely in the general population and that per se they do not necessarily give rise to peptic ulcer.

Duodenitis and gastritis, with similar histological appearances to those observed by us in the human cases, have been described by several workers (Faber,[108] 1927, 1935; Johnston,[107] 1934; Friedenwald and Feldman, loc cit.; Fitzgerald,[110] 1931; Wellbrock,[106] 1930; Judd and Nagel,[105] 1927; Kellogg,[107] 1933; Konjetzny,[104] 1923; and others). (Smith[102] 1902-3) records that he found on many occasions, when ulcer was suspected, no ulcer but only small erosions. Microscopically, these were follicular abscesses which ruptured and

were thought to be the beginning of ulcers. Simonds (1938) described the mode of origin of experimental gastric ulcer induced by cinchophen. The following sequence is interesting when compared with our findings:-

1. OEdema of single or multiple villi.
2. Diffuse infiltration of villi with plasma cells and lymphocytes.
3. Superficial erosions.
4. Focal accumulation of polymorphs in the villi, just above the muscularis mucosae often accompanied by liquefactive necrosis.
5. Narrow fistula-like channels extending from such foci to the surface.
6. Large deep ulcers.

The superficial mucosal erosions formed by the breaking down of one or more of the lymphoid follicles, tend to heal rapidly and may not leave a trace. Conceivably a number of such follicles rupturing close together might coalesce into an ulcer which would become chronic on account of its size and the continued action of forcibly ejected highly acid gastric juice. One reason why ulcer is confined largely to the pyloric antrum and duodenum may be the greater accumulation of lymphoid elements in these regions and the possibility of multiple follicular abscesses

coalsecing to form one large ulcer. Miller[40] (1906) has given a closely similar description of the early phases of a peptic ulcer.

The pathological changes found in the Auerbach's plexus are interesting in relation to the neurogenic theory of the genesis of peptic ulcer. Most of the animals fed on the deficient diets showed degenerative changes in the ganglion cells before any mucosal infiltration was noticed. From a study of serial sections in animals killed after various periods of deficient feeding, it was evident that the earlier pathological lesions in the nerve cells were degenerative; in the later stages, however, the plexus shared with the mucosa the general inflammatory change. The lesions of Auerbach's plexus reported here closely resemble those described by Stöhr[93] (1932) in stomachs resected for ulcer.

The significance of changes in Auerbach's plexus in relation to peptic ulcer is obscure, as the exact function of the plexus is not clearly understood. It is generally agreed that the plexuses of Auerbach and Meissner act as local nerve centres for the gastro-intestinal tract. Alvarez (1928, 1929) believes that the centre of control of muscle movement and secretion lies in the muscle wall itself and the complicated impulses of the vagus and sympathetic are co-ordinated in Auerbach's plexus. Possibly

degeneration of the plexus may lead to spasm, hypersecretion, and abnormality in function of the delicate mechanism of the pyloric antrum and pylorus. Evidence in support of this hypothesis has been brought forward by several workers who have studied cardio-spasm and Hirschsprung's disease. Etzel[114] (1937) investigated cases of cardio-spasm occurring among the poorer people of Brazil and described changes in Auerbach's plexus in the oesophagus, closely similar to those observed in this study. Robertson and Kernohan[115] (1938) reported similar changes in the myenteric plexus in Hirschsprung's disease.

McCarrison (1921) found degenerative changes in the myenteric plexus in animals (monkeys and pigeons) fed on deficient diets. These changes were frequently associated with motor inbalance spasm, and intussusception. The fact that two dogs fed on the 'tapioca diet' died of intussusception is of interest in connection with the above findings. Similar observations were also made by Magee, Anderson and McCallum (1929) with cavies fed on deficient diets.

The frequency of intussusception in adults in Travancore was pointed out by Orr[116] (1932) and it was suggested then that an overaction of the vagus might be the cause, but at that time possible changes in the bowel wall had not been considered.

In this connection, mention may be made of the theory which associates peptic ulcer in Europeans with nervous strain and anxiety, leading to hyperperistalsis, pylorospasm, and hypersecretion.

It has been shown that degenerative changes in the plexus occur in cases of peptic ulcer and also in cases likely to develop ulcer at a later stage. Chronic inflammation of the mucosa accompanies or follows these lesions. Such inflammatory changes have been observed in individuals living on rice or tapioca diets, not suspected of gastroduodenal lesions. In rats and dogs fed on ill-balanced rice or tapioca diets, similar changes in the plexus and less marked changes in the mucosa of the stomach and duodenum have been noted. In the North Indian specimens examined, inflammatory changes in the mucosa, which in the other clinical and experimental specimens were found in combination with plexus degeneration, were not present.

CONCLUSIONS.

From the clinical information gathered in different parts of India, associated with the histological findings in human beings and experimental animals, the final conclusion as to the etiological factors at work and the mode of development of chronic duodenal ulcer in South India

is as follows:-

The South Indian diet, being deficient in protein and animal fat and also in Vitamin A & B, leads to a condition simulating, but not identical with the vagotonic diathesis. These changes are associated with hypersecretion and muscular inbalance or spasm. This inbalanced condition is common in large numbers of people in South India.

Furthermore, the rough irritating nature of much of the food and the septic condition of the gums of a large proportion of the poorer classes, leads to a condition of chronic gastritis and duodenitis.

Neither of these two conditions, inbalance of motor function and hypersecretion on the one hand and chronic gastritis and duodenitis on the other, cause ulcer per se, but the continued effect of a hypermotile spastic and hyperacid stomach on the follicular ulcers of gastritis and duodenitis is to prevent healing and to favour the development of chronic ulcer.

The history of a typical South Indian duodenal ulcer is:-

1) Deficiency in diet leads to degenerative changes in the plexuses of Auerbach and Meissner.
2) This degeneration leads to inbalance in the motor and secretory activities of the stomach resulting in hypersecretion, hyperperistalsis and pylorospasm.

3) The irritating nature of the food plus the infection from pyorrhoea alveolaris and the lowered resistance to infection resulting from the vitamin A deficiency, bring about a round-celled infiltration of the mucosa of the stomach and duodenum, with hypertrophy of lymph follicles.

4) Liquefactive necrosis of the follicles results in their rupture on to the surface forming minute ulcers.

5) These microscopic ulcers coalesce.

6) Healing is prevented on account of the continued trauma of highly acid gastric juice forcibly ejected through a spastic pylorus.

7) The ulcer becomes chronic.

PART VII

THE TREATMENT OF DUODENAL ULCER.

In a surgical thesis it is scarcely necessary to go into details concerning medical treatment and the following section will be confined to the surgical aspects of the case. This does not mean that the author depreciates medical treatment, on the contrary he feels that a full course of medical treatment should be given a trial before surgery is undertaken, but as he has nothing original to contribute to the subject, time and space will not be wasted by reiterating what has been so well said by Hurst and others.

Reference has already been made in the Historical Section to the history of surgical treatment. The early attempts at short circuiting and resection have been recorded and an attempt will now be made to the present position and place of surgical procedures in the treatment of duodenal ulcers with special reference to the experience of the writer in India.

In spite of cunningly devised plastic operations and resections, the majority of surgeons still employ modifications of the posterior gastro-enterostomy operation for duodenal ulcer and some form of resection for gastric ulcer.

The value of gastro-enterostomy is most apparent when some degree of stenosis is present and the value of the operation seems to depend on the rapid emptying of the stomach and the rest afforded the ulcer and to a lowering of the acidity due to biliary regurgitation. Lindsay and Evans[177] examined by the Ewald test meal a series of sixty cases, before and fourteen days after operation and again six months to eight years afterwards. They found that the initial reduction of acid was not maintained in more than 42% of the cases and they noted that many of the cures were cases in which a high acidity persisted after the operation. This is not in agreement with the majority of writers such as Lewishon and Gunzberg[176] who noted that if acid persisted at a high level after a posterior gastro-enterostomy the patient was likely to have trouble later and they state that in only 3% of cases is the acid permanently reduced by a gastro-enterostomy.

The incidence of gastro-jejunal ulcer, following the operation has been variously estimated by different writers. Luff[27] reporting a follow-up of 2609 cases places it at 2.8%. Walton records 1.69%,[178] while Hinton[179] places the incidence as high as 16.4%.

Wright[180] of Manchester reviewed a large series of cases and found that when posterior gastro-enterostomy had been performed for duodenal ulcer 4.04% developed gastro-

jejunal ulcer as proved by operation and 4.45% suffered from symptoms suggestive of an anastomotic ulcer. In 507 cases of posterior gastro-enterostomy for gastric ulcer 5.32% developed anastomotic ulcers and 5.13 were suspected.

The wide disparity in the figures of different surgeons is due probably, not so much to differences in technique as to selection of cases. Those who publish a comparatively low rate of gastro-jejunal ulcer incidence scrupulously avoid the gastro-enterostomy operation in cases with high transverse rapidly emptying stomachs with high acid curves and confine the use of the operation to cases where there is definite stenosis and the acidity is not high.

In the joint series of cases published by the writer in collaboration with Mr. Howard Somervell, 2,500 cases of duodenal ulcer operated on in the ten year period 1927-1936, 3% developed gastro-jejunal ulcer, proved by operation. This rather high figure may be accounted for by the fact that most of the cases, for economic reasons, returned to the unsuitable diet of the country.

From this series of cases much has been learned concerning the technique of the operation and ways of preventing the complications early and late which are apt to occur.

Early Complications.

Acute dilatation of the stomach

Regurgitant vomiting.

Post-operative haemorrhage.

Lung complications.

Acute dilatation of the Stomach.

This has rarely been seen in this series of cases and has never been allowed to develop to a dangerous degree. A stomach tube is always passed on any patient showing a sudden rise in pulse rate. If no haemorrhage is demonstrated, the patient is turned on his face for some time with the stomach tube in position. This has never failed to relieve the condition.

Regurgitant vomiting.

The so-called "no loop anastomosis" is a theoretical rather than a practical consideration. Some length of jejunum must exist between the duodeno-jejunal junction and the anastomosis if the stomach is to be allowed freedom to move during the process of digestion. Considerable change can be seen during a barium meal in the position of a stomach practically empty and the patient in the recumbent position and a full stomach with the patient erect. An anastomosis which anchors the stomach to the posterior abdominal wall will cause kinking and bring about the very

complication that the "no loop anastomosis" is designed to avoid.

The writer has found that a vertical stoma directly under the cardiac orifice with its lower end almost at the greater curvature of the stomach is the most suitable. About two inches of jejunum are allowed between the duodenum jejunal junction and the anastomosis. This gives sufficient free play and yet is not long enough to form a loop which might get kinked. Since this stoma was adopted nine years ago, there have been only two cases in the writer's series requiring re-operation for regurgitant vomiting and both these cases were complicated by some other condition and were in no way connected with the functioning of the stoma or proximal loop. One case was an Indian who succeeded in evading the vigilance of his nurses and consumed a vast meal of rice on the fourth day after the operation. The result was no doubt an oedema of the suture line due to excessive straining. The second case was a European lady who suffered from diverticulitis of the transverse colon in addition to an ulcer, and the inflamed colon became adherent to the efferent loop eight inches below the stoma and obstructed it. Occasionally a patient vomits bile in the first forty-eight hours, but stomach lavage never fails to bring about relief of the condition

The mere fact of entrance of bile into a stomach which has been deprived of bile for several years due to stenosis, may irritate the organ and cause vomiting till tolerance is established. An acid mixture sometimes acts like a charm in these cases.

Post-operative Haemorrhage.

This complication has also been almost non-existant in the writer's last five hundred cases. The points in technique which prevent this complication are:- 1) Ligature of any large vessel seen to be running into the suture line. 2) The adoption throughout of through and through continuous sutures. The writer does not employ Connell's inverting suture in this operation, because it gives a less efficient control of the bleeding from the cut edge.

When haemorrhage has occurred on account of failure to take the above precautions, it has been successfully treated by washing out the stomach with soda bicarbonate and when the washing contains no old blood running in 60m of adrenalin 1-1000. This runs on to the suture line and relieves congestion and lessens bleeding. Only two fatal cases of post-operative bleeding are recorded in this series and they occurred in the early cases and

were due to failure to observe the above technique.

Lung Complications.

The majority of the patients earlier in this series, were operated on under chloroform and ether inhalation anaestheia and as the teeth were often infected, lung complications were frequent, and accounted for most of the fatalities. The introduction of spinal anaesthesia was expected to lower the incidence of this complication but did not do so. The temporary paralysis of the lower intercostal muscles and the less effective aeration of the lung in the three hours following operation, possibly accounted for this disappointment. In the last fifty operations gas and oxygen anaesthesia with avertin, premedication has greatly reduced the liability of the patient to post-operative bronchitis and pneumonia, particularly if CO_2 and O are administered at the close of the operation. In cases with chronic bronchitis, who would obviously be bad risks for inhalation anaesthesia, local block anaesthesia has given good results and though in most cases the bronchitis was troublesome for a few days, no fatal cases have been recorded. The use of M & B 693 has certainly lowered the mortality, though it is not well tolerated by gastric cases and often gives rise to vomiting. On the whole, it might

be said that a quick operation & light handling of the viscera, contribute as much as good anaesthesia and medication to the prevention of serious lung complication.

Late complications.

Stoma ulcer.

Intussception of small intestine through the anastomosis.

Adhesions causing obstruction.

Recurrence of pain and non-healing of the original ulcer.

Stoma Ulcer.

This subject will be discussed in detail in a later section but some technical considerations may be discussed here. The use of clamps have been blamed for this complication, so also have the use of inabsorbable sutures, but still most surgeons use clamps and a few still use silk sutures. Experiments on dogs showed that trauma by crushing with clamps played but a small part in the causation of ulcer. The writer uses Somervell[1]'s clamp, which is so designed that there is equal pressure along the entire length of the segment of bowel within the grasp of the clamp. This avoids pinching the ends of the stoma which is liable to occur with the ordinary type of clamp.

Several cases of anastomotic ulcer seen by the writer, had portions of unabsorbed silk suture in the anastomosis and one at least healed rapidly after the silk had been removed, without any other treatment.

The most important point in technique in the writer's opinion is the accurate apposition of the mucus membrane, so that no gaps occur through which highly acid gastric juice can get at the cut edge of the muscle coats. The posterior suture line is a through and through running suture which draws the mucus membrane neatly over the muscle but the returning or anterior part of the running suture is more difficult to apply. If Connel's suture is adopted the mucus membrane is inverted into the lumen of the gut but it does not necessarily cover the cut edges of muscle. The illustration shows this clearly. In the writer's technique the suture is passed on a large curved needle which passes through the sero-muscular coat of the stomach a sixth of an inch from the cut edge, but is so directed that its point traverses the stomach mucosa near its edge. The needle point passes to the edge of the mucosa of the opposite side and the tip of the needle carries this edge within the lumen of the gut and then pierces the muscle coats and serosa of the jejunum, a sixth of an inch from its cut edge. The result is that the mucosal edges lie in close apposition inside the lumen of the bowel and

the junction of the mucosa is not opposite the junction of the muscle coat. This prevents any part of the cut edge of the muscle coats coming into contact with the gastric juice. This is easier to demonstrate than to describe but the drawing illustrates the point. PLATE V

An additional point in suture technique is possibly more of theoretical than practical interest but it aims at avoiding any suture running between the cut edges from within out. Such sutures are potential drains which might provide a track for infective material from within the lumen to find its way into the muscle layers. In the technique here described, the knots are tied outside the lumen and on the serous surface and the suture is led into the lumen through all the coats of the bowel wall and never passes between the cut edges. When the returning continuous suture comes to be tied off it is tied to the free end which lies outside on the serous surface. PLATE V

Trimming of redundant edges of mucosa is also to be depreciated as tending to predispose to leakage and post-operative bleeding. The stomach is provided with a lax and redundant mucosa in order to allow for expansion and contraction. If the redundant mucosa is trimmed flush with the cut edges of muscle, when the stomach dilates, as it may do within a few hours of the operation, the mucosa

retracts and may even tear out of the suture line. This may result in bleeding and actually did so in several cases where the writer adopted this procedure. Even if no bleeding results, there is serious danger that the retraction of the mucosa will leave the cut edges of the stomach and jejunum exposed with the associated risk of anastomotic ulcer.

Intussception of the small intestine through the anastomosis.

Only one such case is recorded in this series and was relieved by operation. No explanation for it can be given except that intussception of small intestine upon itself is by no means uncommon in South India in adults and this may have been a case of this type.

No case of herniation of the intestine through the rent in the mesocolon has been recorded. Such a complication is obviously the result of imperfect suture of this rent to the stomach.

Adhesions causing obstruction.

These have been rare and one case is described in the paragraph dealing with regurgitant vomiting.

Recurrence of pains and non-healing of the original ulcer.

This has occurred in 5% of the followed up cases and has followed operation on small early ulcers in which there was no evidence of stenosis. The food which was of an irritating nature, continued to pass over the ulcer and prevented healing. A resection of the pyloric antrum and if practicable the ulcer itself has given very striking relief from symptoms. By this procedure the operation is converted into a Bilroth II. A system of one-way traffic is introduced and the ulcer if not resected is allowed to heal. Out of sixty-three cases of this order one eventually developed gastro-jejunal ulcer. It was found that the excision of the antrum did not lower the general level of acidity to any great extent, though it abolished the hormonal phase of gastric secretion.

REVIEW OF POST-OPERATIVE RESULTS OF SOUTH INDIAN GASTRO-ENTEROSTOMY OPERATIONS.

In a country district in India where the patiets come from small villages often two hundred miles from the surgical centre, follow-up work is extremely difficult. Post-cards and letters are rarely answered and accurate information is most difficult to obtain, concerning the well-being of post-operative cases.

At great labour and expenditure of time, it was possible to visit centres in different parts of Travancore

and South India. Notice was given in the local papers, with a request that post-operative cases should report themselves. 635 persons reported and were examined. 210 persons were classified according to the time elapsed since their operation, but as no useful information was obtained by this classification, the remainder were classified only as regards the result of the operation.

The following table illustrates the findings:-

Length of time after operation.	Excellent result.	Good result.	Some pain ? duodenal	Incapacitated by pain	TOTAL
5-10 years	19	7	5	1	32
2- 5 "	44	3	14	6	67
1- 2 "	24	5	6	2	37
Under 1 year	24	5	15	10	54
Unclassified	345	42	30	28	445
Totals	456	62	70	47	635
Percentages	71.5	10	11	7.5	100

From this it is seen that 81.5% showed good results, leaving a rather high proportion in whom the results were bad. It is interesting to notice, there was a higher percentage of poor results in patients with a post-operative history of less than a year and suggests that these cases tend to settle down eventually. It must also be

remembered that many of the cases were quite unable, for economic reasons, to follow up a suitable post-operative diet and went back to the tapioca and rice diet. The bad results were among cases with high acidity and rapidly emptying stomachs and the proportion was sufficiently high to cause the operators some disquiet and urge them to seek ways and means of dealing with the 18.5% who are, by reason of their high acidity and economic environment, unsuitable for the gastro-enterostomy operation.

A second follow-up was employed in another district employing test meal examinations in order to determine to what extent the operation of posterior-gastro-enterostomy lowered the gastric acidity. Forty-four cases were examined. Thirty-seven were in good health and the result could be classed as excellent. In seven there was some complaint. One had pain as bad as he had before operation. Two had pain which was troublesome, but did not incapacitate them and four had slight pain related to food but were much relieved by the operation.

An interesting feature of the test meal study of these cases was that in no case was there achlorhydria. In two there was a low normal acidity, twenty-four had normal free acid curves. Eleven had hyperacidity curves. The seven unsatisfactory cases were among this group. Another interesting thing about the cases in which the results were poor was that the fasting juice was of high

acidity. In some cases it was 50-60 c.c. $\frac{10}{N}$NaOH. and never less than 30 ccs. As will be brought out later, the view of the writer is that a high fasting juice or a high night secretion is a more serious matter from the point of view of recurrence, than a steeply mounting peak when the stomach is full, falling again to normal as the stomach empties. In the majority of the successful cases a marked drop was present at the end of one and a half hours, but in the unsatisfactory cases the curve was still rising at the end of two hours when all food must have completely left the stomach. These findings the writer feels to be most important, suggesting as they do the importance of the vagal aspects of gastric secretion which maintain a high constant secretion stimulated by psychic factors. This he feels ought to be taken more into consideration, in estimating the fitness of patients for the gastro-enterostomy operation, than the hormonal secretory curve.

The writer has come to believe that the stomach may vary enormously in different individuals in tone peristaltic activity and secretory curve and that certain persons create a problem for the physician and surgeon alike. They are the people with what Hurst calls the ulcer diathesis. Even with the greatest care in medical treatment the ulcer tends to recur and if surgery is employed the

results will be disappointing to say the least of it and may be tragic.

The type of case in which poor results follow surgery is the one with hyperperistalsis, hypersecretion and pylorospasm. It is in such persons that gastro-jejunal ulcers arise and most of the poor results in the above follow-up series have belonged to this class.

There are four phases of gastric secretion: a) the continuous secretion which goes on day and night independent of food and is of vagal origin. b) the psychic phase which is also vagal and depends on stimulation from the senses of taste and smell c) the hormonal or chemical phase, which depends on stimulation of the pyloric antrum by food, resulting in the formation of a hormone which acts on the cells of the fundus, causing them to pour out acid secretion.

d) A late phase which is also hormonal and results from stimulation of the small intestine.

These phases vary in importance in different people and an operation designed to abolish the hormonal phase of secretion may fail because the vagal sources of acid secretion are the most important for these particular people and remain unaffected by the operation.

Numerous methods have been devised to lower the gastric secretions in peptic ulcer cases and depend more or

less on a radical resection of the acid secreting parts of the stomach and these operations fall into two main groups:- Fundesectomy and gastrectomy.

Fundesectomy operations.

These have been carried out mainly on experimental animals with somewhat disappointing results. They aim at removing a sufficient area of the acid secreting portion of the stomach to bring about a permanent lowering of the acidity. Connell[102] carried out this operation in human beings for peptic ulcer but did not publish a follow-up record. He quotes seven cases so treated. One died, all the others became symptom free but he does not go into the question of post-operation test meals. Seely and Zollinger[103] showed that the greatest concentrations of acid secreting cells lay in the greater curvature and fundus of the stomach. They carried out radical fundesectomy which resulted in a big drop in acidity immediately but with a tendency to rise again after some months and they finally came to the conclusion that the operation was of no value. Watson[104] has contributed a scientific study of the subject. He made duodenal and gastric fistulas according to the technique of Mann and Bolman and showed that by radical fundesectomy, a diminished acid reaction to meat and hista-

miner[illegible] resulted. This only happened after extensive resections and the acid curve tended to return to normal later.

Such operations therefor have met with little or no favour with the general body of surgeons.

Gastrectomy.

The rationale of the gastrectomy operation.

The expected effect of the gastrectomy operation is to lower the gastric acidity curve to a greater or less degree and to provide a system of one-way traffic so that no food passes over the ulcer. It provides for quicker emptying and free regurgitation of bile and if the ulcer is in a position suitable for resection, it permits complete removal of the ulcer. All observers agree that acidity is lowered by gastrectomy and most agree with Lewisohn and Gunzberg[176], that if achlorhydria can be achieved, recurrences or stomal ulcers never occur. Where a divergence of view occurs, is in estimating the degree of effectiveness of the operation in achieving this result. In an early publication on the subject Lake[185] asserted that achlorhydria followed the removal of the pyloric half of the stomach. From his later publications it is evident that he agrees with most observers that it is only in a small proportion

of cases that this limited operation achieves the desired result. Priestly and Mann[67] carried out extensive experiments to throw light on this matter. They found that division of the prepyloric sphincter produced slight lowering of the acidity and later removal of the antrum did not bring about any further drop in the acid curve.
Where a greater decrease was achieved, it was shown that more than the antrum had been removed and an appreciable segment of the body of the stomach had been resected as well. Further lowering of acidity they attributed to freer regurgitation of the duodenal secretions, quicker emptying of the stomach and (a point of great importance) food reaching the upper intestine in a less digested state and thereby failing to stimulate the intestinal phase of gastric secretion as well as fully digested food would do. They come to the conclusion that the pars pylorica plays but a minor part in the control of gastric secretion.

It is disconcerting to find that an operation which brings about a completely desirable result in one patient may be only partially successful in another and may fail entirely in a third. The author of this Thesis holds strongly and will bring forward reasons to support his contention at a later stage, that as several factors both hormonal and vagal act in stimulating the gastric se-

cretory curve and as some of these factors may predominate in one case and others in another, a routine operation cannot be expected to bring about uniform results in a series of cases. He believes that the hormonal or chemical phase of secretion is comparatively unimportant in relation to recurrent or stomal ulceration, as this curve only rises when food is in the stomach buffering the action of the juices, and thereby protecting the gastro-jejunal mucosa. It is the resting juice or night secretion which is present when the stomach is empty which is so dangerous and a study of unsuccessful cases has shewn that it is the case with a high fasting juice, rather than the case with a high hormonal phase, whichgoes on to post-operative pain and an unsatisfactory result.

The removal of the pyloric antrum abolishes the hormonal phase of secretion and when vagal influence is not strong and regurgitation is free achlorhydria results, but where the vagal influence preponderates, as it so often does in duodenal ulcer cases, nothing short of the most radical gastrectomy operation will be effective and as will be shewn later, even the most heroic procedures may fail to produce achlorhydria. Some other operation therefore which will do for these exceptional cases, what gastrectomy will not always do, remains to be devised.

Results of Gastroctomy operations.

In spite of the uncertainty in results of gastrectomy operations, they have come to hold an important place as a means of dealing with duodenal ulcer with high acidity and rapidly emptying stomach. Klein[87] found that removal of the pyloric antrum led to hypoacidity or an acidity in 78% of gastrectomy operations for gastric ulcer and that this rose to 100% six months later, but he found that in only 18% of duodenal ulcer cases, was the acidity lowered immediately after the operation and that after an interval the percentage rose to 66%.

The effect if the gastrectomy operation may be enhanced by removing a large segment of the body of the stomach as well as the antrum. This acts, as does fundesectomy, by cutting down the number of acid secreting cells but at the same time of course, it cuts down the volume of the stomach in which the remaining acid has to act and the concentration of acid is therefore little affected.

The results of the gastrectomy operation for duodenal ulcer have been variously reported. Lake[114] reviewed a series of 320 cases. He had a mortality of 5.3% and an incidence of 2% gastro-jejunal ulcer. He reports good permanent results but it is perhaps too early yet to talk of permanent results. The incidence of 2% stomal ulcer

that
shows/though the risk of this complication is less with the gastrectomy operation, it is by no means abolished. Probably the figure is better than it sounds as no doubt the cases chosen for gastrectomy were those which would have been likely to develop a stomal ulcer after the gastro-enterostomy operation. Gordon-Taylor[17] reviewed a series of 52 cases which had been followed up with great detail, in order to determine the remote results of gastrectomy on the human body.

In this series 44% showed definite anaemia, but this was symptomless and was only discovered by laboratory methods. It did not resemble the pernicious type and no evidence of the recurrence of pernicious anaemia was found.

Free hydrochloric acid was found in 20% of the cases, Fibrin was present in the faeces of 50% and there was a general tendency to an increase in the faecal fat. Some increase of the intestinal flora was found but without increase of any specific type of organism.

Cases with a rapid gastric emptying, showed a sudden drop in the specific gravity of the urine following a test meal. The importance of the pyloric control of water absorption is hereby demonstrated. An increase in the blood chloesterol and uric acid, were the only abnormalities found in the chemical examination of the blood.

Garnell & Talbot examined 26 cases after the gastrectomy operation and their findings are worth recording.

65% showed post-operative achlorhydria and the height of the post-operative curve had no relation to the height of the pre-operative curve. They appear to agree with Lake that regurgigatation of bile is important in the reduction of acidity and point out that only two of twelve patients having bile in the fasting juice or in the first specimen, had any free acid later.

No gross blood changes were noted. The emptying time of the stomach was reduced 79% and there was no evidence of dilatation or hypertrophy.

58% gave a history of some form of internal unrest and eight had irritable colons. All stools were negative for undigested food or blood except in the recurrences.

Two of the 26 or 7.7% showed recurrence which is a figure rather higher than that reported by most operators.

50% maintained weight, 30% gained weight, 20% lost weight and 43% complained of being easily tired.

The general impression left by the study of the above reports is that we have not yet found the best method of dealing surgically with duodenal ulcer in a vago-

tonic individual. No serious harm appears to follow the removal of large segments of the stomach but the mortality is moderately high and the risk of recurrence is by no means abolished.

Ogalvie[170] published a series of cases where he left the pyloric antrum intact and removed a large segment of the body of the stomach, on the assumption that the antrum would cease to stimulate the acid curve if no food passed into it. The resection aided the lowering of the acidity by removing a large portion of the acid secreting cells. This operation, which is comparatively easy and quick, appeared to be rational, but experience has shown that for the maximum effect the pyloric antrum must also be removed.

The writer of this Thesis has had experience of these operations and carried out a series of thirty-seven without a death. The initial result appeared to be most satisfactory though complete achlorhydria was only obtained in 22% as found by a test meal two weeks after the operation. The remainder showed a change from the pre-operative high level acidity curve, to one of more gradual rise, maintaining an even moderate level. Apparently the hormonal phase of secretion was eliminated for the time being and only the vagal and intestinal phases operated.

A follow-up test meal examination was made in

as many of the cases as could be persuaded to present themselves for re-examination. Only fifteen could be followed up completely with post-operative periods of 8 months to 3 years. Eleven or 73.3% were well and the result could be classed as excellent, in spite of the fact that the patients had largely discarded the medical and dietetic measures shortly after leaving hospital.

Four complained of pain after meals and one possibly had a small stomal ulcer. The follow-up test meals were disappointing, in that permanent achlorhydria had only been achieved in two. The others presented free acidity curves within normal range but flatter than normal, but in two cases the curve was high. The achlorhydria cases are among those with good results and the high acid cases were among those with unsatisfactory results. Whether the removal of the pyloric antrum will improve these results remains to be seen but Ogalvie has re-operated on several of his cases and removed the antrum with benefit.

A review of the statistics of the writer and his colleague, Mr. Somervell are interesting. 88 gastrectomies were carried out for duodenal ulcer with two deaths, 2.3%. (The death rate for the posterior gastro-enterostomy cases was 1.5%). Both of these deaths were due to leaking duodenal stumps where the sclerosis of the ulcer had pre-

vented the proper invagination of the stump. As has been pointed out, the method which leaves the antrum, or part of it intact, makes the operation much safer and easier. In 46 gastrectomies for gastric ulcer five died (11%). In 18 for carcinoma only one died, while in sixty for gastro-jejunal ulcer eight died (13.3%).

This indicated that gastrectomy on a stomach not in itself inflamed ulcerated or adherent, if conducted well, is not in itself a dangerous operation. The mortality in the gastric ulcer and gastro-jejunal ulcer cases was due to increased time taken to overcome the technical difficulties of the operation, to leaky suture lines made in inflamed and unhealthy tissue and in two cases too early perforation of a stomal ulcer.

Disease	Number of gastrectomies.	Deaths	Percentage
Duodenal ulcer	88	2	2.3
Gastric ulcer	47	5	10.6
Gastric carcinoma	19	1	5.3
Gastro-jejunal ulcer	60	8	13.3
	214	16	7.8

GASTRO JEJUNAL-ULCER.

The literature on this subject is enormous and a few typical references will serve to show the general trend of opinion in relation to this most important complication. Wright[196] places the incidence at 4.45% of proved cases, in series of 1730 posterior-gastro-enterosomies for duodenal ulcer but the incidence is probably higher, for only proven cases are included in the figures. In a series 507 gastro-enterosotomies for gastric ulcer the incidence is 5.32%. In 29 patients who had Polya gastrectomy for duodenal ulcer the incidence was nil and in 199 gastrectomies for gastric ulcer the incidence was .8%.

Lahey and Swinton[191] quote widely varying figures. From 1.69% given by Walton[171] to 16.4 recorded by Hinton[179] following gastro-enterostomy. In two large series of gastrectomy operations 0.6% and 0.7% are recorded and Lake[164] records 2% from his gastrectomy series.

Walton[178] expresses the view that if sufficient stomach is removed at the gastrectomy operation, achlorhydria results and there is no recurrence. A view which the present writer has reason to doubt as will be shewn hereafter.

75% of the recurrences are to be found on the suture lines and 25% in the jejunum itself opposite the

stoma. That is, at the point on to which the gastric contents impinge when they leave the stomach.

Etiology of Gastro-jejunal Ulcers.

Numerous causes or combinations of causes have been given but the commonest causes reported by various authors may be divided into:-

1) Constitutional factors in the patient.
2) Infective factors in the patient.
3) Faults in technique.
4) Failure of proper pre- and post-operative care.

1) Constitutional factor.

This is described by Hurst and Stewart as the Ulcer Diathesis. It is found in vagotonic persons, that is those with high gastric curve, hyperperistalsis and hypertonicity. Undoubtedly such people are liable to form ulcer at the slightest provocation and the sudden exposure of the jejunal mucosa to highly acid gastric juices, is more than its resistance powers can cope with. Steinberg and Proffit[19] made an interesting study on the part played by the force with which the stomach secretions are ejected on to one spot, in causing ulcer. They carried out the Mann and Bolman duodenal drainage operation and re-established the anastomosis in different ways. If a kink was made in the jejunum near the stoma, the ulcer formed on the jejunum just proximal to the kink, showing

that it was the part of the bowel on to which the highly acid gastric contents impinged, which tended to ulcerate. If an end to end anastomosis was made, the ulcer occurred at the junction in all. If an end to side anastomosis was made the ulcer occurred in 43% and then it was on the jejunum just opposite the stoma. If the antrum was excised, ulcer occurred in 12% only, showing that a wide stoma, from which all force was removed, was safer than a narrow stoma. Even if a kink was introduced in the jejunum in such an anastomosis, no increase in the ulcer incidence occurred, as the factor of forceful ejection on to the part had been eliminated. 25% of Gastro-jejunal ulcers occur in the jejunum opposite the stoma and are presumably the direct result of the force of highly acid gastric juices ejected by a hypermotile stomach through a small stoma.

75% of ulcers occur in the suture line itself, however, and other factors come into play, such as:-

Infection.

This may be from the patient's teeth *and/or* from gastritis. The frequency of gastritis associated

with duodenal ulcer appears to vary. In Continental clinics and in South India it is the rule rather than the exception to have the ulcer complicated with gastritis. Walters & Church[57], however, mention that it is uncommon in the ulcers seen in the Mayo Clinic and opinions are divided in Great Britain, but the use of the gastroscope has tended to increase the frequency with which gastritis is diagnosed.

It is easy to understand that a gastro-enterostomy, carried out through an infected stomach wall, will lead to infection of the suture line, poor healing and possible ulceration. Furthermore if the mucus membrane is not accurately approximated to protect the cut edge of the stomach and jejunum, infection swallowed from the teeth, tonsils or nasal sinuses will find its way into the muscle layers and delay healing and may result in ulcer.

Poor Technique.

Emphasis has already been laid on the importance of accurate suturing, avoiding passing the sutures between the muscle coats and so forming pathways for infection from the lumen to reach the muscle layers. The use of clamps does not appear to play a part, as experiments on dogs have shewn that quite severe trauma can be applied to the stomach without ulcer resulting. Unabsorbable

suture material is rarely used nowadays, but no doubt it played a part in the past in the formation of stoma ulcer. In the author's South Indian series of gastro-jejunal ulcers two cases of stoma ulcer healed spontaneously after the removal of an old piece of silk suture had been removed.

Pre- and Post-operative medication and Care.

This in the writer's opinion is all important and may play a big part in combating the effects of an ulcer diathesis and infection. The removal of septic foci is an obvious precaution and the treatment of gastritis by bland diet, H202 stomach washes and milk of magnesia, help to provide a clean field for the performance of the operation. It is in the days immediately following an operation that the seed of a gastro-jejunal ulcer is laid. Once the mucosa has soundly healed and the cut muscle edges are completely protected, the chances of ulcer are much reduced in the opinion of the writer. This does not mean that symptoms of ulcer show themselves soon after the operation but that an imperfectly healed mucosa, associated with infection of the underlying muscle coats, leaves a weak spot which may become an ulcer in time. In the case of an ulcer on the jejunum opposite the stoma however, it is likely that a considerable period of time

elapses before the continued ejection of highly acid gastric juices, undermine the resistance power of the jejunum. A continuance of careful dieting after the operation associated with alkaline medication and belladonna, serves to some extent to protect the jejunum from the effects of its new relationship to the gastric juices.

The Prevention of Gastro-Jejunal Ulcer.

From the foregoing, certain points stand out which may help to lessen the risk of this complication.

1) Avoidance of the gastro-enterostomy operation in the vagotonic stomach.

2) If medical treatment fails to cure or at least control the ulcer in the vagotonic stomach, some form of operation calculated to lower the gastric acidity must be employed.

3) A careful estimation of the acidity curve to determine the most active phase of acidity for each patient and the choice of the type of operation based on that knowledge.

4) Pre-operative dietry and medication and removal of septic foci to reduce gastritis.

5) Careful technique in suturing.

6) Prolonged post-operative medication and dietry.

A review of the cases of gastro-jejunal ulcer operated on by the writer and his colleague in South India, show the results of the various methods of attack in a series of 85 cases in a ten year period.

The following Table sets out the type of operation carried out in each case with results so far as are known at present.

PGE - posterior-gastroenterostony, AGE - anterior gastro-enterostomy, GJ - gastro-jejunal ulcer D - duodenal ulcer J - jejunal ulcer, C - gastrocolic fistula, B - Billroth, P - Polya. F - Finsterer high gastrectomy, E - excision of ulcer.

Serial No. or date.	Original operation.	Interval	Complication.	Second operation.	Remarks.
446	PGE	2½ yrs.	GJ	E	8 yrs.later recurrence.
320	PGE	3 "	GJ	E	Satisfactory
308	PGE	2 "	GJ	P	Pain later due to kink relieved by entero-anastomosis
557	PGE	9m	GJ	E	Satisfactory
520	PGE	3 yrs.	GJ	BII	Satisfactory
522	BI	1 "	GJ	BII	Secondary ulcer in jejunum excised.
768	PGE	?	GJ	E	Satisfactory
781	PGE	3½ "	GJ	E	Continuance of pain.
882	PGE	5m	GJ	E	Died.
888	PGE	4 yrs.	GJ	E	Unsatisfactory. pain continued.
717	PGE	1 "	GJ		Satisfactory.
893	PGE	1 "	GJ	E	Satisfactory
1929-6	PGE	3 "	GJ	E	Satisfactory.
1929-9	PGE	1½ "	GJ	E	Satisfactory.
1929-11	PGE	2 "	GJ E	AGE in Y	Satisfactory.
1929-3	PGE	4 "	G D	P	Satisfactory.
1325	PGE	1 "	GJ C	AGE in Y	Satisfactory 1 year.
1350	PGE	1 "	GJ	BII	Improved.
1932-10	PGE	2 "	GJ	P in Y	Satisfactory.
1932-10	PGE	1m	GJ	P in Y	Satisfactory
1028	PGE	2 yrs.	GJ.	E	Satisfactory.
1036	PGE	1m	GJ	P in Y	Satisfactory.
1126	PGE	1m	GJ	E	Ulcer recurred.
1130	PGE	6m	GJ G	E	Satisfactory.
1174	PGE	4m	GJ	E	Recurrence relieved 2½ yrs.later by B.

Serial No. or date	Original operation.	Interval	Complication.	Second operation.	Remarks.
1190	PGE	4 yrs.	GJ	E	Recurred relieved 1½ yrs. later by BII.
1209	PGE	2 "	GJ	E	Satisfactory.
1261	PGE	3 "	GJ	BII	Satisfactory.
1344	PGE	3 "	GJ C	E	Stormy convalescence but now well.
1359	PGE	1½ "	GJ	P in Y	Satisfactory
1398	PGE	2 "	GJ	E Y	Recurred
1454	PGE	2 "	2GJs	P	Died - subphrenic abscess.

1457	PGE	2yrs.	GJ+ C	P	Satisfactory
1518	PGE	4yrs.	GJ	BII	
1589	PGE	4yrs.	GJ C	BII	Satisfactory
1590	PGE	6yrs.	3Gs	BII	Satisfactory
1620	PGE	6m.	GJ+C	E	Died.
1646	PGE	8yrs.	J	E	Complications necessitated new anastomosis.
1636	PGE	3yrs.	GJ	BII	Satisfactory.
1688	PGE	4yrs.	G J	P	Died.
1692	PGE	1 yr.	GJ+C	P in Y	Satisfactory
1736	PGE	1½yr.	GJ	BII	Satisfactory, silk thread in PGE suture found.
1758	PGE	1½yr.	GJ	BII	Satisfactory.
1762	PGE	2½yr.	GJ.	P in Y	PGE found done the wrong way round. Satisfactory.
1773	PGE	5yrs.	GJ	P in Y	Died
1809	PGE	6m.	GJ	BII	Satisfactory, silk thread.
1891	PGE	4yrs.	GJ	BII	As No. 1736. Re-operated five months later for intussusception of small intestine. Recovered.
1901	PGE	6 yrs.	GJ+ J	P in Y	Satisfactory.
1903	PGE	7m	GJ	E	Bad position of original operation corrected. Hence no gastrectomy.
1926	PGE	3yrs.	J+C	E BII	Satisfactory
1930	PGE	6yrs.	GJ	BII	Satisfactory.
1933	PGE	3yrs.	J	P in Y	Satisfactory
1965	PGE	7yrs.	J+C	E BII	Satisfactory
1969	PGE	8yrs.	GJ	BII	Satisfactory.
2005	PGE	3 yrs.	GJ	E	Pain and tenderness over Stoma
2028	PGE	4yrs.	GJ	P in Y	Satisfactory.
2073	PGE	1m.	GJ	BII	Satisfactory but slight discomfort daily.
2082	PGE	9yrs.	GJ.	P	Satisfactory.
2152	PGE	6 yrs.	GJ	BII	Satisfactory.
2226	PGE	1m.	GJ.	E	Satisfactory.
2230	PGE	5m.	GJ.	BII	Slight pain over stoma one year later.

2233	PGE	1yr.	GJ	P	Satisfactory.
2285	PGE	1yr.	GJ	E BII	Satisfactory
2293	PGE	7yrs.	GJ	E	Died from leakage.
2300	PGE	11 days.	GJ	P in Y	Died.
2313	PGE	4yrs.	GJ	P in Y	Satisfactory
2321	PGE	?	GJ	E BII	Satisfactory
2344	PGE	4yrs.	GJ J	P	Died two months later.
2334	PGE	8yrs.	D2	BII	Satisfactory
2372	PGE	6m	GJ	F	Satisfactory.
2382	PGE	?	GJ	P	Died of cerebral oedema.
2383	PGE	?	GJ GJ C	P in Y	Satisfactory.
2476	PGE	12yrs.	GJ.	P in Y	Satisfactory.
A1	PGE		GJ.	F	Satisfactory.
A2	PGE		GJ.	F	Satisfactory.
A3	PGE		GJ	F	Satisfactory
A4	PGE		GJ	F	Satisfactory.
A5	PGE		GJ C	F	Satisfactory.
A6	PGE		GJ	F	Satisfactory
A7	PGE		GJ	F	Subphrenic abscess, finally recovered.
A8	PGE		GJ	F	Satisfactory.
A9	PGE		J	F	Developed dysentry and finally died of perforation of stomal ulcer.
A10	PGE		GJ C	F	Satisfactory.
A11	PGE		GJ	F	Haemorrhage on fourth day and died of perforation on sixth day.
A12	PGE		GJ	F	Satisfactory
A13	PGE		GJ	F	Pain developed twelve days after operation and re-operation showed jejunal ulcer penetrating abdominal wall. Died.

Operation for Gastro-jejunal Ulcer	No.	Died	Recurrence to date.
Excision of ulcer and reforming stoma	24	4	8
Bilroth II	28	-	1
Polya	20	5	1
Finsterer	13	2	1
	85	11	11

Reference has been made to the Finsterer operation but actually the operation is a modification of Finsterer's technique. It consists in dividing the stomach either proximal or distal to the pylorus depending on the position and scarring of the original duodenal ulcer. The jejunum is divided above and below the anastomosis and the ends sutured in an end to end anastomosis. The stomach is resected high up above the old stoma and the reformed jejunum anastomosed to the cut end. The advantages of the operation over excisions and plastic operations of the stoma are that all the work is done on healthy tissue well away from the ulcer. The amount of stomach removed is sufficient to lower the acidity and may bring about an achlorhydria. PLATE IV

One case may be quoted to show that sometimes even the most radical gastrectomy may fail to bring about the desired achlorhydria if the fasting juice is very high. The case is No. A12 on the list.

He was an old man with a gastro-jejunal ulcer. His acidity curve was exceptionally high, even for the Deccan, and a high gastrectomy of the Finsterer type was carried out and the immediate results were and still are, so far as is known satisfactory, but a test meal three weeks after the operation showed that the level of aci-

dity was still appreciable. This case and three which died of perforation from jejunal or stomal ulcer soon after this operation show that it cannot be depended upon to bring about a complete achlorhydria, and its success depends to some extent on what degree of biliary regurgitation is present and how high the initial fasting juice was before the operation.

An Experimental Method of Dealing with the Vagotonic Stomach.

The author is indebted to Mr. Wilson Hey of Manchester for introducing him to an operation technique which bids fair to bring about a marked lowering of the v a g a l phase of secretion without the disadvantages of a mutilating operation.

Hey's operation, which has not as yet been described in public in this country, pending the fullest follow-up of a large series of operations, consists in a massive ligation of all the main arteries of supply to the stomach. Hey has employed this method for three years and is satisfied from his follow-up that the reduction of acidity is maintained over a period of years and that healing of duodenal, gastric, and gastro-jejunal ulcers occurs.

The writer of this Thesis has personally operated on twelve cases by this method and as the results, so far observed, have been most satisfactory, a description of the method and its results will now be given.

The ligation itself sufficies for gastric and gastro-jejunal ulcers, provided that they are associated with a high night secretion and hypertonic stomach. The only case in this series which did not respond well was one in which the pre-operative acidity was low. In duodenal ulcer cases it is well to perform a gastro-enterostomy at the same time as the ligation, as the healing of the ulcer often causes stenosis of the duodenum and a gastro-enterostomy may be required later for this complication.

The ligation is carried out as follows:-
A high mid-line incision is made and the stomach inspected and the ulcer verified. The stomach is drawn down and to the right and the operator's finger is passed up towards the cardiac orifice till the coronary artery can be grasped between the finger and thumb. With a blunt aneurysm needle, a silk ligature is passed round the artery and tied and traction made on the ligature. Another ligature is then passed round the artery as it

reaches the lesser curvature. The left gastro-epiploic artery is found and ligated as close to the spleen as possible and the vasa brevia are treated in a like manner. Then the pyloric artery and the right gastro-epiploic arteries are ligated. Finally, a few ligatures are passed round the vessels of the gastro-colic omentum. If the operation is being carried out for duodenal ulcer, a posterior-gastro-enterostomy is performed and the abdomen closed in layers. In no case was there any evidence that the stomach was devitalised. Apparently sufficient blood enters the organ through the cardia and pylorus to maintain the vitality. PLATE VI.

The Immediate Effects.

The stomach becomes visably smaller and of a greyish blue colour when the ligation is completed.

A barium meal, carried out eight weeks later showed that the stomach emptied more slowly, the peristalsis was slower and less powerful and the pylorus less spastic, unless a gastro-enterostomy had been carried out as well, in which case the stomach of course emptied rapidly through the stoma. Test meal examinations showed a gratifying fall in the acidity and in most cases there was a complete achlorhydria of the fasting juice, though the curve tended to rise later in some cases in response to hormonal stimulation.

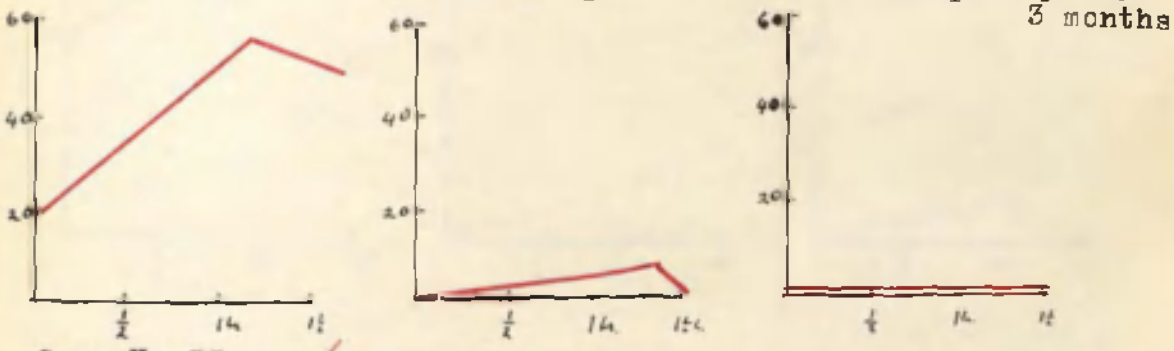
A follow-up of at least three years will be required before this operation can be said to have won a place in the surgical treatment of peptic ulcer but so far, the results are most encouraging with the vagotonic case.

How the operation acts is not clear. No doubt the reduction in the blood supply would account for the drop in acidity but it would appear that the whole character of the stomach changes from the hypertonic type to the atonic type. The relief of symptoms is most marked and possibly when the matter has been studied more, it will be found that nerve changes have taken place in addition to devascularisation.

Review of cases after the Wilson-Hey Operation.
Only six have so far been followed up.

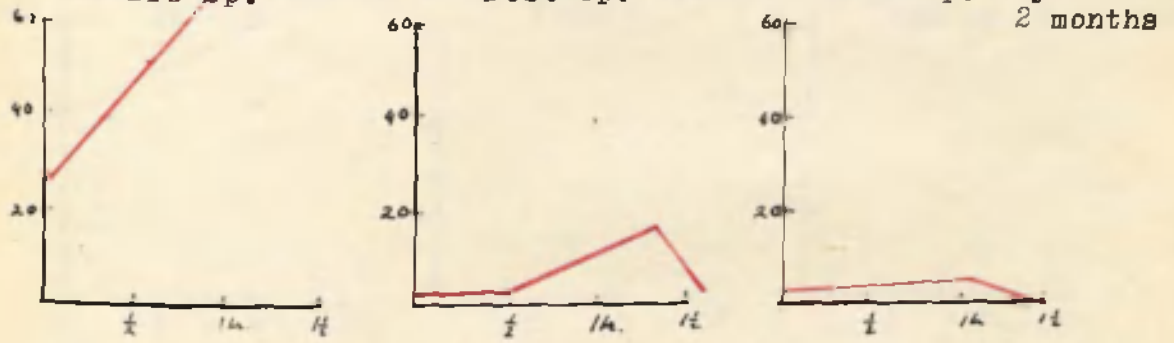
Case No.I
Man aged 52. Duodenal Ulcer. Operation- Posterior Gastro-Enterostomy and ligation. Result one year afterwards.- Excellent, doing hard work as farm hand.

Pre- op. Post-op. Post-op. 1 year. 3 months



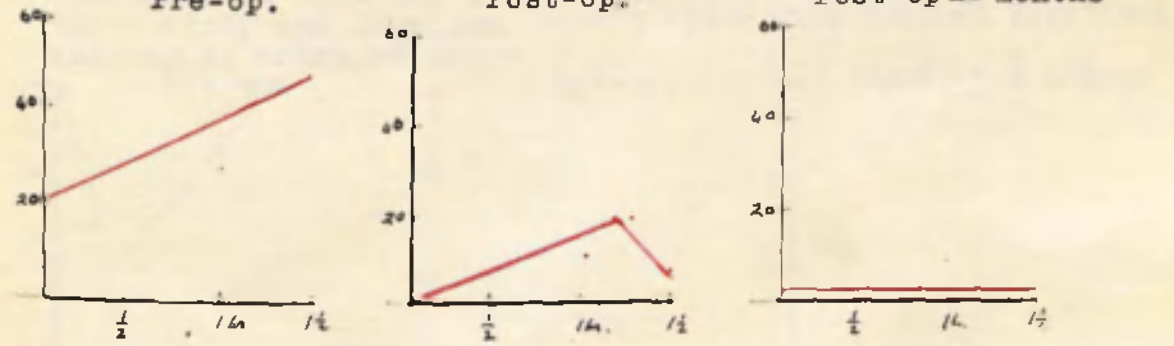
Case No.II
Man aged 30. Duodenal Ulcer. Operation- Posterior Gastro-Enterostomy and ligation. Result one year afterwards.- Excellent, doing hard work as labourer.

Pre-op. Post-op. Post-op. 1 year. 2 months



Case No.III
Man aged 24. Gastric Ulcer. Operation- Ligation only. Result one year afterwards.- Excellent, working as labourer.

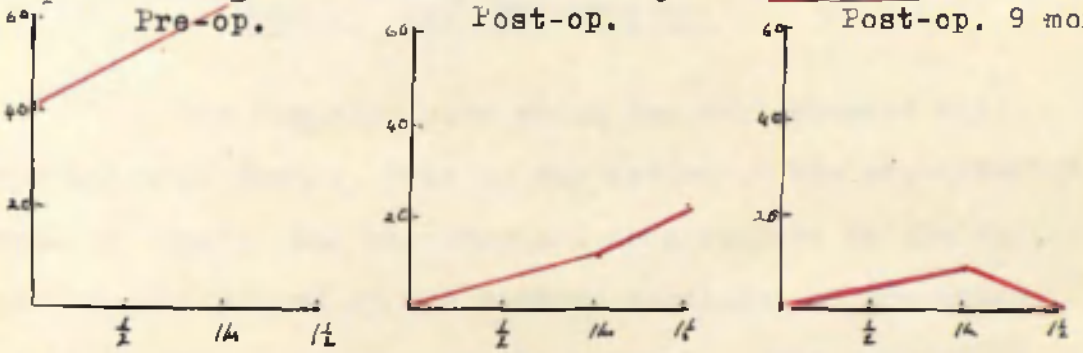
Pre-op. Post-op. Post-op 12 months



NOTE the marked fall in the fasting juice.

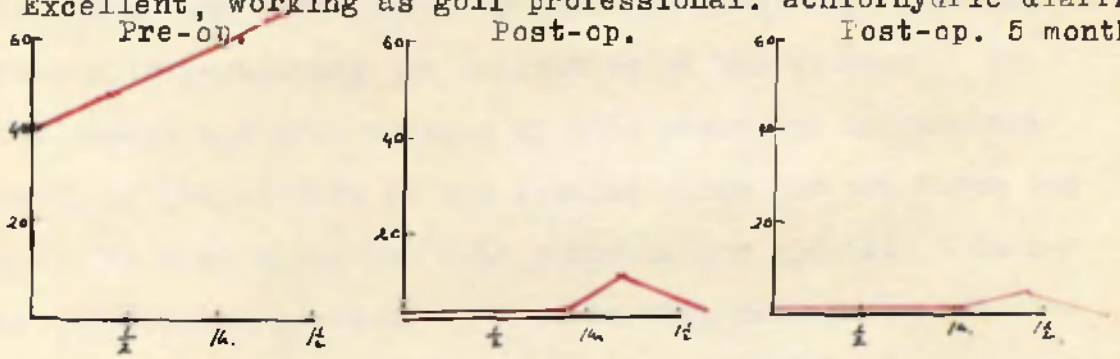
Case No. IV

Woman aged 55. Housewife. Had Posterior Gastro-Enterostomy four years previously for duodenal ulcer. Developed Gastro-Jejunal Ulcer shortly afterwards and anastomosis undone. Operation again- Gastro-Enterostomy and Ligation. Result Good.



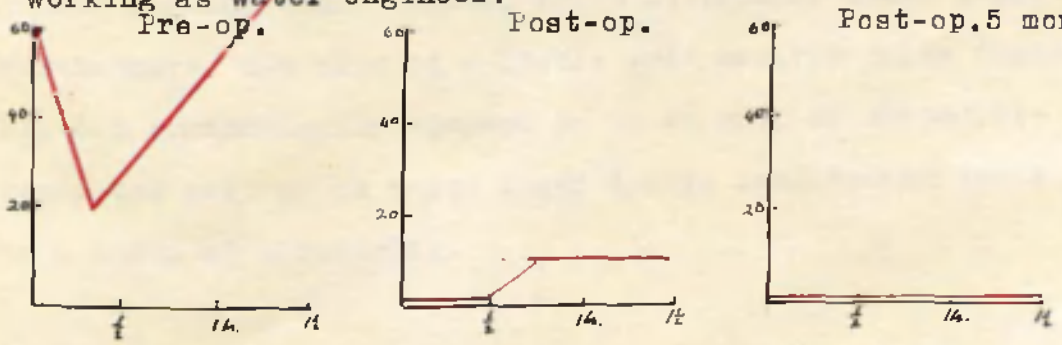
Case No. V

Man aged 57. Duodenal Ulcer. Operation- Posterior Gastro-Enterostomy and ligation. Result six months afterwards- Excellent, working as golf professional. achlorhydric diarrhoea.



Case No. VI

Man aged 47. Duodenal ulcer. Operation- Posterior Gastro-Enterostomy and Ligation. Result after five months- Excellent, working as water engineer.



NOTE. All the above six cases are English and were operated upon in England.

PART VIII

SUMMARY AND CONCLUSIONS.

The dominant note which has been sounded all through this Thesis, both in the review of the experimental work of others and the original observations of the author, is the part played by the nervous inbalance of the motor and secretory mechanism of the stomach. The section on physiology of the stomach, has brought out how delicate is the balance between the vagal and sympathetic impulses and the important part played by Auerbachs Plexus and Meissner's Plexus in regulating the activities of the stomach. On the smooth and even working of this mechanism depends the level of the acidity in the fasting juice and the force and rapidity with which the acid contents are ejected. Mechanical defects, produced by experimental methods, have demonstrated that the factors of spasm and forceful ejection of acid secretion against one part of the bowel, over a period of time, lowers the resistance of that part and prepares the ground for the other factors which ultimately cause ulcer. Furthermore, the fact of a highly acid gastric juice forcibly and spasmodically ejected on to an area of mucosa, already the seat of an acute ulcer delays healing and tends to a state of chronicity.

A review of the epidemiology has shewn that ulcer occurs with great frequency in some Eastern races and is rare in other races and that diet seems to play an important part in this, and that the effect of the faulty diet is to produce a state of inbalance.

It has also been brought out that this state of inbalance, characterised by hyperperistalsis, hypersecretion and pylorospasm may be induced by quite different factors. With some races it is a psychological disorder and the increase of duodenal ulcer as against gastric ulcer, which the historical section has revealed, suggests that modern conditions of living, with increased strain and hurry, have tended to increase the number of persons in Western Countries with a vagotonic diathesis.

On the other hand, experimental work on animals by many workers has shewn that it is possible to bring about a state simulating vogotonia in animals by deficiency diets, particularly diets rich in carbohydrate, poor in protein and this effect may be enhanced if the factors of vitamin A & B deficiency are added. The effect may be still further enhanced if periods of starvation are introduced.

The experimental work carried out by the author on rats and dogs leads to the conclusion, that the effect of these diets is to bring about in the first place, a

degenerative change in the plexuses of Auerbach and Meissner in the stomach wall and it is suggested that it is the failure of these plexuses to perform their normal function of control of the nerve impulses reaching the stomach through the sympathetic and vagus, that leads to the state simulating vagotonia. Furthermore, the study of groups of Indians in the areas where ulcer is extremely common and in those areas where it is rare, points to the conclusion that the peoples liable to ulcer tend to a state simulating vagotonia, as evidenced by the barium and test meal examinations of normal persons. An added significance is given to this finding when it is realised that the deficiencies in diet in South India, are almost exactly those deficiencies which have produced hypertonic state and ulcers in animals, and the same degenerative changes have been found in the plexuses of Auerbach and Meissner in South Indian ulcer patients as are found in experimental animals of the deficient diets. As these changes have been found in persons suffering from ulcer symptoms but in whom no ulcer could be found at operation, the nerve cell changes are evidently the precursor and not the result of ulcer.

Weight is added to the above findings when it is remembered that Sthor in Germany and Holsti in Finland have described similar nerve cell degenerations in ulcer

cases in these countries.

In the review of the literature related to peptic ulcer etiology, it was shewn that infection played a part and that it was possible to induce peptic ulcer by the administration of certain toxins and the injection of certain organisms. German literature expresses the view that chronic gastritis and duodenitis are precursors of ulcer formation, though American and British opinion is divided on this question. All, however, agree that the removal of septic foci is an important factor in the ultimate healing of an ulcer.

Experimental methods of producing ulcer have shewn that lymphocytic invasion, hypertrophy and liquifactive necrosis of lymph follicles and the rupture of these follicles on to the surface of the mucosa are the steps by which the ulcer develops. This same series of events can be traced in the stomachs of persons in South India, not only in those who develop ulcer or pre-ulcer symptoms, but it is commonly found in the stomachs of so-called normal people in the tapioca and rice-eating races.

How then can one bring together two separate pathological processes, one leading to nervous inbalance of the gastric secretions and peristalsis and the other

leading to microscopic erosion and follicular /ulcers? The secretory and motor inbalance, whether it be due to a vagotonic state of psychological origin as in Western Countries, or to a lack of control of nervous impulses, due to degeneration of the nerve cells in the stomach walls, as in South India, prepares the soil and renders the person liable to ulcer, given the addition of infection.

An irritating, highly spiced diet of a bulky nature, often eaten after a long fast, induces an irritable condition of the mucus membrane and discharge from septic teeth or sinuses, brings about infection resulting in follicular abscesses. This stage is simply a gastritis or duodenitis and may exist through a persons adult life without ulcer developing, but when such a condition develops in a vagotonic stomach or in a stomach, the secretory and motor functions of which have been upset by nerve cell degeneration, the minute follicular abscesses fail to heal and may coalease to form an ulcer which becomes chronic on account of the hypersecretion, hyperperistalsis and pylorospasm. The author believes that the symptoms of duodenal ulcer are frequently present before any ulcer crater can be demonstrated by the X-Ray or at operation. The typical symptoms are the result of vagotonic or inbalanced stomach irritating the follicular ulcers with

highly acid secretion ejected with force by a hypermotor organ through a spastic pylorus.

The rôle of treatment therefor, whether medical or surgical, is to remove sources of infection and irritating articles from the diet but most important of all to bring about a condition of the stomach in which the secretions will be less acid, the pylorus less spastic and the peristaltic waves less powerful. The place of rest both mental and physical, alkalies, olive oil and belladonna are too obvious to require further mention, but what of the stomachs which cannot be controlled by these measures? What of the individual, who for economic reasons cannot afford the time to rest and must ignore the advice "not to worry"? What of the person in South India with an unsuitable and deficient diet, who cannot obtain the varied vegetables and whose religion forbids the animal fats and proteins? For these people some operation is necessary which will not only cause the original ulcer to heal but will so alter the physiology of the stomach that the conditions which make chronic ulcer a possibility are removed.

The uses and deficiencies of the gastro-enterostomy and gastrectomy operations have been discussed and an alternative method of altering the secretory activity of the stomach suggested. This must await further trial and experimentation before publicity can be given to it but

it is the considered opinion of the author, that the most radical form of gastrectomy does not always achieve its purpose and that until a safe and simple operation can be devised which will permanently reduce the stomach secretion and remove the factor of spasm, the surgery of duodenal ulcer remains in an unsatisfactory state.

That such an operation will be devised and perfected there is little doubt and this remains a fruitful field for further experiment and enquiry. For the immediate needs of the people of South India, for whose sake this study was originally instituted, far-reaching reforms in food growing and dairy farming will be necessary. It will become the duty of the Government to subsidise efforts to cultivate foodstuffs better suited to the needs of human beings.

School authorities will have to provide for the needs of the children under their care (and are in many cases doing so) and to cultivate a taste for cereal grains, milk products and eggs, for without the desire to have these things, the efforts of legislation will fail.

The author wishes to acknowledge his gratitude to the Indian Research Fund Association for their financial assistance in prosecuting this enquiry and to the Director and Staff of the Nutrition Research Institute, South

India, and to the Professor of Pathology, British Post-Graduate Medical School, for the help and facilities they have rendered in the experimental and pathological side of the work.

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Map of India, showing incidence of Peptic Ulcer.

Highest incidence indicated by dark shading.-

Places referred to in the text underlined in red ink.

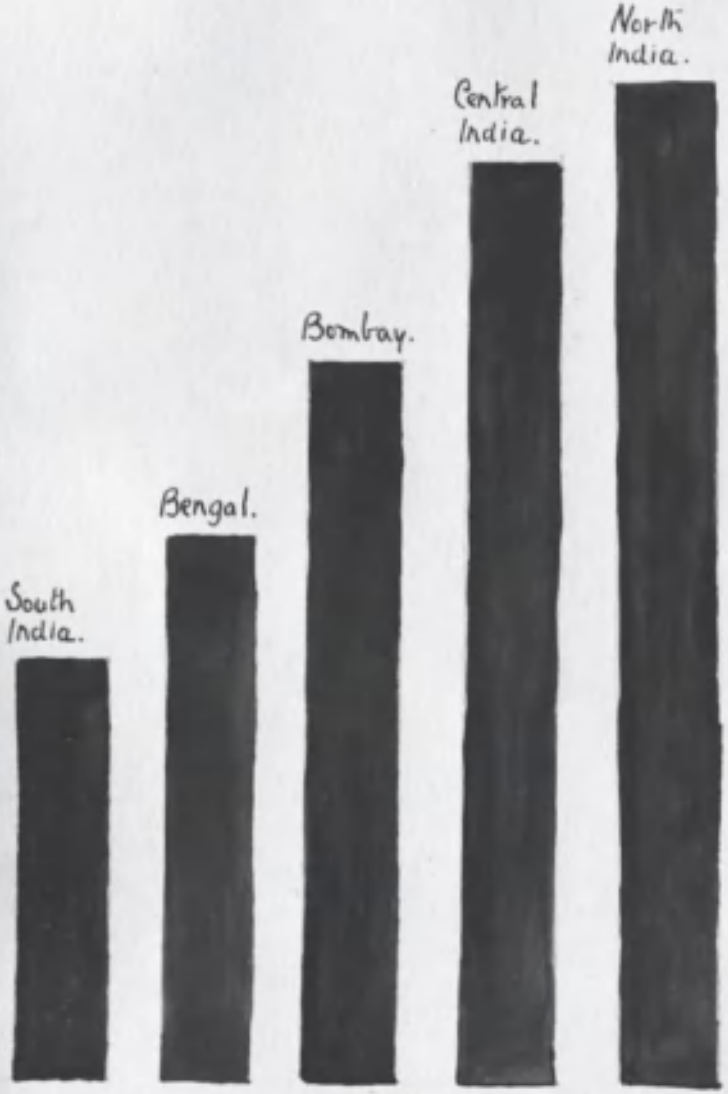
Plate Ia.

Plate Ib.

MAP OF TRAVANCORE.

Map of Travancore, showing Neyyoor in the South; the crosses represent the areas from which peptic ulcer cases come.

Relative value of National Diets in India.
(after Mc Carrison.)



Relative incidence of Gastric & Duodenal Ulcer treated in Hospital. (after Mc Carrison)

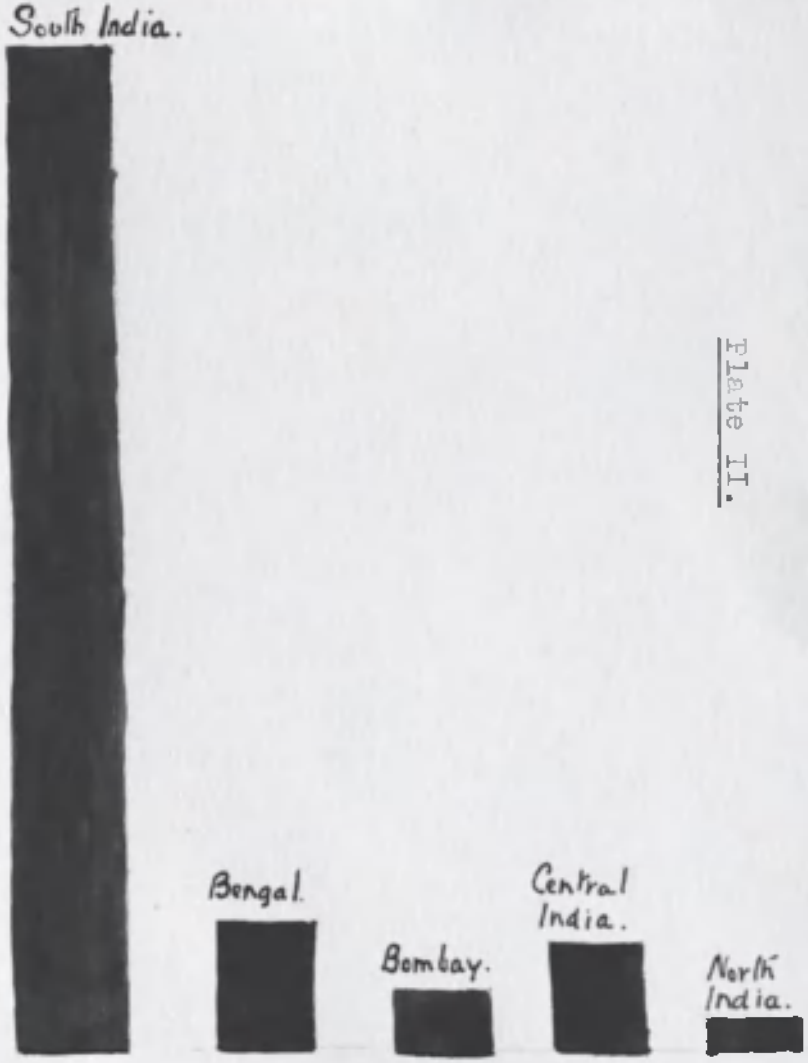
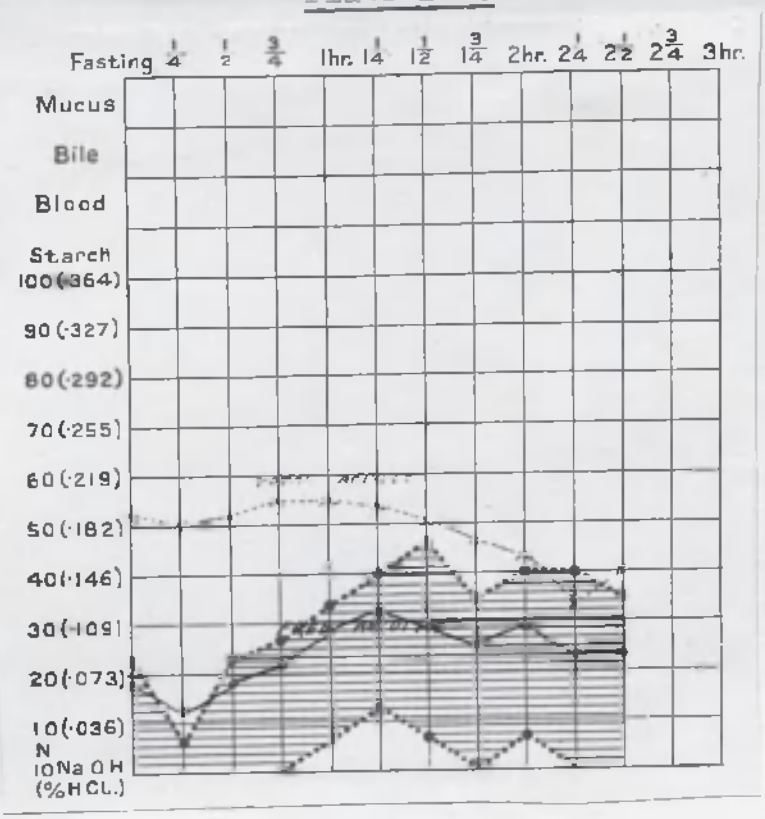
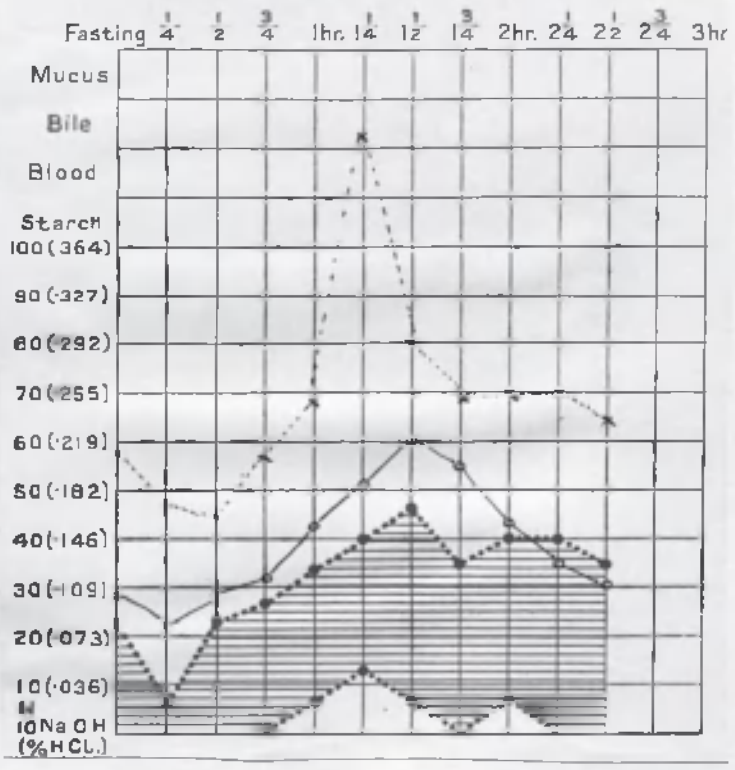


Plate II.

Plate III.



Composite acidity curve of 36 normal Travancoreans.



Composite acidity curve of twenty-seven normal persons in the Deccan.

Steps in the modified Finstrer Gastrectomy for Gastro-Jejunal Ulcer.

Plate IV.

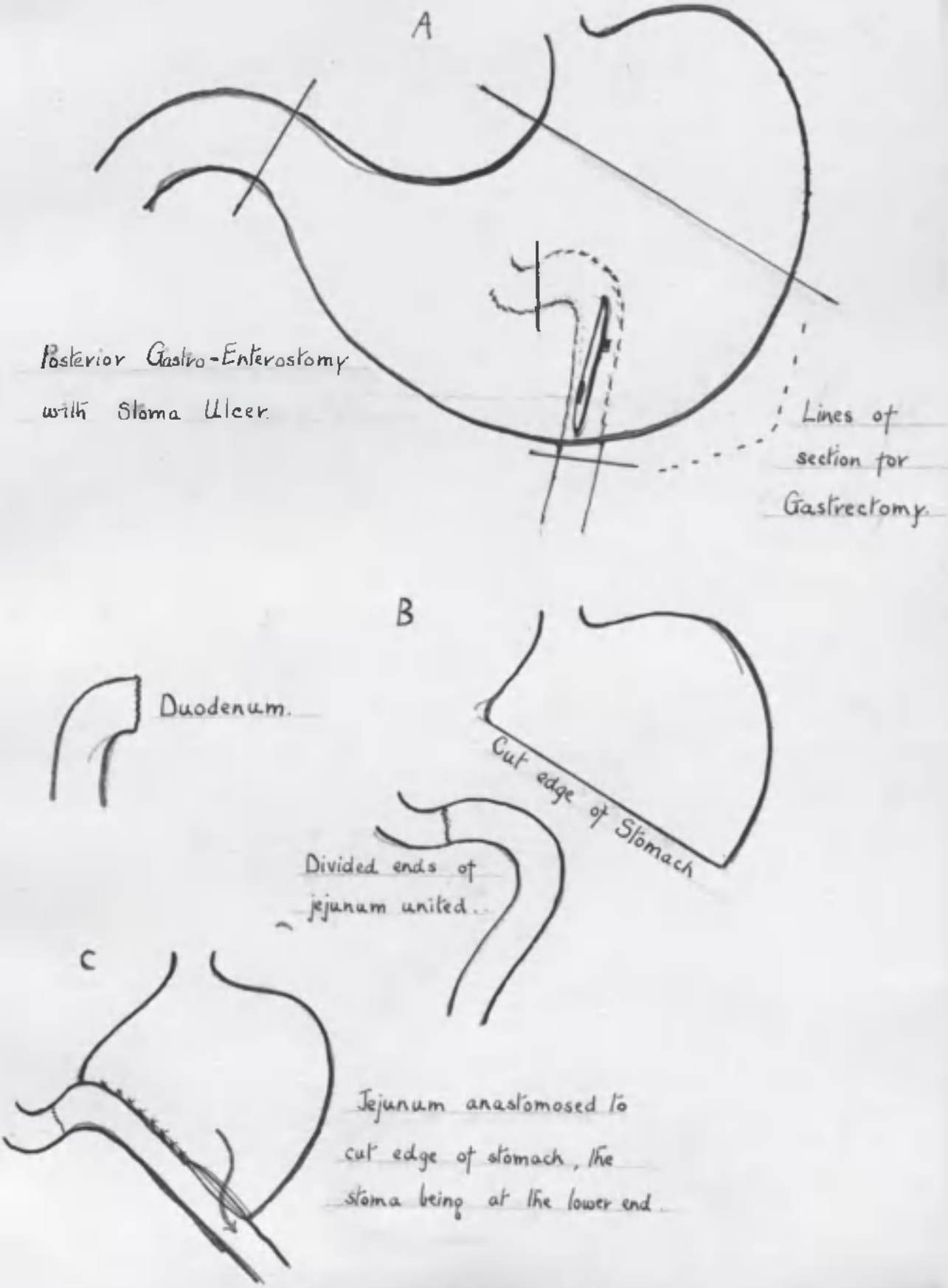
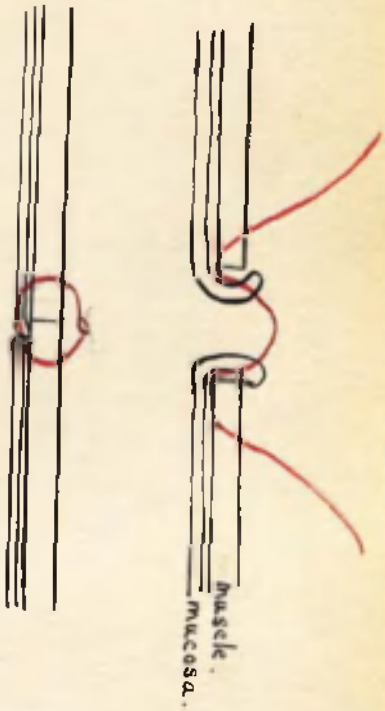
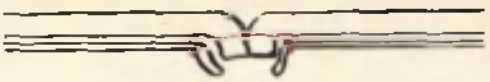


Plate V.

The Authors Suture Technique.

The returning part of the through and through continuous suture of anastomosis takes a big bite of the sero-muscular coats but the point of the needle is so guided that only the tip of the mucosa is picked up. The tip of the needle serves to invert the mucosa before piercing the sero-muscular coat of the opposite side from within out. The result is an accurate apposition of the cut edges of the coats.





Connells inverting suture showing the gap exposing the cut edges of the muscle coats.

The knot of the through and through suture is tied on the outside, one end is left to tie off the returning suture. The needle end is led into the stomach by piercing all the coats and not by passing in directly through the cut.

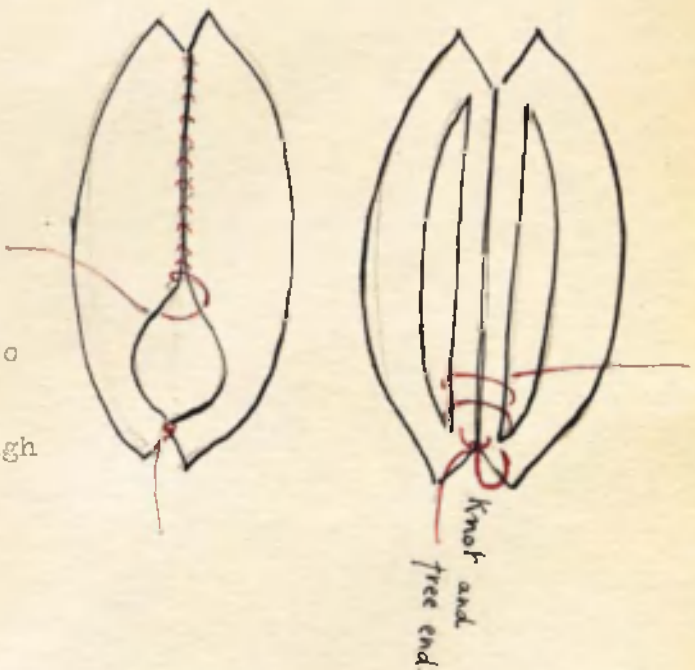


Plate VI.

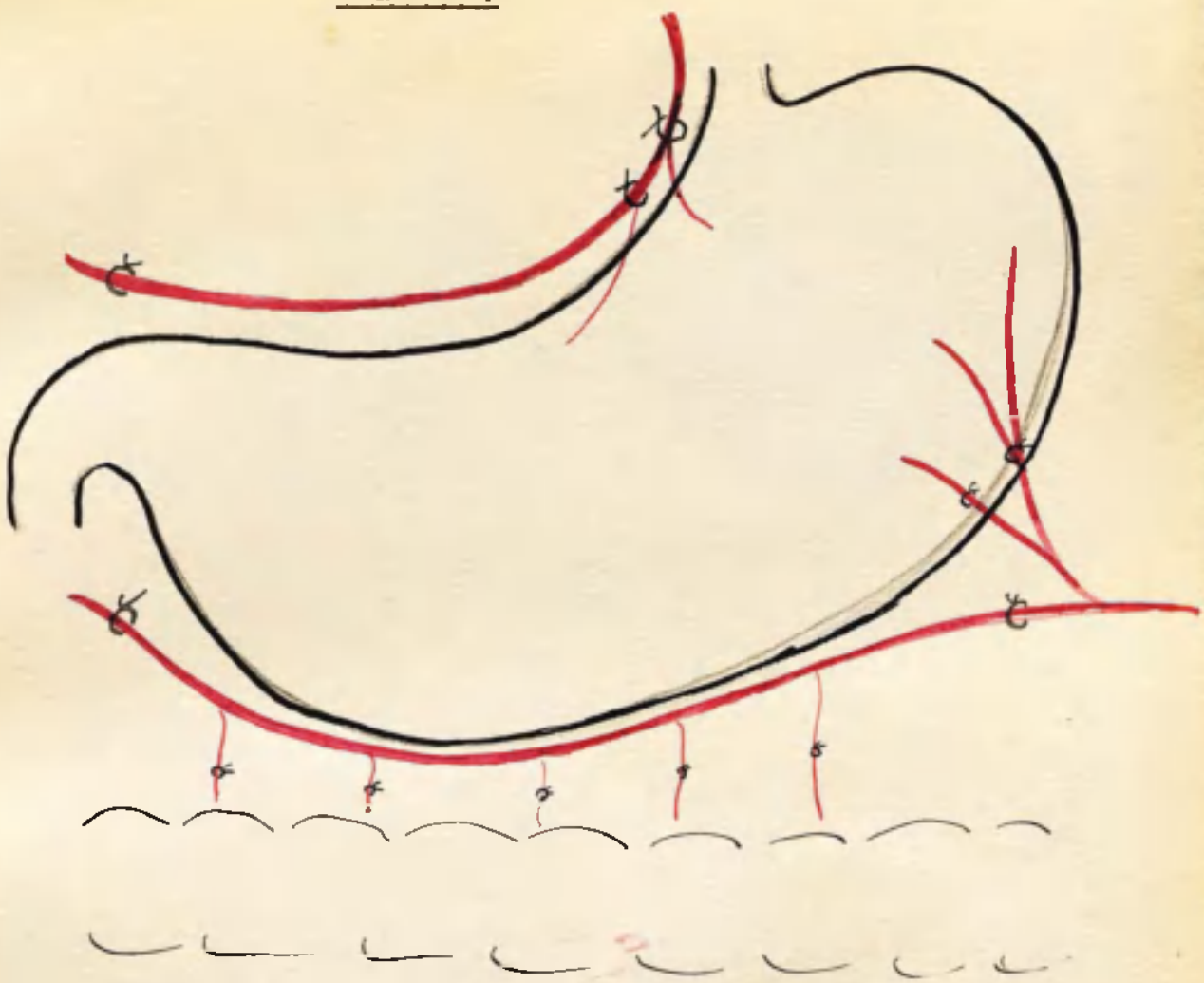
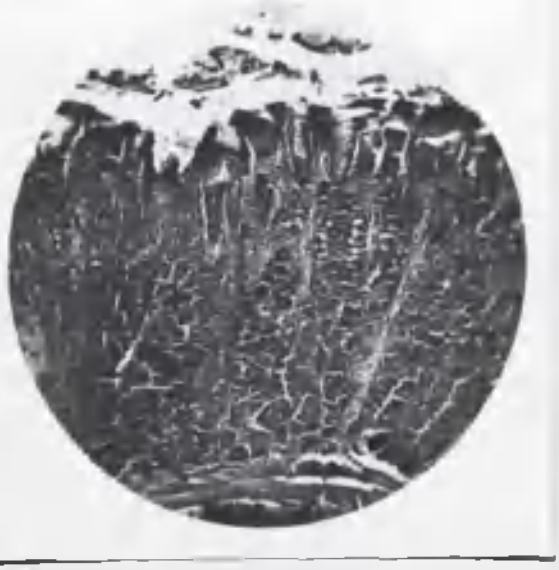


Diagram to show the main vessels of the stomach and the gastro colic omentum and the points at which they are ligatured in the Wilson-Hey operation.

Plate VII



Figs. 1&2. Sections of stomachs from cases of duodenal ulcer in Travancore, showing marked lymphocytic infiltration of the mucosa and hypertrophy of lymph follicles. One follicle has nearly reached the surface. X 50

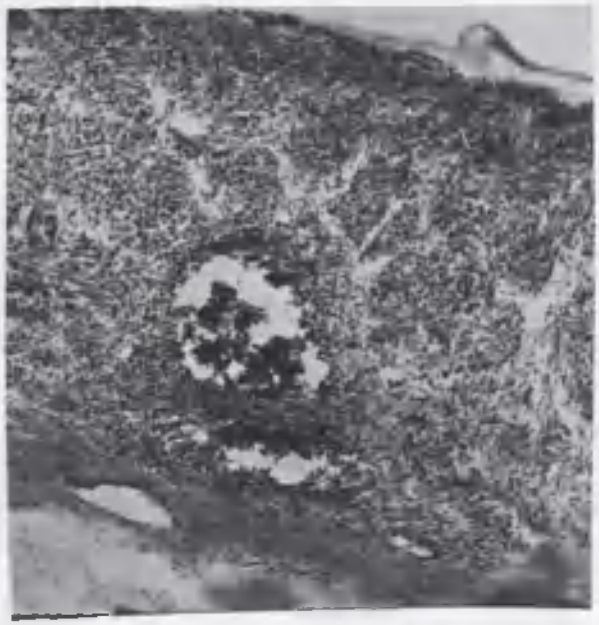


Fig. 3. Liquifactive necrosis of follicle and intense congestion of the mucosa replacing glands. X 90

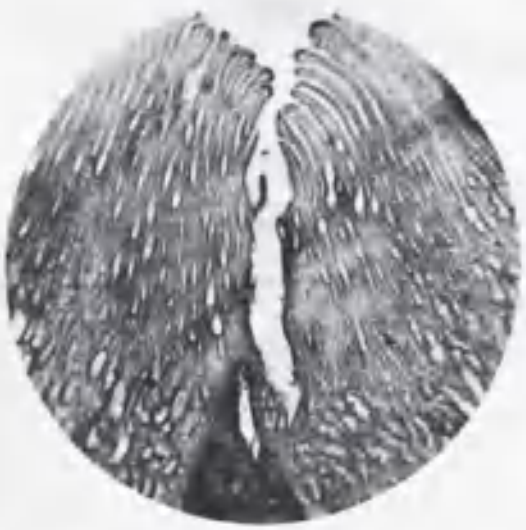
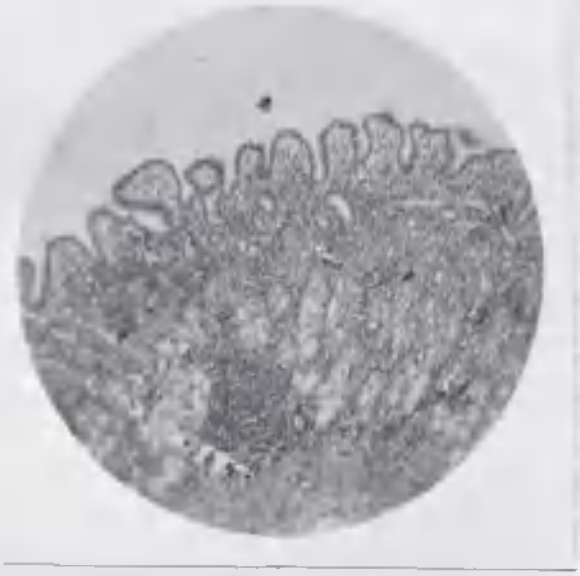
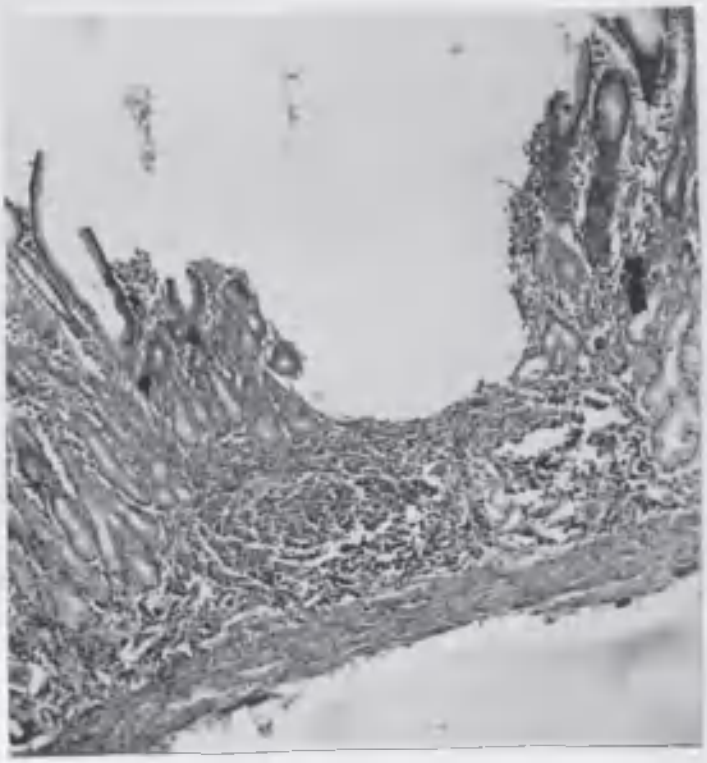
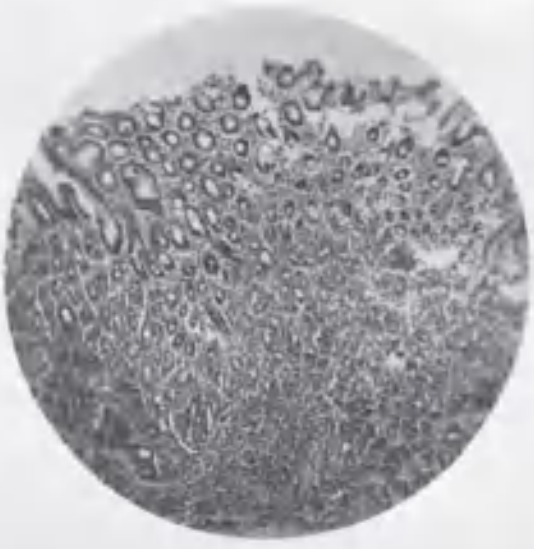


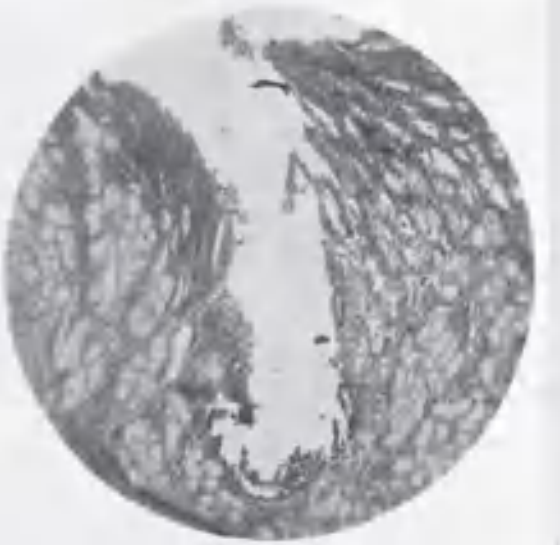
Fig. 4. Gastric mucosa from case of duodenal ulcer showing hypertrophy, lymphocytic infiltration and a follicular abscess forming a superficial erosion. X 50





Figs. 5 & 6. Pyloric antrum and duodenum from persons in South India with ulcer symptoms but no ulcer demonstrated at operation. Showing lymphocytic infiltration, hypertrophy of lymph follicle and rupture of follicle forming microscopic ulcer.





Figs. 7 & 8. Sections from autopsies in Travancore where the persons died by violence, no ulcer being suspected or found. Sections show congestion of mucosa and a lymph follicle which has erupted on the surface forming a superficial erosion.

Plate IX.

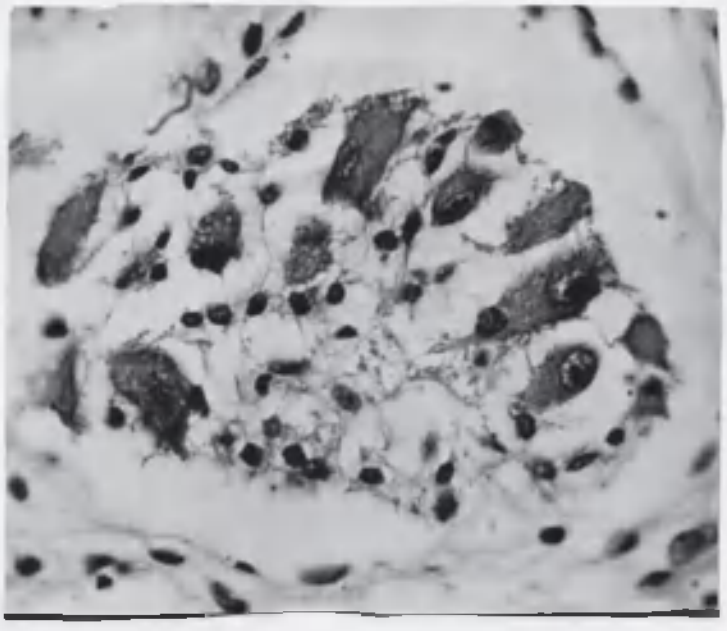


Fig. 9. Auerbachs Plexus in a European stomach showing almost normal features. There is no infiltration of lymph or glial cells or fibroblasts. Most of the ganglion cells are well formed with clear refractile nucleii and well marked nucleolous. X 380

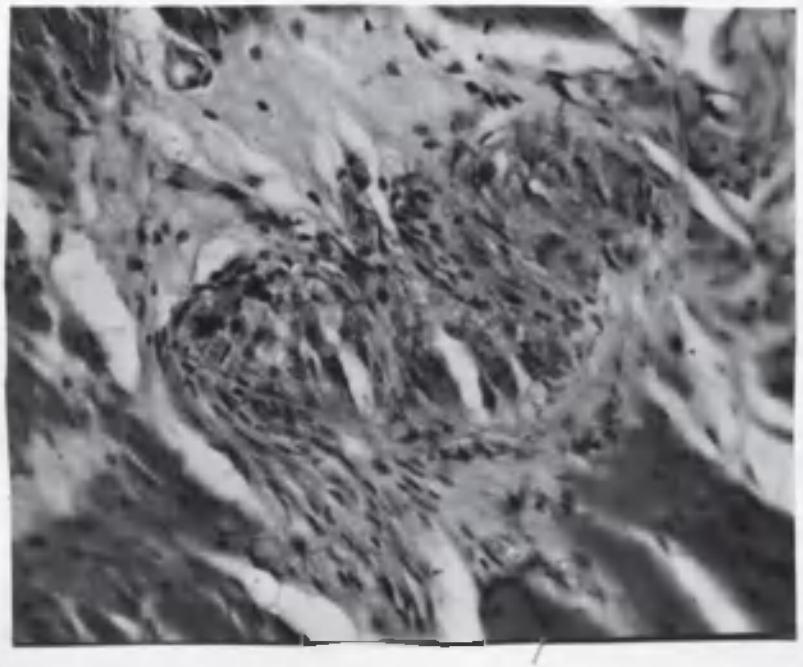


Fig. 10. Auerbachs Plexus from duodenal ulcer case in Travancore showing marked infiltration and degeneration of ganglion cells and the plexus appears to be encapsulated X 285

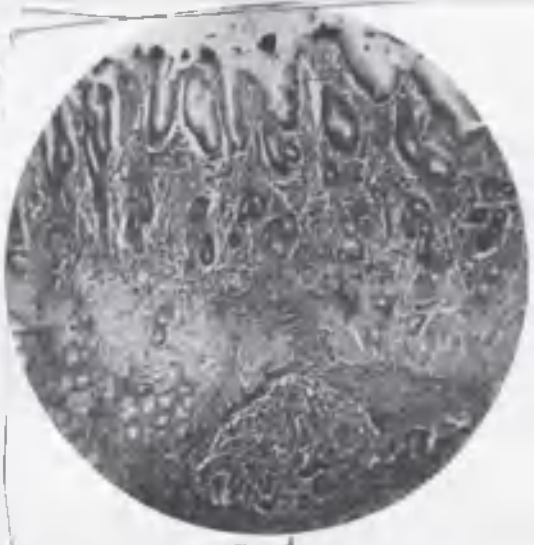


FIG. 1.

FIG. 2.

Figs. 1 and 2. Sections of stomach from a case of duodenal ulcer showing marked lymphocytic infiltration of the mucosa and a lymph follicle in the deeper part of the mucosa (Fig. 1) and the ganglion cells of Auerbach's plexus show degenerative changes (Fig. 2). Fig. 1. × 50; Fig. 2. × 280.

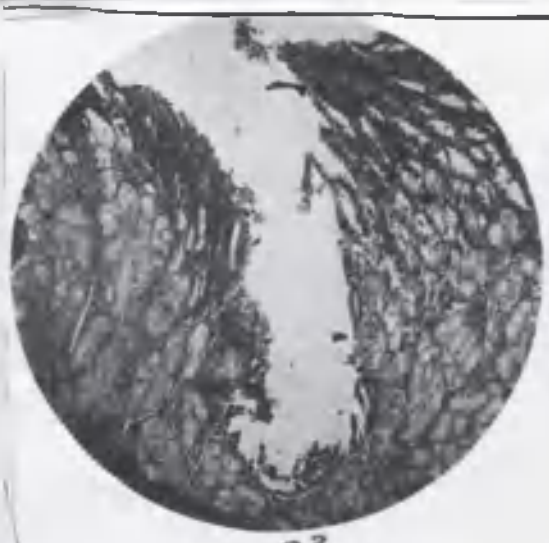


FIG. 3.

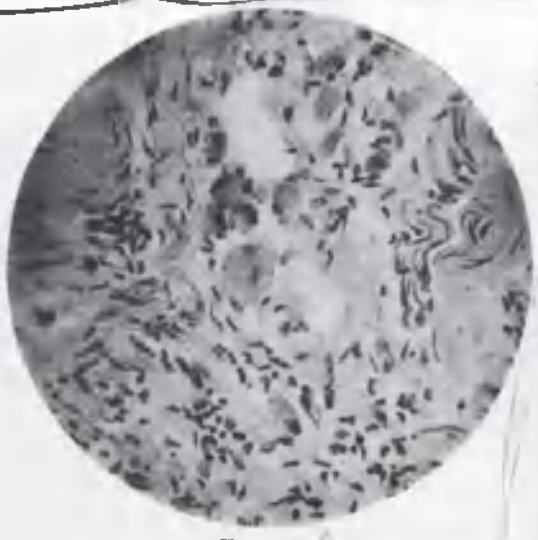


FIG. 4.

Figs. 11 and 12. Sections of duodenum from a person in South India (obtained post mortem), with no history of ulcer, showing round cell infiltration of the mucosa and a lymph follicle which has erupted on the surface forming superficial mucosal erosion (Fig. 11); Auerbach's plexus is swollen and the ganglion cells show degenerative changes. Fig. 11. × 50; Fig. 12. × 280.

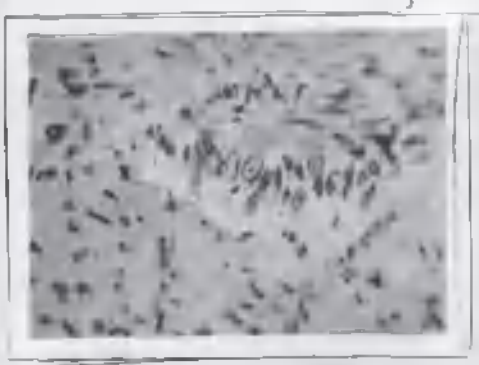
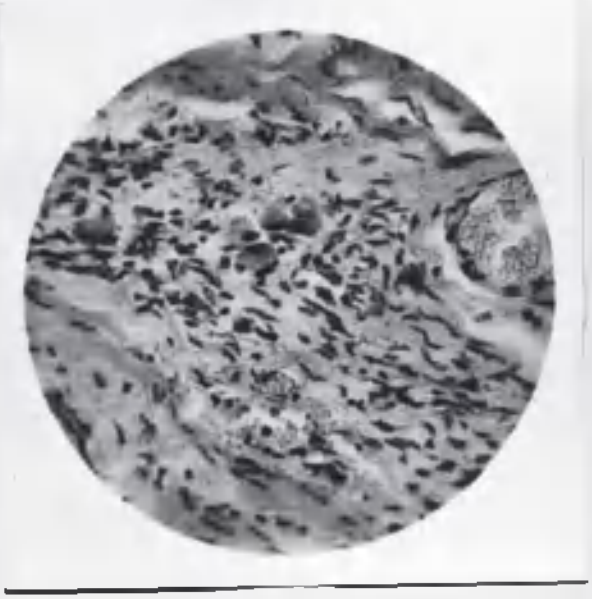


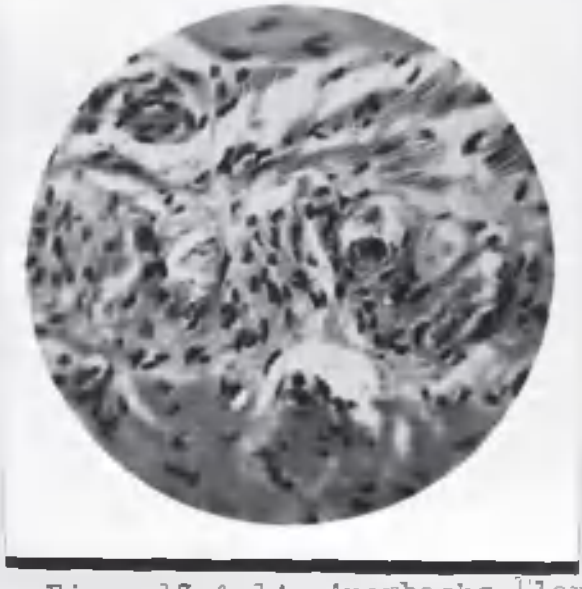
Fig 5.
Normal Stock-fed rat with normal plexus.

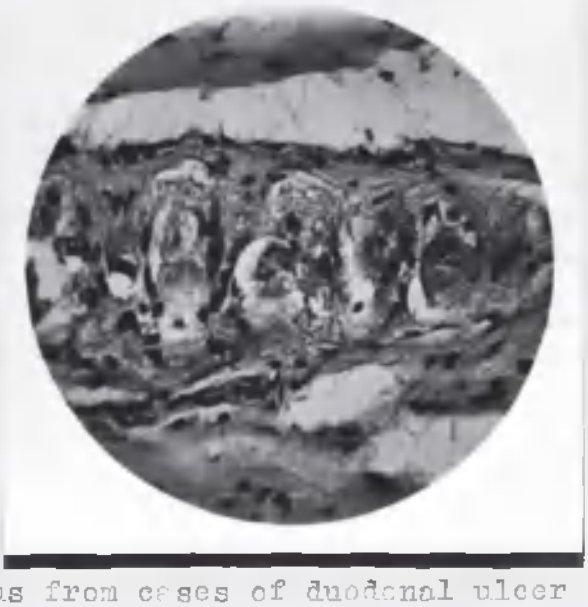
Fig. 6 Rat stomach after six months on S. Indian Diet. Note degenerative changes.

Plate X.



Figs. 11 & 12. Auerbachs Plexus from stomachs of duodenal ulcer cases in S. India showing infiltration of round cells and fibroblasts. Most of the ganglion cells show degenerative changes, the nuclei are pyknotic and flattened and pushed to one side of the cell. X 280





Figs. 13 & 14. Auerbachs Plexus from cases of duodenal ulcer in S. India showing marked degenerative changes in the ganglion cells. X 280

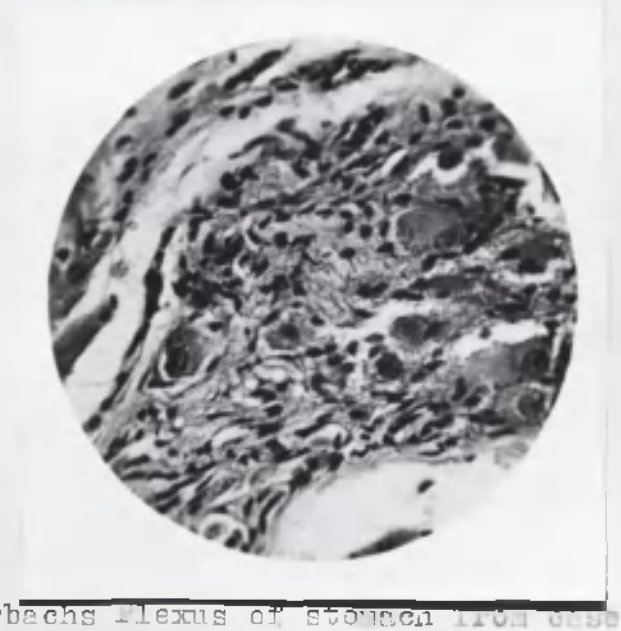


Fig.15. Auerbachs Plexus of stomach from case of duodenal ulcer in S. India showing infiltration with lymphocytes and fibroblasts. Some ganglion cells are normal but most show degenerative changes such as fragmentation of the nucleolous and pyknosis.

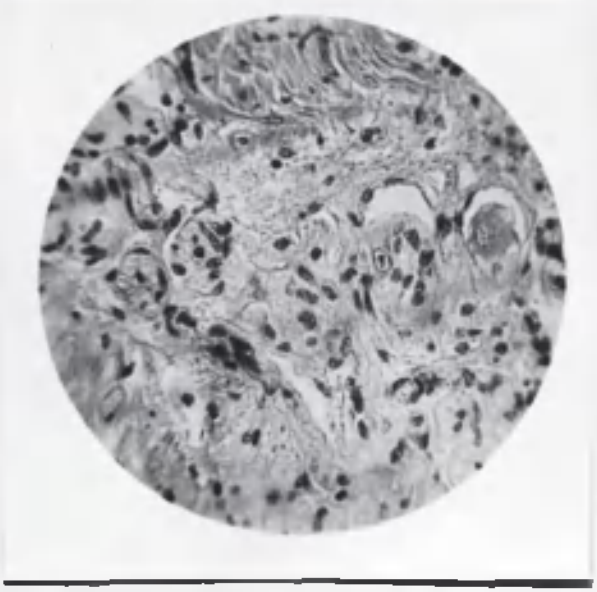


Fig. 16. Auerbachs Plexus from pyloric antrum of case with ulcer symptoms in S. India but in which no ulcer was demonstrated at operation. Ganglion cells show degeneration though infiltration is not marked.

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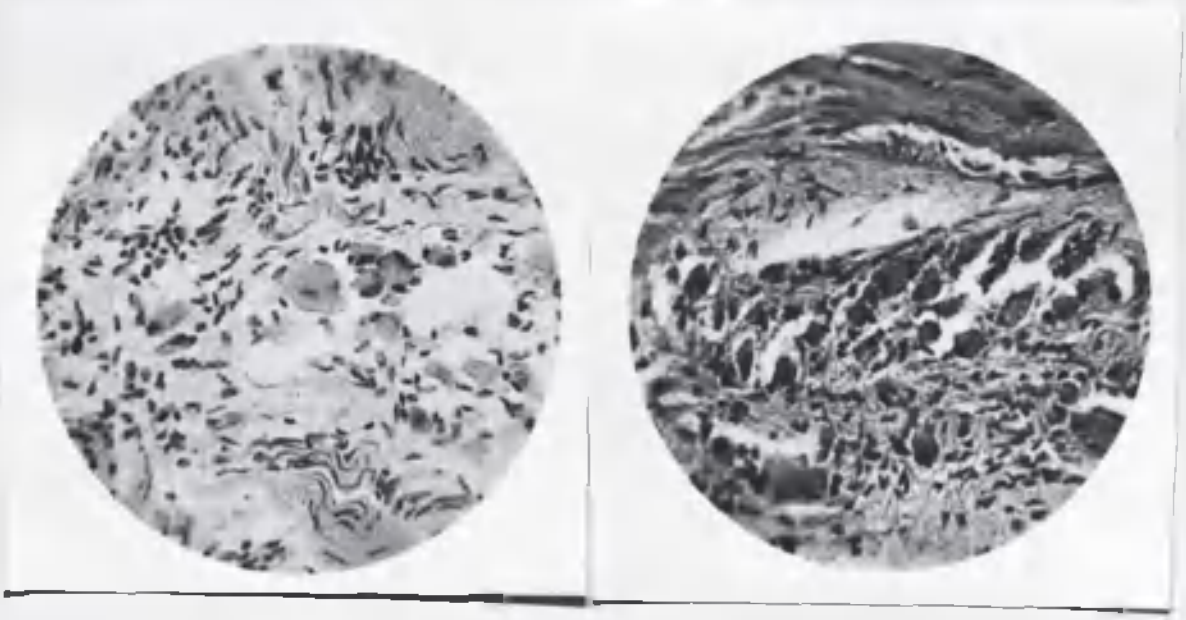
With Mr. Ian M. Orr's Compliments

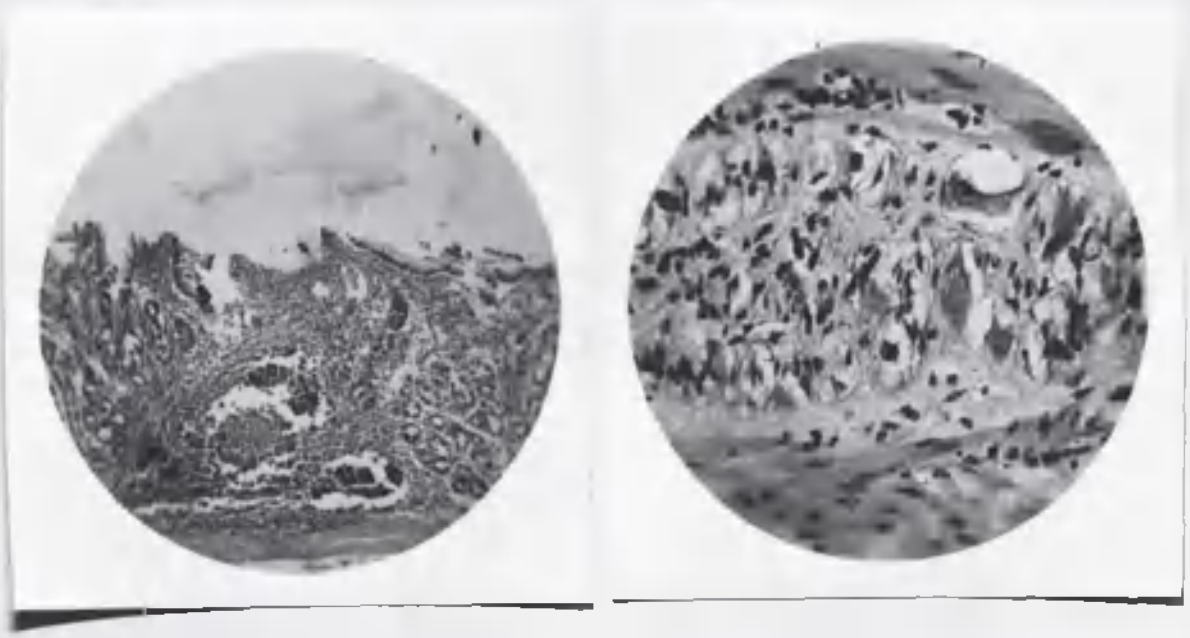
and Many thanks.

Plate XII.

Figs. 17 & 18. Auerbachs Plexus from stomachs of persons in Travancore who died by violence no ulcer being suspected or found. (Sections obtained by post-mortem.)
The Plexus is swollen in both cases and various stages of degeneration are seen. X 280



Figs 19 & 20. Dog III. Sections of stomach removed two months after tapioca feeding, showing lymph follicle of the mucosa which has nearly reached the surface and degenerative changes in Auerbachs Plexus.



PlateXIII.

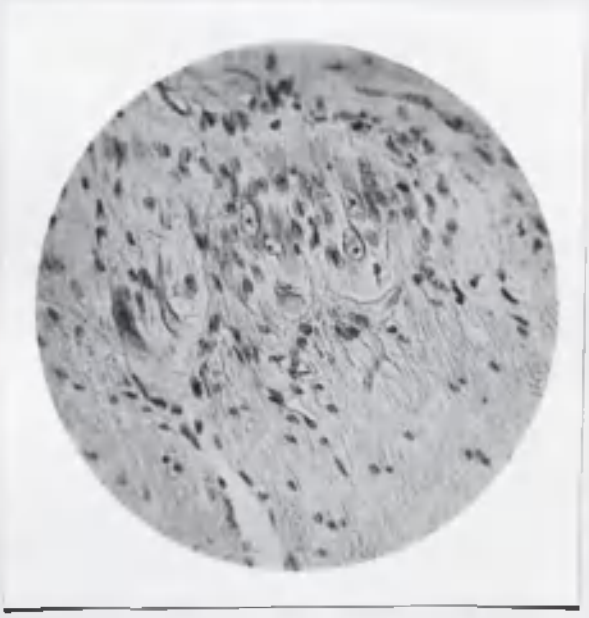


Fig. 21

Fig 22

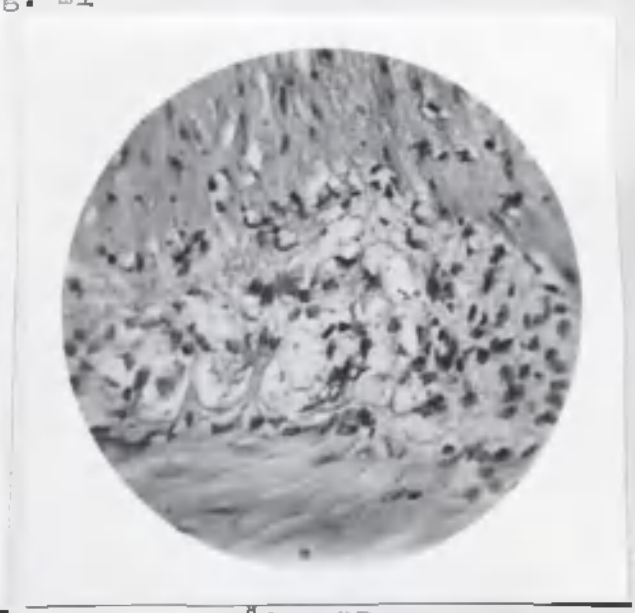


Fig. 23

Figs. 21 22 & 23. Dog No. 1. Auerbachs Plexus of stomach before and after two and four months tapioca feeding. Note the pyknotic and flattened nuclei of the ganglion cells in Fig.22 and the skeletons of degenerated cells in Fig.23.

Plate XIV.

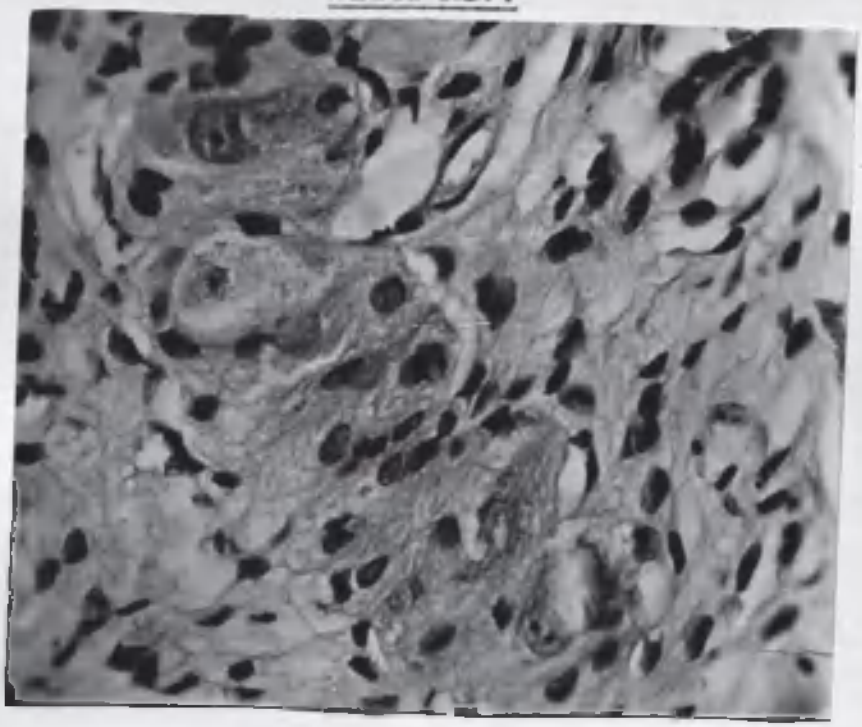


Fig. 25.

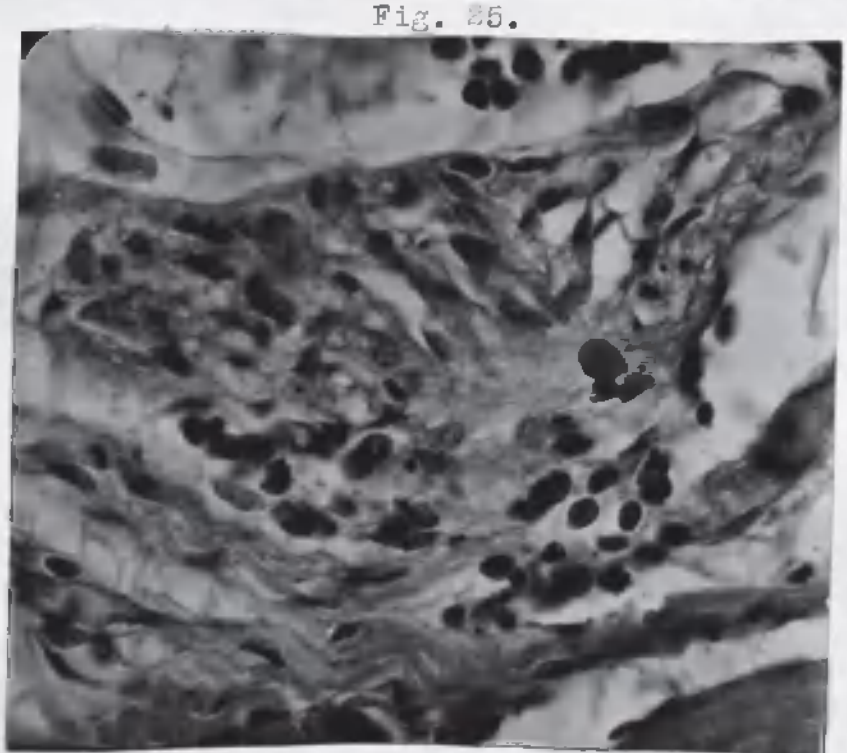


Fig. 26

Figs. 25 & 26. DogII. Auerbachs Plexus of stomach before and four months after tapioca feeding. In the normal section the ganglion cells are well seen with clear refractile nucleii and with well marked nucleolous and nuclear membrane. In Fig. 26 there is infiltration and fibrosis and almost complete disappearance of the ganglion cells.

Plate XV.

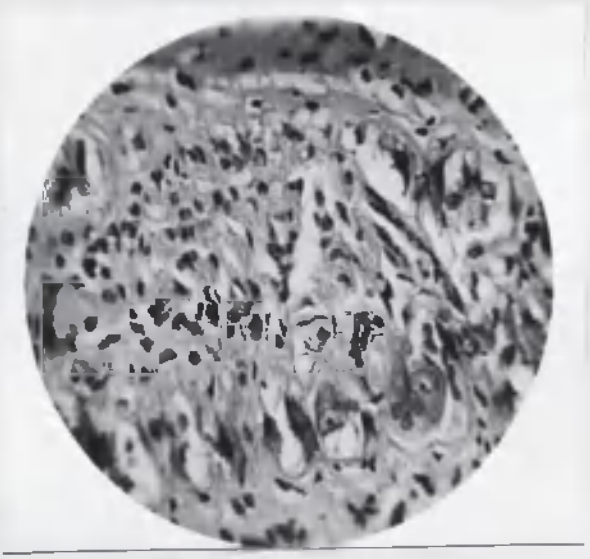
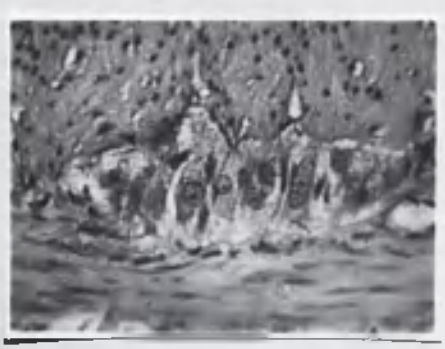
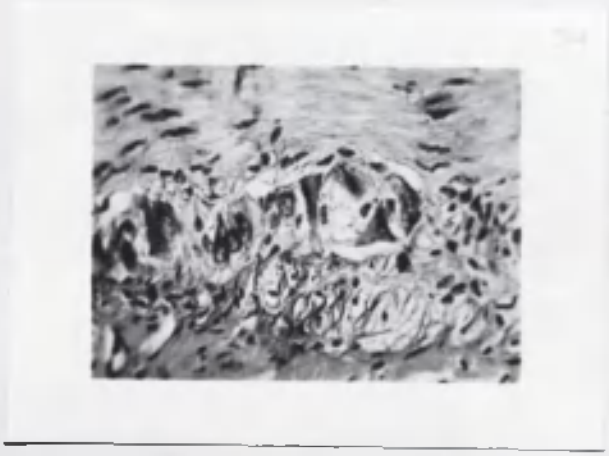


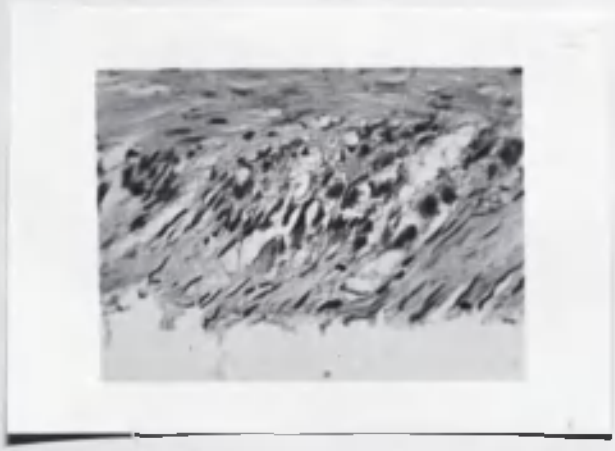
Fig. 24. Dog. V. Auerbachs Plexus of stomach 1½ months after tapioca feeding, showing cellular infiltration and degenerative changes in some of the cells. Note the normal ganglion cells along side pyknotic cells.

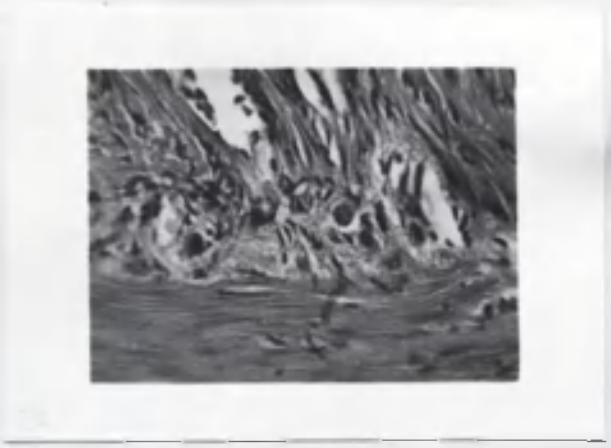


Figs. 27 28 & 29. Auerbachs Plexus of stomachs of rats fed on the stock diet. Note clear refractile nucleus. X 280

Plate VI.

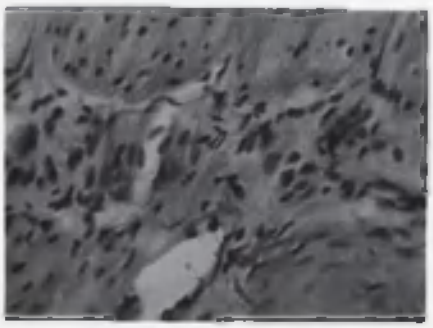






Figs.30 31 & 32. Auerbachs plexus of stomachs of rats fed on the tapioca diet of Travancore for 9,12,& 14 months respectivly. X 280

PlateXVII.



Figs. 33 34 & 35. Auerbachs Plexus of stomachs of rats fed on the cheap Madrassi diet for 9, 14, and 16 months respectivly.
X 280

Plate XVIII.

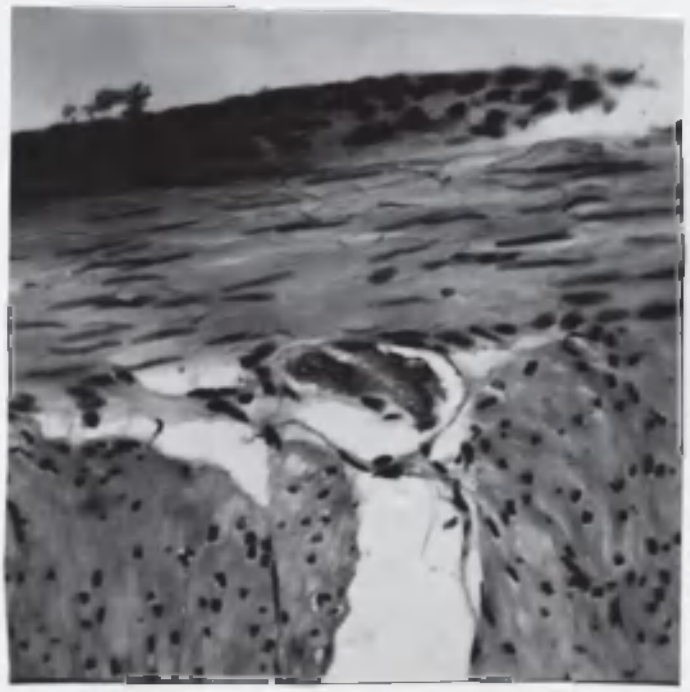


Fig.36. Auerbachs Plexus of a rat fed on the stock diet. X 335

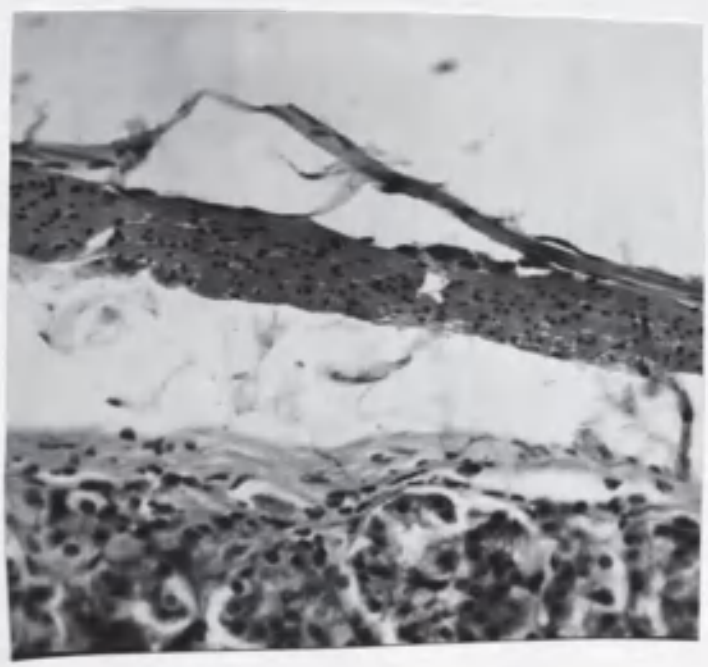


Fig. 37. Auerbachs Plexus of a rat fed on the tapioca diet for six months. Note the thinning of the muscle coats and pykmotic changes in the ganglion cells. X 335.