APPENDICITIS AND ABDOMINAL PAIN

A CRITICAL RE-EXAMINATION OF THE PATHOLOGY OF THE APPENDIX AND OF THE CLINICAL MANAGEMENT OF ABDOMINAL PAIN

A Thesis submitted to the University of Glasgow for the degree of Doctor of Medicine

by

John G.R. Hovie

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INTRODUCTION

Appendicitis is the commonest surgical emergency in general hospital practice and affects mainly an otherwise healthy age group (The Lancet, 1962).

For every 1000 people born, about 150 will have their appendices removed and one will die from appendicitis or the complications of appendicectomy. Of the 150 who have the operation, fifteen will have previously been in hospital with the same symptoms but will have been sent home without an operation. A further dozen will have been subjected to extensive out-patient investigation and several visits to hospital clinics before their operations. Young female patients are particularly likely to be included in these last two groups and are also likely to predominate among the 50 or so operations of the original 150 where a normal appendix will be removed (Harding, 1962).

Despite this high number of apparently mis-diagnosed cases, nearly all the group of 150 patients will be cured or "improved" by their operation and they will be saved the anxiety which is associated with having a "grumbling appendix." However, two or three of the group will be dissatisfied and will seek new advice elsewhere (McLennan and Watt, 1954).

Fifty of the original 1000 patients will be admitted to hospital at some time for observation as possible cases of

appendicitis but will be treated conservatively. Only half of this group have no further trouble after leaving hospital, and a number continue to have the same symptoms and make more visits to their medical advisers for reassurance.

About one quarter of those patients who were treated conservatively will eventually have their appendices out and in 60% of these cases the appendix will be normal.

Thus one in six of the population will be admitted to hospital at some time with a diagnosis of possible appendicitis. Whether appendicectomy will be performed often depends on the untested dogmas of the surgeon-in-charge. The present clinico-pathological investigation is designed to provide and analyse the evidence needed for rational action and therefrom to offer a guide to the management of possible appendicitis where immediate operation is not obviously the treatment of choice.

It is generally accepted that the treatment for acute appendicitis is early operation and that if an appendix is abnormal it should be removed (Rees, 1952; Campbell and McPhaill, 1958; Jewers, 1959; Shepherd, 1960). Even Coldrey, (1956), who advocates

conservative treatment if the acute attack has lasted more than 24 hours, agrees that for a short clinical history, operation is preferable. It is also accepted that exact diagnosis in a patient with suspected appendicitis is often difficult (Wass, 1955) and that mild appendicitis will often settle spontaneously. I have found that where surgeons adopt a radical or predominantly operative approach to the treatment of possible appendicitis, a higher number of abnormal appendices is removed than if the approach is conservative or predominantly non-operative (Howie, 1964).

From this it must be concluded that the conservative approach to treatment results in failure to remove abnormal appendices. It is also true that with improved anaesthetic and surgical techniques, uncomplicated appendicectomy is no longer a dangerous operation; this may have "in some measure hampered the growth of clinical judgement" (Molony et al, 1950). Nevertheless, as mentioned above, removal of a "normal" appendix is often curative whether for physiological or psychological reasons (Shelley, 1938; Alvarez, 1940; McLennan and Watt, 1954; Westlake, 1954; Leak, 1954; McFarlane, 1954; Gallagher and Stevenson, 1955; Ingram and Evans, 1965).

Strong views on the justification of operating on doubtful cases of appendicitis are held by many people and disagreement is

common. Evidence to support the radical or conservative point of view has rarely been given. A good "control" series of patients who have not been operated on is lacking (Wickers, 1954; Brit. med. J., 1955) although it has been argued that patients who have had operations should act as their own controls (Leak, 1954). It is significant that there is not even agreement on what constitutes a normal appendix.

Hertzler's definition of a normal appendix is one "which performs its function, if it has any, in complete harmony with the well-being of the individual" (Hertzler, 1926). In this definition we have the possible answer to the basic difficulty of classification of appendices which is created by the common finding of minor degrees of acute inflammation (which pathologists cannot accept as truly normal) without symptoms of abdominal pain (Aschoff, 1932; Shelley, 1937; Campbell et al, 1961; Stevenson and Sneddy, 1961; Howie, 1964). Three main groups of appendices may be recognised;

(1) those showing histological abnormalities which are normally associated with symptoms;

(2) those showing histological abnormalities the association of which with symptoms has never been satisfactorily established; and

(3) those without histological abnormality.

To find an objective basis for discussion, cases must be

allocated to these groups and examined on the basis of correlation of histological and operative findings combined with a follow-up study of the clinical result.

Only two good reviews of this type are available, the first of which uses histological terminology which is not now acceptable (Shelley, 1938) and the other of which gives no reference to detailed histological changes (McLennan and Watt, 1954). Typical of the difficulties inherent in work of this type is the abuse which McLennan and Watt received for their thoughtful article which included "the naïve assumption that the diagnosis (of chronic appendicitis) was correct if the patient remained free of pain (after operation)", (Van Meurs, 1954). This exemplifies the difficulty in balancing the exacting requirements of scientific proof and the humanitarian ones of providing satisfaction through relief of symptoms.

Boyd (1942, page 293) stated that "today every appendix is condemned by some pathologist somewhere" and called for a study of the type described above, by a surgeon with a training as a pathologist. Campbell et al. (1961) likewise stated "it would seem important to decide 'when is a superficial appendicitis responsible for symptoms and when is it not'" and called for a thoughtful correlation of clinical, operative and histological

findings. Lee (1961) emphasised the need for a British study of this type with particular reference to young females; and he quoted Morris (1957) as stressing the value of the epidemiological approach to a problem of this type to "define its extent and put individual clinical experience in a community perspective."

Good reviews of the problems discussed above are contained in leading articles in The Lancet (1962) and British Medical Journal (1955; 1964; 1965a).

The three purposes of the present work are:

(1) to define the "normal" appendix histologically and separate abnormal appendices into those where the histological changes are shown to be likely to cause symptoms or likely not to cause symptoms. This study introduces the use of the prussian-blue reaction (Howie, 1966) as an index of recent appendicitis and uses it to examine some of the relationships of the appendix to abdominal pain;

(2) to introduce criteria to assess the morbidity and mortality associated with operative and non-operative treatment of abdominal pain and to use these criteria to find the best form of management for the patients whose care is at present the cause of clinical disagreement; and

(3) to review some epidemiological and social problems connected with appendicitis and appendicectomy.

SECTION 1

A CLINICO-PATHOLOGICAL STUDY OF THE APPENDIX

CHAPTER 1

THE HISTOLOGICAL DIAGNOSIS OF APPENDICITIS

Acute inflammation is the only common abnormality of the appendix. Although Cope (1963, page 45) has stated that "the different degrees of inflammation of the vermiform appendix have for many years been well described and understood....," the crux of the problem of defining the relation between the appendix and abdominal pain lies in the fact that this statement is not correct.

Fully developed appendicitis is an easy histological diagnosis to make and correlates well with clinical acute appendicitis. Small foci of acute inflammation however, are commonly found on histological examination both in the presence and absence of abdominal pain. This creates confusion over their interpretation, and thus over the definition of a histologically normal appendix. This absence of standard objective definitions caused three pathologists who each examined one set of material to agree on the diagnosis of only 94 of 165 cases - 56% - (Barraclough et al, in preparation). Another group of two pathologists who examined two consecutive series of cases found a ninefold increase in the number of appendices showing mild abnormality in the second

series (Campbell et al, 1961). Details of these studies and comparison with the results to be obtained using objective histological criteria or purely clinical criteria are given in Chapter 6 of this Section. Before attempting to discuss the significance of any group of histological changes an essential preliminary is to define terms so that different histologists may be able to understand them unequivocably and - accepting their validity as criteria of appendicitis - reach a uniform diagnosis on any given sample of appendices.

Aschoff's "appendicitis fugax," (Aschoff, 1932), the "focal and superficial appendicitis" of Campbell et al. (1961), Shelley's "chronic catarrhal appendicitis," (Shelley, 1937, 1938), Anderson's "focal appendicitis," (Anderson, 1961, page 803) and my own "limited acute appendicitis," (Howie, 1964) may well all be the same abnormality. But my own definition is the only one published which refers to the upper and lower limits of each histological category and is thus able to allow reproducible results.

This chapter enlarges on the terms "normal appendix" "limited acute appendicitis" and "complete acute appendicitis" with particular reference to the borderline changes between normality and abnormality.

Naked-eye examination

The length of a normal appendix shows a considerable range of variation with a mean of 8 cm. It is white and slender, the surface often covered by a network of small veins. In acute appendicitis the organ is tense and swollen, often mottled or gangrenous with a fibrinous covering. Intermediate changes are common.

Many surgeons examine the mucosa of an appendix removed at operation for punctate ulceration or even alterations in colour (Crymble and Forsythe, 1949). This involves opening the unfixed appendix. The traumatic artefact so caused makes later histological examination difficult especially where lesions of limited extent are present. From the pathologist's point of view preliminary fixation of the intact unopened appendix is essential. A block to be sectioned longitudinally is prepared from the tip of the organ and two or more blocks for transverse section are taken from representative portions of the remainder. Trauma from this procedure is minimal and additional blocks can be examined later if required. Because of the rapid longitudinal spread of early appendicitis it is unlikely that evidence of inflammation starting from a source which has escaped sampling by this procedure will be overlooked.

In the present investigations surgeons were requested to submit appendices intact in formalin. This was nearly always done and made a high standard of material available for histological diagnosis. The few opened appendices were submitted by senior surgeons, usually operating on colleagues or their relatives. It is of interest that in these conditions small "lesions" seen only by naked-eye examination of the opened appendix and often not capable of histological confirmation were regarded as diagnostic of appendicitis by surgeons who disputed the significance of histologically demonstrable "limited acute appendicitis," on the grounds that this histological entity may be found on occasions unrelated to abdominal pain. This exemplifies one of the problems facing a histologist working in a clinical field where everyone from house-surgeon upwards is tempted to regard himself as an expert.

The most useful naked-eye finding in separating normal from abnormal appears to be the presence of faecal contents in the lumen of the appendix. Very few appendices containing even a ribbon of soft faeces at the tip show any histological abnormality. An exception to this rule is of course the genuine faecolith which is rarely seen without accompanying obstructive appendicitis. A cylinder of impacted faecal matter should not be regarded as a

fig. 1

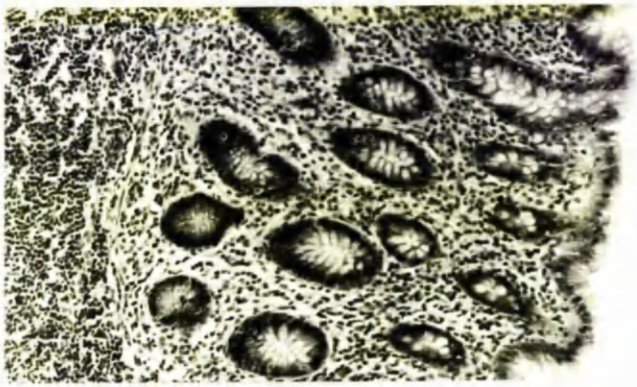


fig. 2

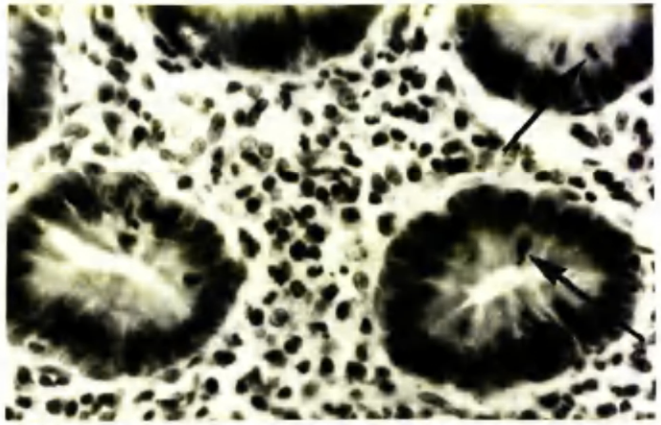


fig. 3

Figure 1 Normal appendix, transverse section (Haemalum and Eosin, x13).

Figure 2 Normal appendix, showing loosely-packed stroma. Note low frequency of mitotic figures in mucosal glands (H & E, x140).

Figure 3 Mild acute appendicitis, showing higher incidence of mitotic figures (arrowed) in mucosal glands (H & E, x340).

Figure 4 Normal appendix, showing typically active germinal centres (arrowed) in lymphoid tissue (H & E, x50).

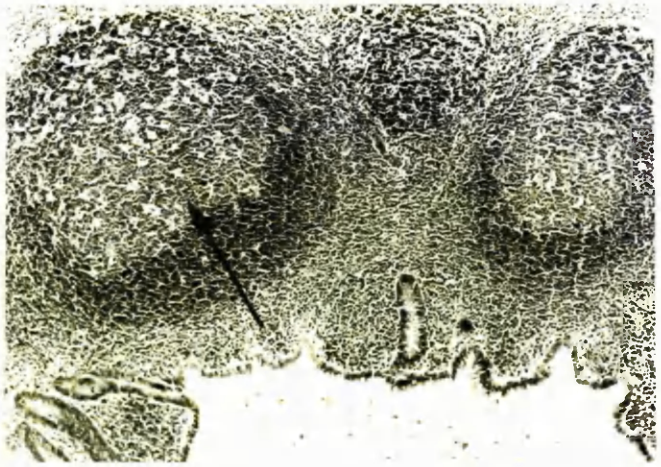


fig. 4

faecolith.

Histological Examination

The Normal Appendix (fig. 1)

The mucosal pattern is that of large bowel although Paneth cells are a normal finding. The stroma is loosely filled with small darkly-staining cells (fig. 2). A densely cellular mucosa is the first indication of possible abnormality elsewhere in the organ. This is in keeping with the early views of Landsdowne and Williamson (1914) who described a packing of the mucosa with lymphocytes as the first change in appendicitis, mucosal ulceration and secondary infection following. Plasma cells and eosinophils may be present in considerable numbers. No relationship appears to exist between mucosal eosinophilia and threadworms in the lumen or even within the mucosa. Mitotic activity in the glands is usually low in normal appendices but may be noticably high in acutely inflamed appendices (fig. 3).

Appendicular lymphoid tissue decreases with age from about a dozen follicles per transverse section (fig. 1) at 20 years of age to less than half after 50 years of age. Germinal centres are usually active (fig. 4).

The amount of lymphoid tissue may vary greatly, however,

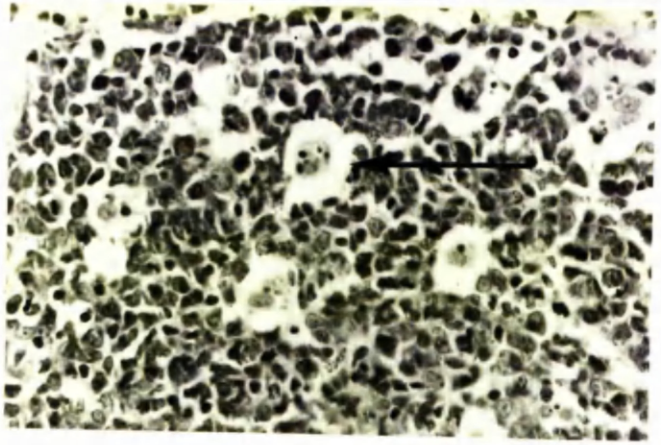


fig. 5

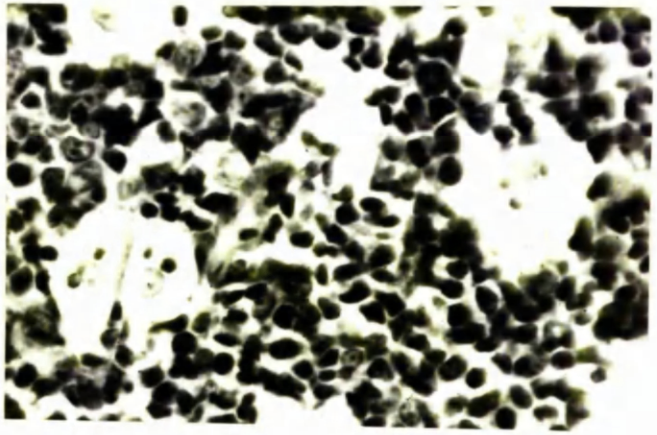


fig. 6

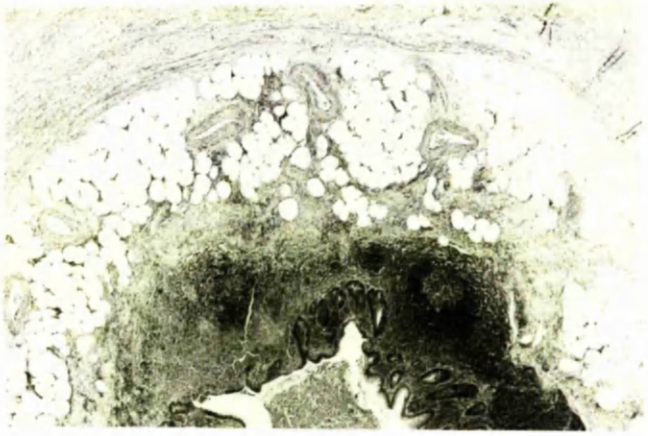


fig. 7

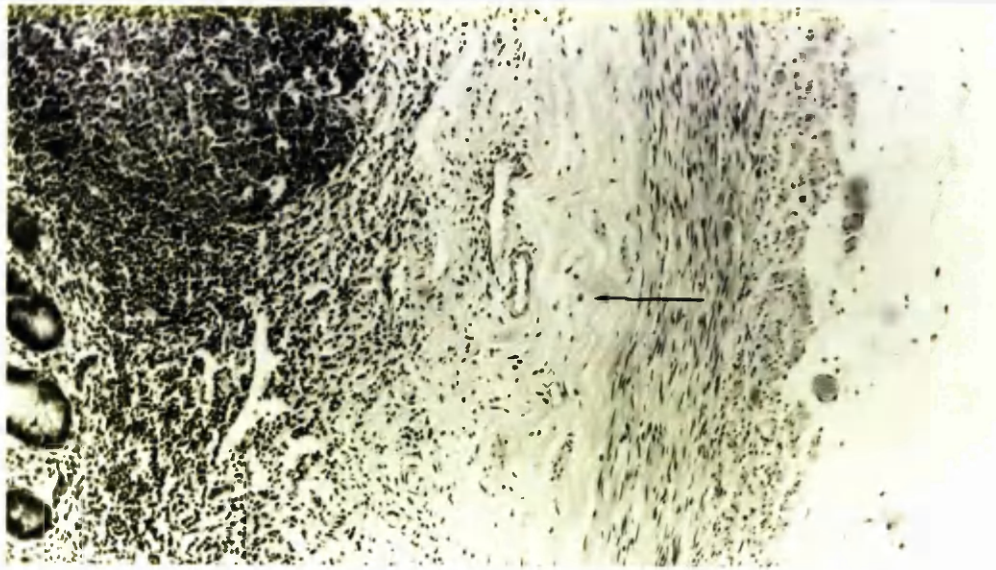


fig. 8

Figure 5 Normal appendix, showing basophilic inclusions (arrowed) in reticulum cells in germinal centres (Haemalum and Eosin, x390).

Figure 6 Normal appendix, showing basophilic inclusions as in fig. 5 at higher magnification (H & E, x630).

Figure 7 Acutely inflamed appendix, showing gross fatty infiltration of submucosa (H & E, x40).

Figure 8 Normal appendix, removed from female aged 16, showing:-

(1) equal thickness of submucosa and muscularis, and

(2) occasional lymphocytes and plasma cells (one arrowed) in submucosa (H & E, x330).

within any age group. Lymphoid hyperplasia does not appear to be a genuine pathological entity and should be regarded only as a descriptive term. The lymphoid cells often contain deeply basophilic inclusions (figs. 5 and 6), probably phagocytosed mucosal debris. Misinterpretation of this appearance may explain why Collins (1955) reported that 8% of appendices showed evidence of histoplasmosis whereas I found no examples of this condition in over 1400 cases. Christopherson et al. (1932) and Stephenson and Snoddy (1961) also failed to find any cases of histoplasmosis in their own series.

The submucosa varies in thickness inversely with the amount of lymphoid tissue. Submucosal fibrosis is thus of doubtful value as an index of past inflammation because of the difficulty of assessing the amount of fibrosis due to lymphoid regression.

Submucosal fat also increases with age and is usually found encircling blood vessels. In young patients it is usually seen only in small amounts but there is no objective division of normal from abnormal. An extreme degree of fatty infiltration is seen in fig. 7. Occasional lymphocytes, plasma cells, or eosinophils may be found in the submucosa (fig. 8). Mast cells may be found in this layer as in the muscularis and subserosa.

The muscularis is approximately the thickness of the submucosa

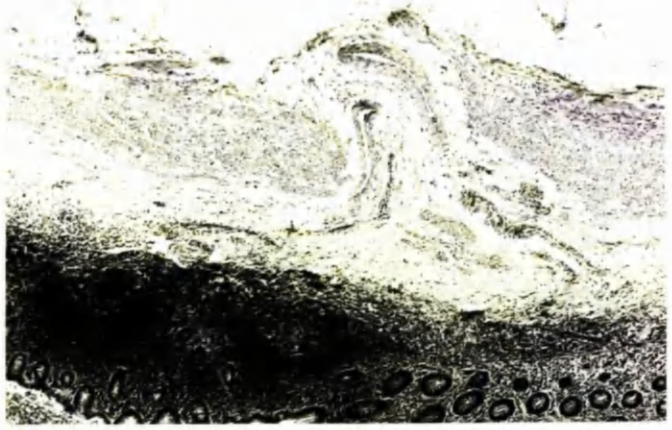


fig. 9

fig. 10

fig. 11

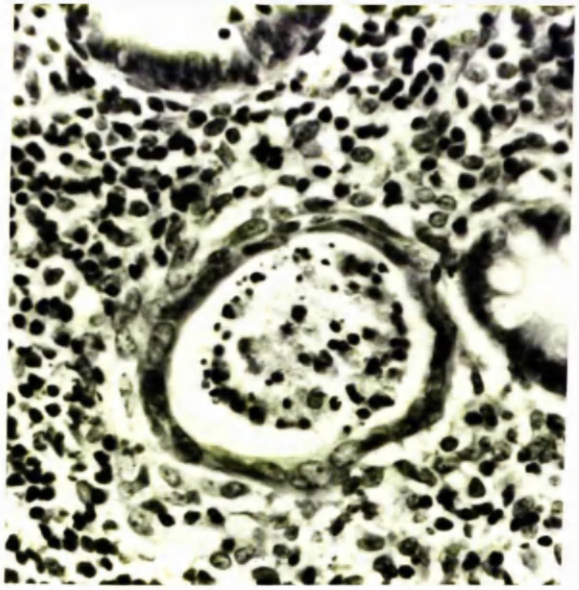


fig. 12

Figure 9 Acutely inflamed appendix, longitudinal section, showing passage of blood vessels through break in muscle layer (Haemalum and Eosin, x45).

Figure 10 Hypertrophy of muscle layer with irregular replacement by fibrous scar tissue probably due to previous episodes of inflammation. This patient gave a history of previous pain suggestive of appendicitis (H & E, x60).

Figure 11 Acutely inflamed appendix, showing lymphoid follicles in the serosa (H & E, x40).

Figure 12 Normal appendix, showing mucosal gland which contains eosinophilic debris but is not associated with surrounding acute inflammation (H & E, x190).

in the adolescent (fig. 8), and about two-thirds that of the thicker adult submucosa. Blood vessels pass through clefts in the muscle (fig. 9) but gross derangement of the muscle by fibrous bands suggests previous inflammation (fig. 10). Inflammatory cells should be absent from this layer.

The serosa is similar to that of serosal surfaces elsewhere. Some plasma cells and lymphocytes or even complete lymphoid follicles (fig. 11) may be a normal finding in the subserosa.

Polymorphonuclear leukocytes may occasionally be seen in small numbers in the appendix wall in dilated blood vessels or lymphatics but are not normally found extravascularly.

Occasional crypts contain eosinophilic debris and are surrounded by an acellular mucosa containing no or only occasional reactive pus cells. These appearances may be accepted as normal (fig. 12).

Pus cells should be absent from the lumen of the normal appendix except in relation to hard faecal masses (fig. 13), foreign bodies or worms (fig. 14). Worms may be associated with large accumulations of pus in the lumen and finding pus cells with a normal mucosa has correctly suggested the presence of worms at another level on several occasions.

All appendices fulfilling the criteria of normality listed

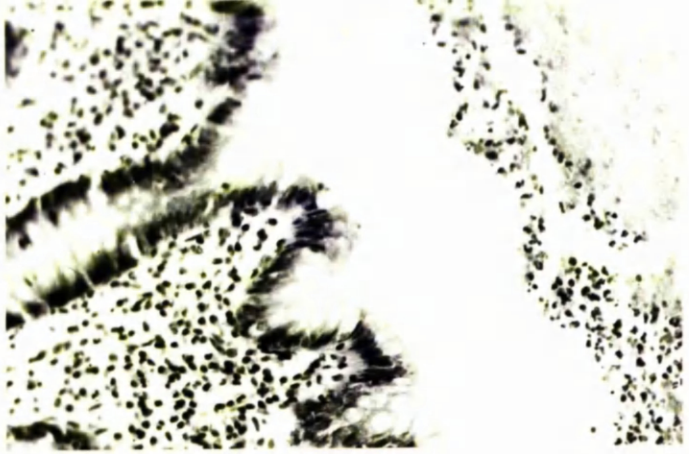


fig. 13

fig. 15

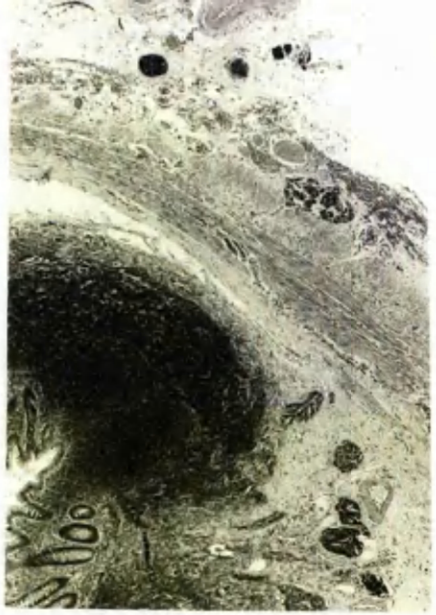


fig. 16

fig. 14

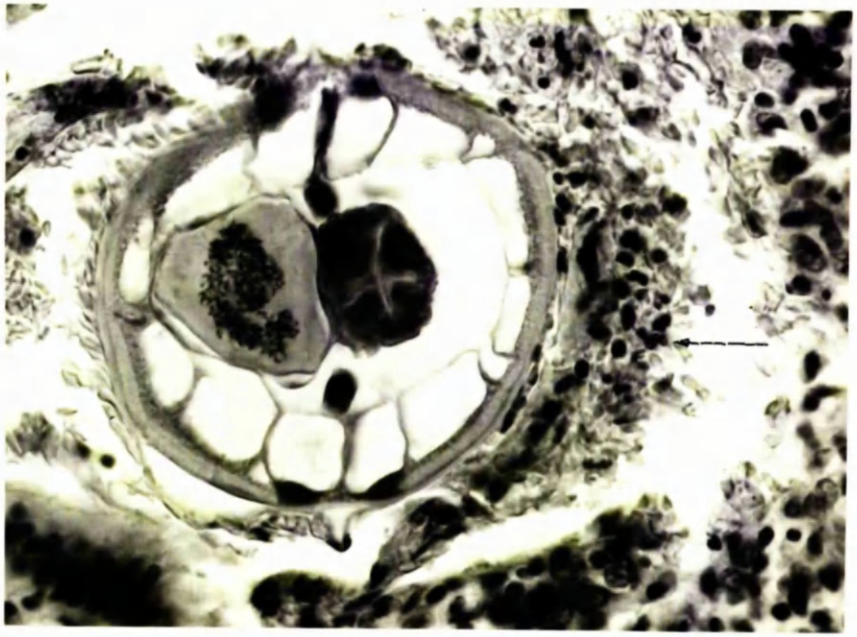


Figure 13 Normal appendix, showing pus cells at edge of piece of hard faecal matter (Haemalum and Eosin, x275).

Figure 14 Normal appendix, showing pus cells (one arrowed) in relation to worm in appendix lumen (H & E, x600).

Figure 15 Normal appendix, showing haemorrhage into lumen and mucosa due to trauma at operation (H & E, x150).

Figure 16 Normal appendix, showing packing of lymphatics with lymphocytes due to trauma at operation (H & E, x140).

above were classed as NORMAL in the present studies.

Traumatic Artefact The histological trauma caused by handling and clamping the appendix at operation is well known and the possibility that minor inflammation may also be an operative artefact is always emphasized by those anxious to dispute a histological diagnosis of mild appendicitis.

The characteristic changes due to trauma are tears or abrasion of the mucosa, haemorrhage within the mucosa and lymphoid tissue, and extrusion of mucosal elements into the lumen of the appendix (fig. 15).

Aggregations of lymphocytes may be found in the submucosal and subserosal lymphatics (fig. 16). In the presence of any of these changes great caution should be used in interpreting changes which would otherwise be diagnosed as appendicitis.

Attempts to study untraumatised post-mortem appendicular histology are not satisfactory because of the rate at which autolysis of the mucosa occurs. The patients coming to post-mortem are also of a different age group from those normally having surgical appendicectomy.

Acute Appendicitis

The obviously abnormal appendix is as easily defined as the

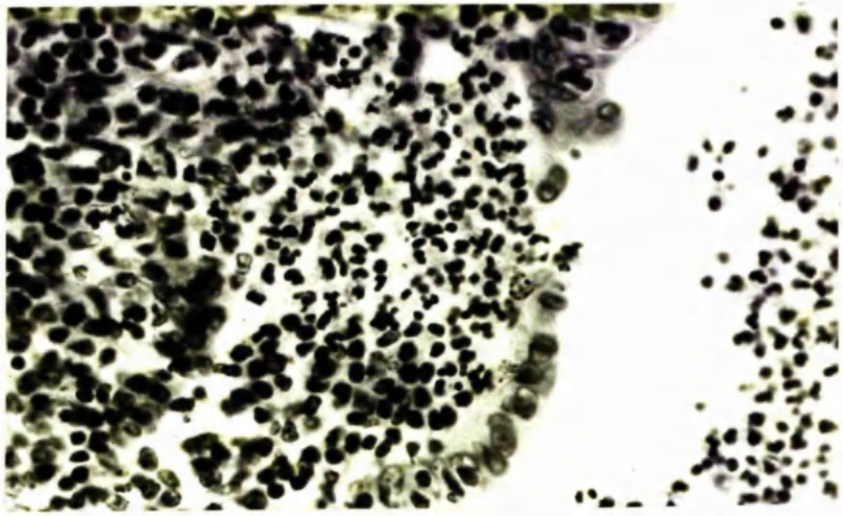


fig. 17

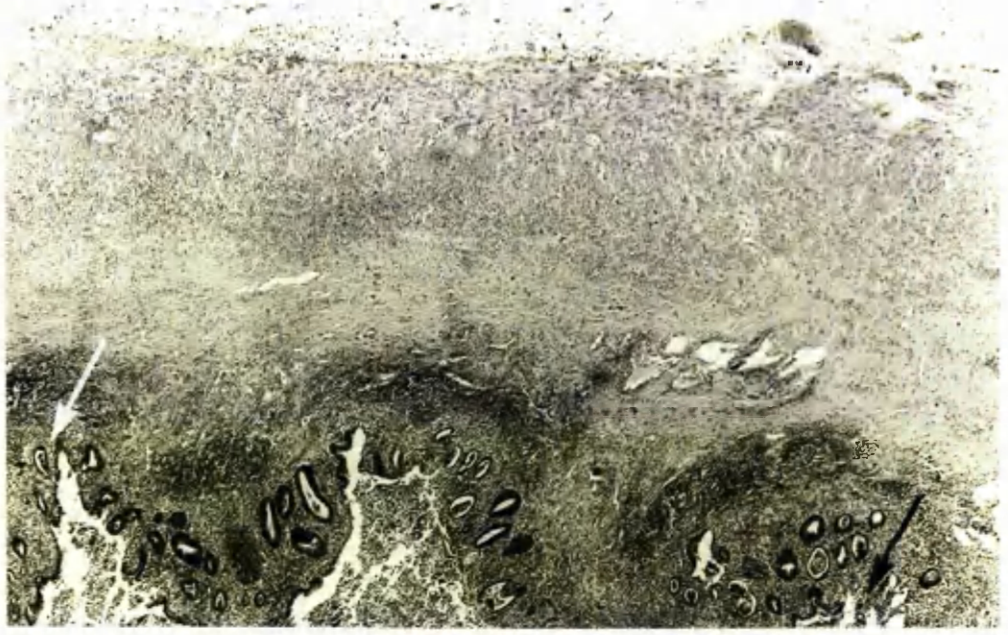


fig. 20

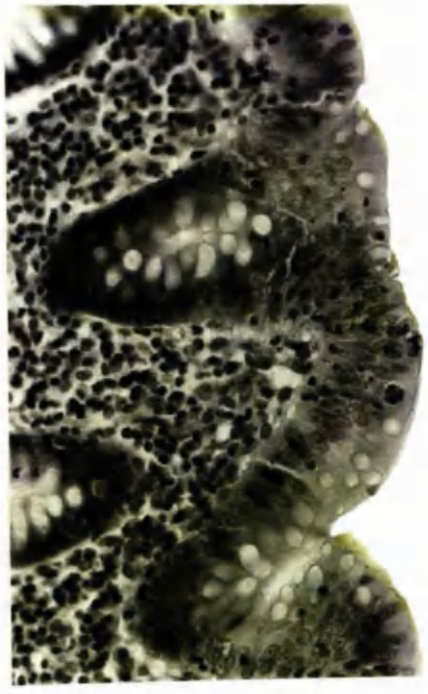


fig. 18

fig. 19

Figure 17 Minimum requirements for diagnosis of acute appendicitis, showing focus of pus cells in mucosa (left), early ulceration of mucosa, and pus cells in lumen of appendix (right) (Haemalum and Eosin, x630).

Figure 18 Same appendix as in fig. 17, showing tracking of pus cells from the mucosa through the mucosal lining (H & E, x285).

Figure 19 Limited acute appendicitis, showing typical mucosal changes but no evidence of abnormality in the submucosa (H & E, x135).

Figure 20 Mild complete acute appendicitis, showing mucosal lesions varying from minimal (white arrow) to fully developed (black arrow) acute appendicitis within one field (H & E, x75).

obviously normal appendix. The dividing line between normal and abnormal, however, is not easy to define and to be of value, must be objective.

The minimum requirements for a diagnosis of appendicitis are:

(1) pus cells in the lumen of the appendix;

(2) a focus of pus cells - even a small one - in the mucosa of the appendix; and

(3) direct communication between these either through an ulcerated mucosa or by definite tracking of pus cells through an intact mucosa (fig. 17, 18).

Where the inflammatory exudate does not extend to the serosa at any part of the appendix the diagnosis is LIMITED ACUTE APPENDICITIS: where the exudate involves the serosa, the diagnosis is COMPLETE ACUTE APPENDICITIS.

This division is generally easily made, most cases of limited acute appendicitis having no or minimal involvement of even the submucosa (fig. 19) compared with the heavy aggregates of pus cells found in all coats in complete acute appendicitis. Figure 20 shows the terminal portion of an appendix with relatively mild complete acute appendicitis; changes progressing from minor localised limited acute lesions to fully developed appendicitis may be seen. Further division of acute appendicitis into

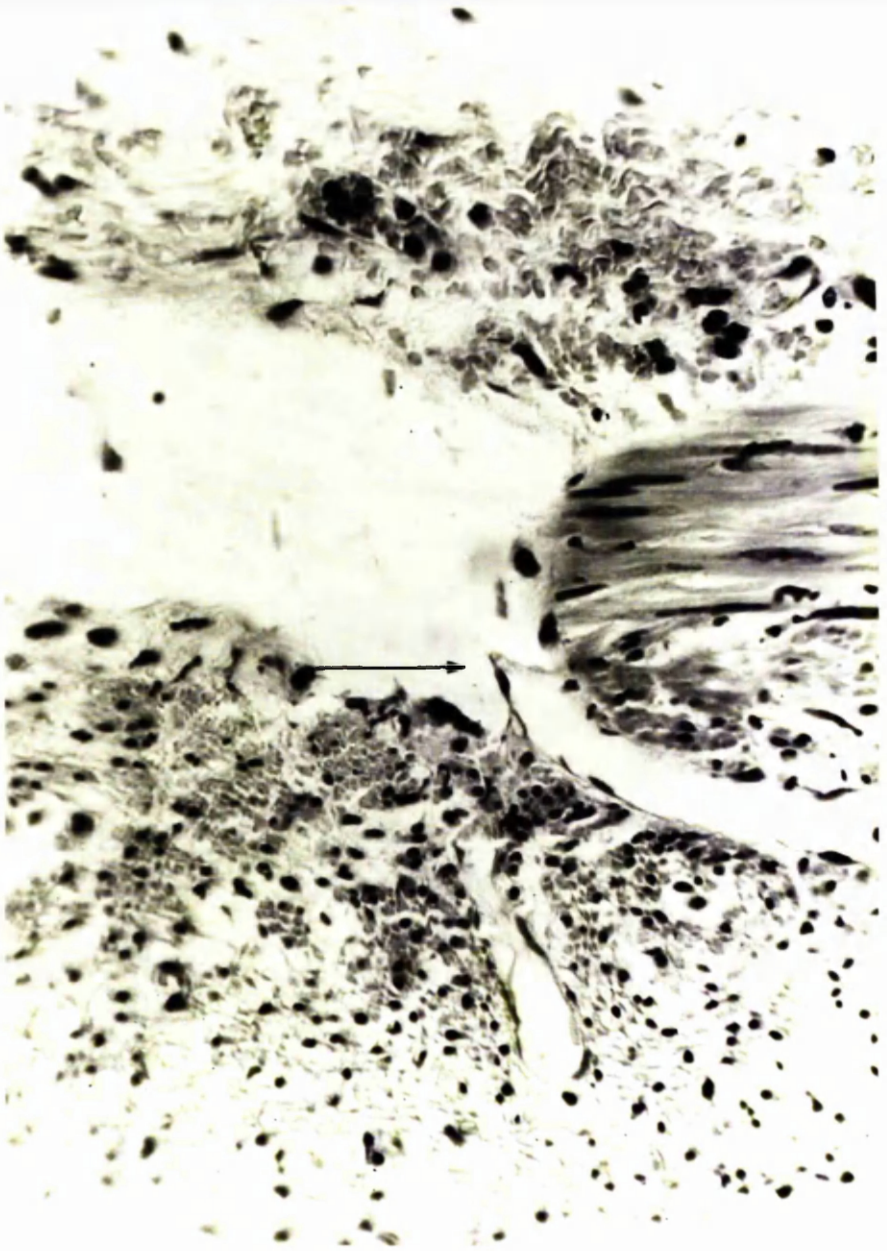


fig. 21

Figure 21 Normal appendix, showing lymphatic channel passing through muscularis from submucosa (below) to subserosa above. Note valve on lymphatic (arrowed) apparently preventing flow of lymph from serosa to submucosa (Haemalum and Eosin, x460).

obstructive, suppurative or mixed obstructive-suppurative classes can be made histologically but is not relevant to this work and has been omitted.

The spread of inflammatory exudate depends on the lymphatic drainage from the primary focus. This was described in great detail by Seng (1932) on the basis of Indian-ink injection studies. He described separate networks in each coat of the appendix with drainage channels transversely through the mucosa and longitudinally along the submucosa and serosa. Because pus spreads easily down the lumen from a primary focus and rapidly along the submucosa and subserosa after preliminary transverse spread from the mucosa, examination of transverse sections will generally suggest the presence of active acute appendicitis even in the absence of mucosal abnormality at that level. The muscularis is usually the last layer to be involved in the inflammatory process. It is unlikely that primary peritonitis can spread backwards to the mucosa to cause secondary appendicitis and I have, in fact, demonstrated a valve on a connecting lymphatic in the muscularis (fig. 21) which would prevent passage of pus cells from serosa to submucosa by the lymphatic route.

Where the appendix appears acutely inflamed in all layers except the muscularis, the diagnosis is still regarded as complete

acute appendicitis because, according to Morley's theory of the genesis of right iliac fossa pain in appendicitis (Morley, 1928), the important clinical change of position of pain coincides with the onset of peritoneal changes.

One of the abnormalities not covered by these criteria is the finding of acute inflammation in all coats of the appendix except the mucosa which itself may appear quite normal. Pus may or may not be present in the lumen. Examination of several blocks from these appendices usually reveals the basic lesion to be a diverticulitis of the appendix. This type of appendix is usually much thickened. It is classed as complete acute appendicitis because of serosal involvement. This appearance is unusual.

If these criteria are adopted, few errors of classification need arise. This is particularly true if careful examination of representative blocks is carried out as described and if pus in the lumen or on the serosa is never allowed to pass unexplained without careful search for appendicitis in several other blocks.

Atypical Appearances

A number of appendices classed as normal because they do not fulfil these criteria of acute appendicitis, differ from the typical appearances of the normal appendix described at the start

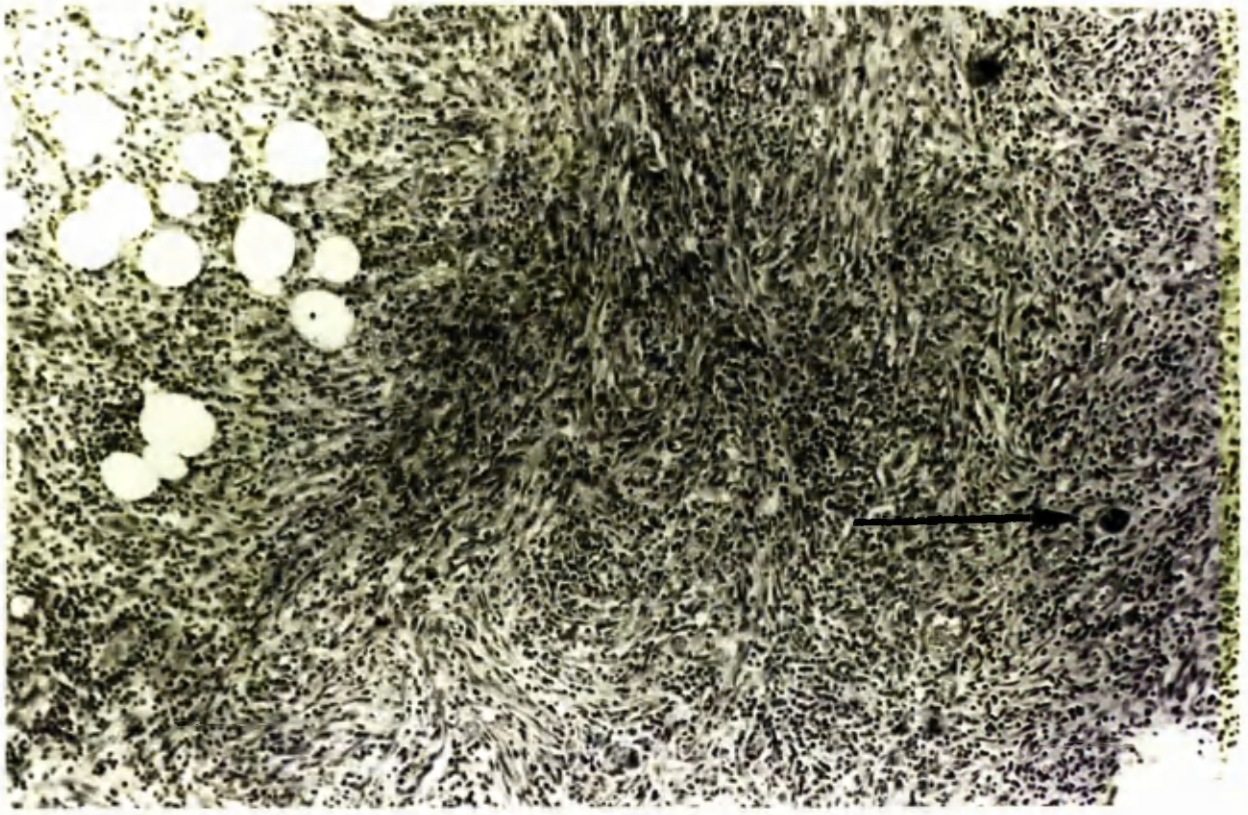


fig. 22

Figure 22 Appendix removed six weeks after clinical diagnosis of appendix abscess had been made; showing submucosa (top left) and muscularis (right) over-run by subacute inflammatory cells including giant cells (one arrowed) (Haemalum and Eosin, x110).

of the chapter. This group of atypical cases (109 of 1412 cases studied) sub-divided into five minor groups (a-e below) for separate consideration. Although each is small, the combined size of the five groups is large enough for misinterpretation of their significance to alter materially the results of a histological survey.

(a) Unrelated inflammation Cases in this group showed acute serosal inflammation with no evidence of primary appendicitis. Usually the appearances were explained by the operative finding of perforated peptic ulcer, salpingitis or some similar acute intra-abdominal lesion. If this was not so, cases were only included under this heading after careful examination of several blocks of appendix.

(b) Resolving appendicitis Cases in this group had one of two appearances. The more common was the mixture of polymorphs, subacute inflammatory cells, fibroblasts, and sometimes foreign body giant-cells seen in the wall of an appendix removed some time after an appendix abscess (fig. 22). The active mucosal lesions which would allow a diagnosis of active appendicitis to be made were absent. The second appearance showed a breach of mucosa plugged by polymorphs, often apparently meshed in fibrin but not associated with passage of pus cells from mucosa to lumen.

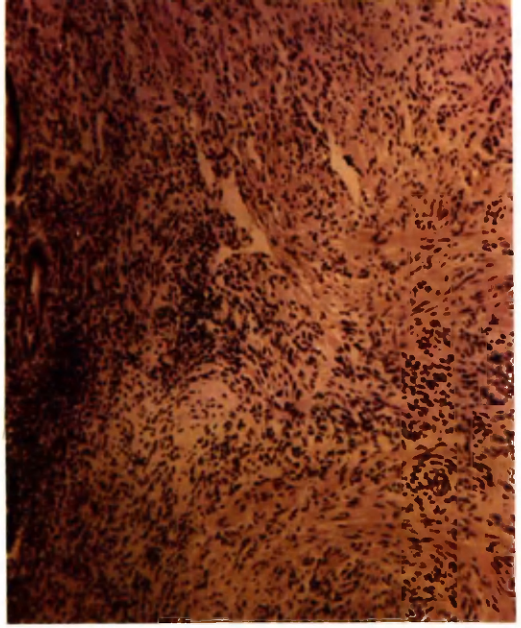


fig. 23

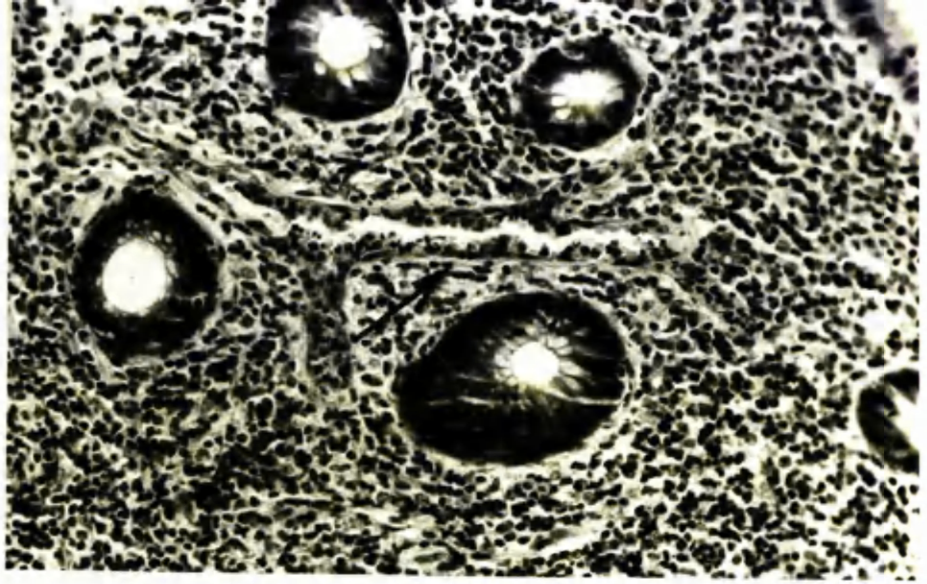


fig. 25

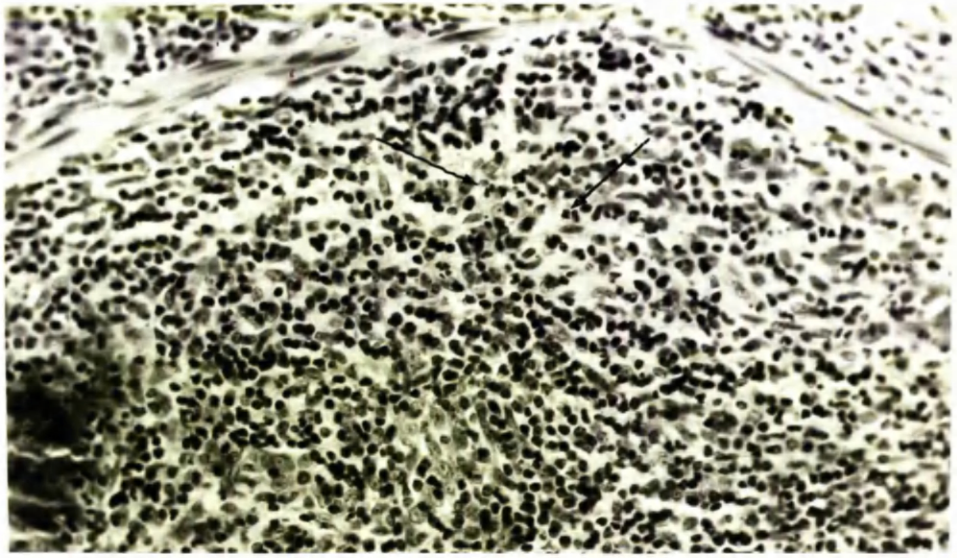


fig. 24

Figure 23 Subacute appendicitis, showing numerous eosinophils in inflammatory exudate in submucosa. No evidence of acute appendicitis elsewhere in appendix (Haemalum and Eosin, x100).

Figure 24 Pre-acute appendicitis showing polymorphs in mucosa (two arrowed) of appendix which was otherwise within normal limits (H & E, x300).

Figure 25 Pre-acute appendicitis showing mucosal lymphatic containing numerous polymorphs (arrowed) in appendix which was otherwise within normal limits (H & E, x190).

Indeed there were usually no pus cells in the lumen. Cases of this type were not common, totalling six in all.

(c) Subacute and chronic appendicitis Although subacute and chronic appendicitis are terms commonly used by clinicians very few appendices show histological changes to justify the use of these terms by pathologists (Brit. med. J., 1955). In this series large numbers of lymphocytes (in chronic appendicitis) or eosinophils, or plasma cells or both (in subacute appendicitis) were required to be present in the submucosa to allow this classification to be used (fig. 23). For this classification these cell types must not be associated with traumatic changes or with acute inflammation elsewhere in the appendix. It is possible that this represents the continuation of the process described under the heading of resolving appendicitis.

(d) Pre-acute appendicitis This arbitrary term describes

(1) the presence of small numbers of polymorphs within the mucosal stroma of the appendix but not related to crypt abscesses (fig. 24), or

(2) the presence of larger numbers of polymorphs within dilated lymphatics in the mucosa (fig. 25). It was not clear whether these changes were due to operative handling or represented the earlier changes of appendicitis. It seemed more probable that the

fig. 26

Figure 26 Fibrous obliteration of lumen of appendix showing remains of two lymphoid follicles and numerous lymphocytes in the surrounding submucosa (Haemalum and Eosin, x36).

fig. 27

Figure 27 Fibrous obliteration of lumen of appendix with no visible lymphoid remnants and no lymphocytes in the submucosa (H & E, x30).

former was correct and this group of changes was regarded therefore as within normal limits.

(e) Fibrous obliteration of the lumen Fibrous obliteration of the lumen has been the subject of extensive writing mainly discussing the relative parts played by involution and past inflammation in its production (Collins, 1934; Muller, 1959b; Thackray, 1959; Stephenson and Snoddy, 1961; Rukstinat, 1963). Most authorities believe that fibrous obliteration is post-inflammatory in nature: all agree that it is not a cause of abdominal pain. For cases to be included in this category, no mucous membrane must be present at any level (fig. 26). The amount of lymphoid tissue present in these appendices was variable but always less than in appendices with a normal mucosa. Loss of activity of germinal centres was an early change and the lymphocytes remaining become gradually dispersed throughout the fibrous tissue until they were eventually removed (fig. 27). This disruption of lymphoid follicles may have been interpretated in the past as "chronic inflammation," a diagnosis which has retarded the understanding of the causation of abdominal pain by many years.

Degrees of fibrosis and fatty infiltration of considerable extent, but short of total obliteration, were commonly seen.

Such appearances are widely reported as indices of previous appendicitis. The time relationship between these hypothetical past attacks of appendicitis and the onset of recognisable fibrosis has never been discussed and there is no evidence to suggest that it is short enough to be of clinico-pathological value in individual cases. Even appendices removed three months after abscess formation cannot be identified by the pattern of their submucosal fibrous tissue. New criteria for the diagnosis of recent appendicitis are needed to make the diagnosis of "evidence of previous appendicitis" other than a meaningless cliché. A new test for recent appendicitis is discussed in the next chapter.

Summary

Four main histological categories are described as the basis for this work. These are "NORMAL," "ATYPICAL," "LIMITED ACUTE APPENDICITIS" and "COMPLETE ACUTE APPENDICITIS."

The incidence and significance of each group is discussed in detail in Chapter 3 of this section.

CHAPTER 2

THE PRUSSIAN-BLUE REACTION IN THE DIAGNOSIS OF PREVIOUS APPENDICITIS

As stated above, no satisfactory or objective criteria exist for making a clinically useful diagnosis of recent past appendicitis.

Having noted large deposits of haemosiderin in appendices removed from patients who had had recent appendix abscesses, I applied the prussian-blue reaction to a series of appendices in the hope that this might prove a useful test for recent appendicitis (Howie, 1966). No similar work had been previously reported.

Materials and Methods

669 appendices removed at operation during the year beginning February 1963 were studied. This total represented all appendices removed for any reason during the period of study in the Western Infirmary, Glasgow.

Sections were taken from each specimen in the manner described in the last chapter and examined after haemalum and eosin staining.

Duplicate sections were examined by Perls' prussian-blue technique (Pearse, 1960, page 683) with a carmalum or neutral red counter-stain.

The case records of the 669 patients were examined with particular attention to any past history of abdominal pain and to the surgeon's operation notes. The criteria used are defined below:-

Pathological diagnosis

For this study "acute appendicitis" included limited acute appendicitis, complete acute appendicitis, and any appendices clearly showing resolution of recent acute inflammation. All other appendices were labelled normal. All cases (14 in number) diagnosed clinically as having had appendix abscesses were included in the "acute appendicitis" group on the grounds that the original diagnosis was established with reasonable clinical certainty.

History of previous appendicitis

This was defined as "positive" if the case record implied that the patient had, in the six months before operation, experienced a similar or related type of illness to that for which his appendix was eventually removed. All other cases were

fig. 28

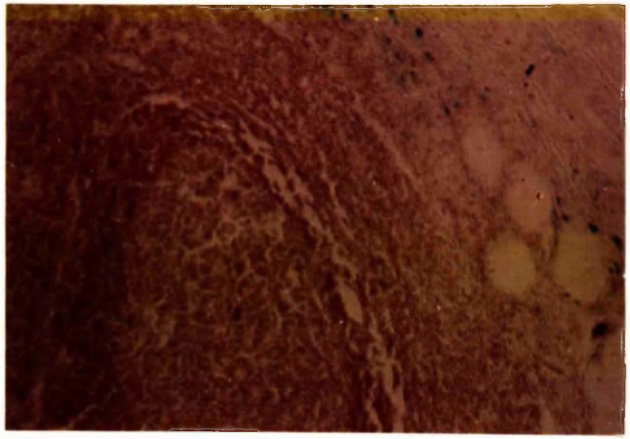


fig. 29

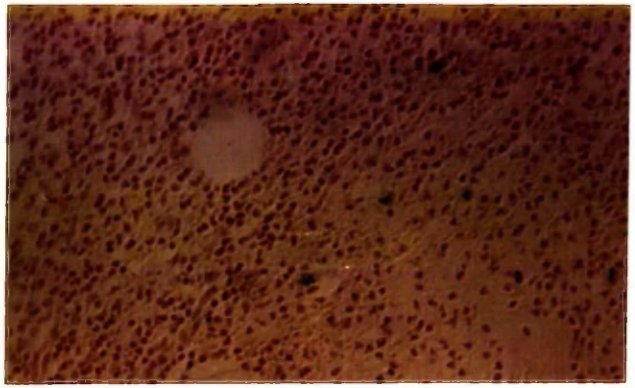


fig. 30

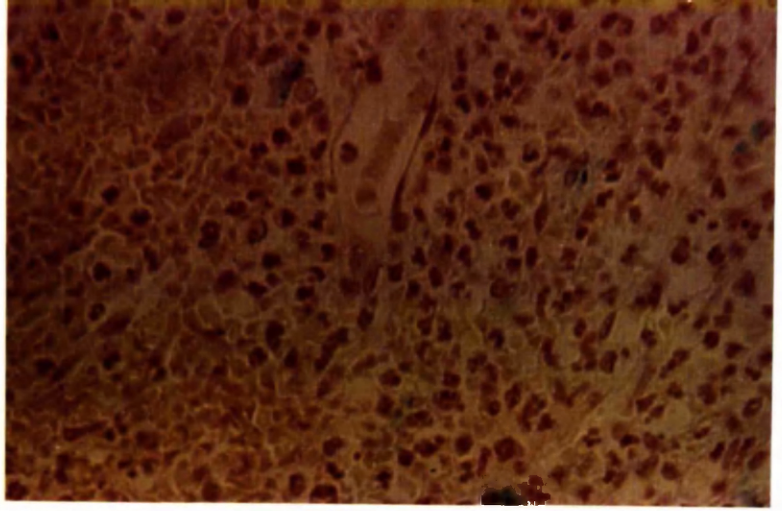


fig. 31

Figure 28 Iron strongly positive. Appendix removed two months after clinical diagnosis of appendix abscess had been made (Perls' prussian-blue, x90).

Figure 29 Iron strongly positive, with heavy deposits in submucosa, one field representative of many being shown in this illustration. Appendix removed two months after clinical diagnosis of appendix abscess had been made (P.P.B., x300).

Figure 30 Iron positive, showing fairly numerous phagocytes containing iron all within a restricted area at only one level of the appendix. Recurrent episodes of abdominal pain for one year; present attack of 16 hours duration (P.P.B., x350).

Figure 31 Iron positive, showing only scanty phagocytes containing iron. Previous episode of pain 6 weeks before current attack. Appendix contained faecolith and showed acute obstructive appendicitis (P.P.B., x450).

regarded as having a "negative" past history.

As an exception to this rule, if patients with recurrent pain had histologically normal appendices removed and were noted to have other lesions which might account for their symptoms (for example, mesenteric adenitis, or right-sided ovarian cysts), this alternative pathology was assumed to be the cause of the recurrent symptoms. In such cases the history of previous appendicitis became in retrospect "negative."

Iron

Stainable iron was assessed as negative, positive or strongly positive. In all negative cases there was complete absence of stainable iron. The strongly positive group contained cases with either a very marked focal distribution of iron or cases with a diffuse distribution of iron covering several fields (figs. 28 and 29). The intermediate "positive" group thus contained a wide range of intensity from very scanty deposits of stainable iron to fairly considerable quantities. Some representative appearances are shown in figs. 30 and 31. The division between positive and strongly positive was a subjective one.

TABLE 1.

The Prussian-blue Reaction as an index of recent appendicitis - classification of cases with respect to clinical, pathological and operative findings.

Mode of clinical presentation \ Class		No history of earlier attacks of appendicitis. A	Positive past history of appendicitis: Acute appendicitis at operation B	Positive past history of appendicitis: No acute appendicitis at operation. C	"Silent" appendicitis D
Emergency operation	539	(No acute appendicitis found) 109*	81	24	0
		(acute appendicitis found) 325+			
Interval operation after appendix abscess	14	0	14	0	0
Planned operation for recurrent R.I.F. pain	62	(other pathology found) 15	16	31	0
Incidental removal at unrelated operation	54	32	0	0	22 †
Total	669	481	111	55	22

* includes 16 cases where a past history of abdominal pain was given, but a possible alternative explanation was found at laparotomy

\+ includes 24 cases where a past history of appendicitis more than 6 months before operation was given.

† "silent" appendicitis = cases removed incidentally and found to be surgically abnormal or to show histological evidence of acute appendicitis.

Clinico-pathological Classification

Appendices are removed under circumstances varying from emergency operations to planned interval procedures. These differences are in some cases artificial, and the classification used in this study took this into account. Four classes were defined as follows:-

Class A: Patients with no past history suggestive of appendicitis.

Class B: Patients with a past history suggestive of appendicitis whose appendices showed histological changes of acute appendicitis at operation.

Class C: Patients with a past history suggestive of appendicitis whose appendices were histologically normal at operation.

Class D: Patients whose appendices were incidentally removed during unrelated operations but were grossly abnormal in the surgeon's opinion or showed histological evidence of acute appendicitis.

The distribution of cases to each class is shown in table 1.

Results

The numbers and percentage of cases showing stainable iron in each of the classes defined above are shown in table 2. Direct comparison was made between classes A and B, A and C,

TABLE 2

Distribution of cases showing stainable iron in clinico-pathological classes defined in text.

Class	Description	Iron		Total	% positive
		Negative	Positive		
A	No history of earlier appendicitis	343	138	481	28.7
B	Positive past history appendicitis at operative	39	72	111	64.9
C	Positive past history no appendicitis at operation	28	27	55	46.1
D	Silent appendicitis	9	13	22	59.1
	Total	419	250	669	37.4

The difference between A and each of the three test classes is highly significant ($P < 0.01$).

and A and D. Highly significant differences ($P < 0.01$) were observed between each class and class A, the control group for the series. There was thus a significant association between the presence of stainable iron and a past history suggestive of appendicitis or, in class D, an abnormal appendix.

Ideally, control material should match test material for age and sex; but in the incidental operations in this series where normal appendices were found, there was a predominance of females and the age group was an older one. The patients were generally undergoing cholecystectomy, hysterectomy, or resection of tumours. The number of cases in this group (32) was in any case too small to act as an adequate control series. Table 3 shows the composition of the various sub-groups of class A. It will be seen that in no group does the number of iron-negative cases differ significantly from the number for the class as a whole. Thus the class is homogeneous and appears to be as true a control group with respect to the absence of previous symptomatic appendicitis as can be expected in a study of this type.

Post-mortem material was not accepted as a control both because the age group was different from the test series and because the appendix undergoes autolysis with great rapidity after death. A pilot study of 50 post-mortem appendices showed 12 iron-positive cases.

TABLE 3.

Subdivision of Class A with respect to clinical and pathological presentation to demonstrate homogeneity of material.

Type of operation	Operative and pathological findings	Cases	Total iron negative		% iron negative	
			Expected	Observed		
Emergency	Normal histology; No past history; with or without other surgical lesion	93	66	64	68	109*
Emergency	Normal histology; positive past history; + other surgical lesion	16	11.3	7	44	
Emergency	Acute histology; no past history; with or without other surgical lesion	301	214	222	74	325*
Emergency	Acute histology; positive past history - distant; with or without other surgical lesion.	24	17	15	62	
Planned	Normal histology; positive past history; + other surgical lesion	15	10.6	11	73	
Incidental	Normal histology; normal gross appearance; no past history + other surgical lesion	32	22.7	24	75	
	Total	481	-	343	71	

* These total figures show distribution of emergency operation cases in Class A in Table 1

No significant differences between rows ($X^2 = 8.25$, $P < 0.1$ not significant.

20 pieces of normal ileum and colon from surgically removed specimens were all found to be without stainable iron.

Relationship of iron deposits to the acute episode

Exudation of red blood corpuscles is a well-known feature of the acute inflammatory reaction, and it is equally well-known that within a few days iron from those red blood corpuscles can be demonstrated as haemosiderin in macrophages (Muir and Niven, 1935). Niven (1935) showed that a diffuse blue colouration can be expected in macrophages grown in tissue culture with red blood corpuscles in about 72 hours.

In class A, 88 of the 138 iron-positive cases showed acute appendicitis. 15 of the 88 had a present history of more than three days and 6 had one of more than two days. In 88 controls from class A matched for sex and also showing acute appendicitis but iron-negative, only 6 cases had a present history of more than three days but 15 had one of more than two days. It appears that when the clinical history exceeds 72 hours stainable iron may be in the process of being formed and that in cases of acute appendicitis this should be borne in mind as a cause of positive stainable iron.

Where the appendix was normal histologically and contained iron (50 cases) 5 cases had a history of more than three days'

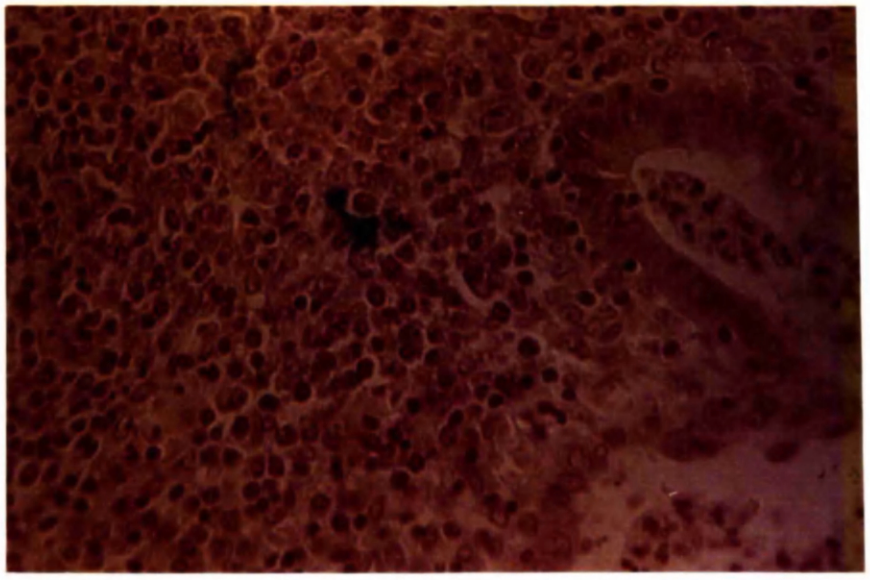


fig. 32

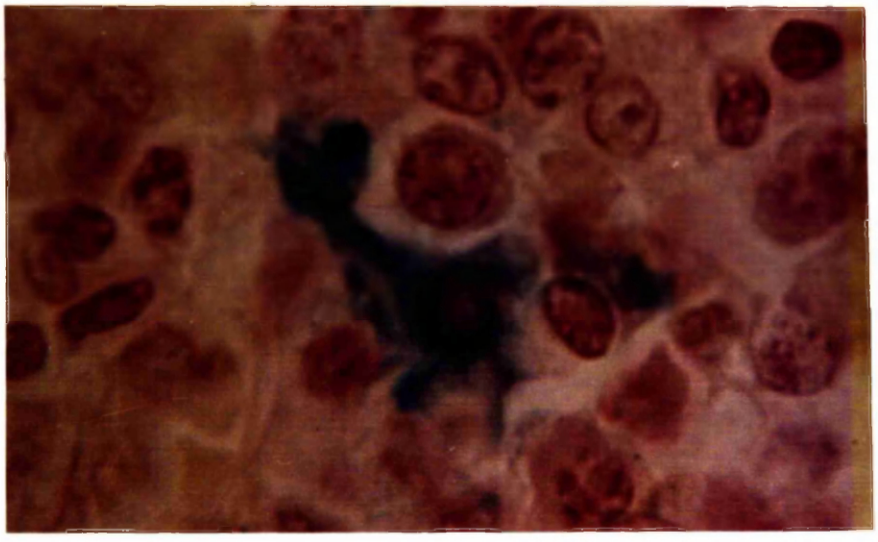


fig. 33

Figure 32 Focus of stainable iron in mucosa of acutely inflamed appendix removed at emergency operation. Present attack of 12 hours duration. No history of previous abdominal pain (Perls' prussian-blue, x250).

Figure 33 Higher magnification showing diffuse blue colouration suggesting recent formation of pigment, compatible with very recent asymptomatic episode of limited acute appendicitis (P.P.B., x1000).

duration and this was exactly equalled by the control series matched for sex and past history but iron-negative.

In 19 cases in class A stainable iron was present in the mucosa only (figs. 32 and 33). All these 19 cases showed acute appendicitis. In other words 19 of 88 cases of acute appendicitis had deposits of iron confined to the mucosa. None of the 50 normal iron-positive appendices had any iron in the mucosa. Only one of the 19 cases had a clinical history of three days, one had a history of two days and 13 had a history of less than 24 hours. Clearly a small focus of limited acute appendicitis in an asymptomatic form had preceded the major lesion. The stainable iron found in cases of acute appendicitis may be due to asymptomatic limited appendicitis immediately preceding operation, but this appears to apply to iron in the mucosa only. Other distributions of iron seem to be as frequently found in acute and normal appendices, and are therefore not likely to be attributed to the acute episode.

Table 4 shows the distribution of class B cases (positive past history) making allowance for the possibility that stainable iron in the mucosa alone or present with an acute episode lasting over 72 hours may be due to the current attack. Excluding such cases there was still a highly significant difference ($P < 0.01$)

TABLE 4.

Distribution of stainable iron in Class B cases (positive past history of appendicitis), allowance being made for a concurrent attack of acute appendicitis.

	Iron		Total	% Positive
	Positive	Negative		
Appendicectomy following appendix abscess	12 ¤	2	14	84
Planned operation for recurrent right iliac fossa pain	13 +	3	16	81
Positive past history, present episode 72 hrs.+ or focus of mucosal iron+	24	5	29	80
Positive past history excluding cases in line above	23 ‡	29	52	45
Total	72	39	111	64.9

¤ includes one case with operation due to recurrence of symptoms where acute current history exceeds 72 hours.

+ includes three cases with no current symptoms where stainable iron is confined to the mucosa.

‡ When this group is compared with class A, $X^2=8.5$ $P<0.01$, highly significant.

between each constituent group of class B and the control group, class A. The cases of previous appendicitis showed 12 of 14 cases positive, 11 of the 12 being strongly positive. The amount of stainable iron in these cases was often very marked (fig. 28). Indeed, absence of stainable iron might well cast doubt on the accuracy of the clinical diagnosis. (In one of the negative cases in this group a mucocoele was found at operation). The 16 cases having planned appendicectomy for recurrent right iliac fossa pain in which acute appendicitis was found, had 13 iron-positive cases only one of which was strongly positive. Of the 81 cases in this class which had emergency operations, 47 were iron-positive, 19 of these being strongly positive. Deposits of iron appeared to bear a quantitative relationship to the severity of the previous episodes.

Observer error

The material from 400 cases was reassessed by the same observer and the same results were obtained in 93% of cases. A second observer assessed 50 cases selected at random and agreed in 42, disagreed in 3, and was uncertain in 5. The disagreements were not biased to either positive or negative. These findings suggested that the probable degree of observer error was small and not likely to have affected materially the highly significant

findings obtained.

Discussion

The highly significant difference between the number of iron-positive cases in classes A and B must be emphasised. All patients in class B appear to have had appendicitis within the six months before operation. The choice of six months is an arbitrary one, there being no evidence of the length of time necessary for complete removal of iron deposits from the appendix. Most previous episodes of pain suggestive of appendicitis fall within this period before operation. Class A and class B appear to differ from each other only in respect of the presence of the past history of appendicitis, and it thus appears that there is a strong correlation between the presence of stainable iron and a probable past episode of appendicitis.

Why are all the class B cases not positive? It may be that stainable iron was present but was totally removed by macrophages or lost by sloughing off the mucosa during healing of the appendix. Alternatively, it can be argued that some of the episodes of inflammation are accompanied by relatively little tissue destruction, and that the sections examined missed a small focus of stainable iron. In some cases of "catarrhal" appendicitis oxudation of red blood corpuscles into the appendix stroma is not a feature and in

such cases no stainable iron may in fact ever be formed. This would account for some of the negative findings in patients with mild recurrent appendicitis without stainable iron.

Stainable iron, with or without a positive past history of appendicitis, is less commonly found in females than males. The significance of this is not clear and is discussed in the next chapter. Probably the clinical diagnosis is more difficult in females and perhaps the turnover of iron is faster. Either possibility would account for false-negative cases with the criteria of this study. Mild appendicitis is more frequently found in females than in males (Muller, 1959a). Perhaps female patients complain of pain and have appendicectomy for mild episodes which in males do not give rise to pain. These attacks thus appear as past asymptomatic episodes in male patients with an increased percentage of iron-positive cases.

Class C cases, all of which had a history of previous abdominal pain, did not show acute appendicitis at operation even though about half of them (24 of 55) were operated on during an acute attack of their recurrent pain. These 24 cases probably represent false-positive past histories of appendicitis in which no alternative explanation of the clinical picture was found. Class C is therefore an intermediate group between

class A and class B probably containing a mixture of genuine and false-positive past histories.

Errors of classification

Errors in recording the past history are likely to be mainly of failure to elicit or record previous episodes of abdominal pain. Such errors would cause the inclusion in class A of cases which should be in class B and would thus weaken the correlation between the presence of stainable iron and a positive past history of abdominal pain.

Failure of the surgeon to elicit or record findings such as ovarian cysts or mesenteric adenitis would tend to enlarge class C with inappropriate cases and so again weaken the correlation between stainable iron and previous appendicitis.

Accepting that there is no reason to believe that the iron causes appendicitis, is there any mechanism other than absorption of red blood corpuscles from the inflammatory exudate which might account for the presence of stainable iron? McCarthy, Reid and Gibbons (1964) recently described the presence of stainable iron in macrophages removing mucus from the alveoli of rats in the apparent absence of haemorrhage. They suggested that the accumulation of acid mucopolysaccharides in macrophages causes absorption of iron from oedema fluid which may in turn be the

result of a variety of pathological processes. The relevance of this to the present study is not clear, but in any case the process leading to the deposition of iron appears to be pathological, and inflammation is the most probable cause.

Cappell (1958-59), in 5 cases of conditions characterised by excessive iron storage, showed that the ileum and colon contained no stainable iron. It seems unlikely, therefore, that the deposits of iron in the appendix in this series can be due to diseases or peculiarities of iron storage.

As iron has been traced in its deposition during the acute episode, it appears reasonable to conclude that, except where the clinical history of the acute attack exceeds 72 hours or the iron in a case of acute appendicitis is confined to the mucosa, stainable iron in the appendix is probably due to recent past appendicitis.

This technique has proved to be of clinical use in individual cases, both when positive and negative. Its value in the broader epidemiological study of appendicitis becomes apparent in the remaining chapters in this section.

CHAPTER 3

INTERPRETATION OF HISTOLOGICAL CHANGES

Discrepancies among pathologists over the interpretation of histological changes in the same appendices have resulted in pathologists' opinions on appendicitis being frequently disregarded by clinicians. Barnes and his colleagues in particular recently stated (Barnes et al, 1962) that gross operative findings are of more value than histological findings and Barnes (1964) repeated this view, stating that the changes which I described as limited acute appendicitis were of theoretical interest rather than practical value. This suggests that discussion of the management of abdominal pain is not assisted by differentiating accurately between normal and abnormal appendices or by understanding the natural history of appendicitis. This is surely incorrect, but it may be agreed that the onus is now on the pathologist to demonstrate the correctness of his criteria and their usefulness in applied clinico-pathological study.

This chapter attempts to demonstrate the clinical significance of the changes defined in the previous two chapters.

Materials and Methods

Clinical and histological classifications

This part of the inquiry is based on the study of 1412 appendices submitted to the Pathology Department of the Western Infirmary, Glasgow between 1st February, 1963 and 31st January, 1965. This total represents all but 20 appendices removed in the hospital over the two years of the study. It includes 8 appendices removed in private practice by members of the hospital staff. All patients were aged 12 years or older.

Each appendix was examined in the manner described in the preceding chapters and assigned to one of the four main histological groups - namely

(1) NORMAL;

(2) LIMITED ACUTE APPENDICITIS;

(3) COMPLETE ACUTE APPENDICITIS; and

(4) ATYPICAL APPEARANCES.

Each case was also described as positive or negative for stainable iron. The degree of observer error was small and is discussed in Chapter 6 of this section.

All patients were allocated to one of 4 main clinical classes (A-D) depending on the method of clinical presentation.

Class A contains all patients having emergency operations; class B contains patients admitted from the hospital waiting list for appendicectomy because of recurrent right iliac fossa pain; class C contains patients being re-admitted for "interval" removal of an appendix previously diagnosed as the site of abscess formation; and class D patients had appendices removed incidentally at other operations for unrelated lesions including gall-stones, resection of abdominal tumours and surgery for perforated peptic ulcers.

Occasional difficulties of classification arose on this basis. These involved 11 patients and were dealt with as follows:-

(a) Three patients on the waiting list for interval appendicectomy after an appendix abscess, developed a second acute episode before their expected date of re-admission. These patients were considered twice over and allocated both to class A and to class C.

(b) Five patients were operated on as cases of acute appendicitis but four were found to have perforated peptic ulcers and one to have a ruptured spleen. These patients were allocated both to class A and to class D, because their symptoms were, in retrospect, clearly not due to appendicitis.

(c) One patient while in hospital awaiting planned appendicectomy for continuing right iliac fossa pain (class B) developed an acute episode on the morning of her operation. Her case was categorised as both A and B.

(d) Two patients admitted to gynaecological units for laparotomy for recurring right iliac fossa pain were found to have a left-sided ovarian cyst and fibroids respectively. They have been given double classifications of B and D.

Thus 11 of the 1412 cases are duplicates, but for ease of calculation this has been ignored.

All other cases were allocated to the single most relevant class.

Assessment of result of operation

The interpretation of the significance of debatable histological changes requires a clinical follow-up of patients in these categories and comparison with follow-up studies of patients having obviously normal and abnormal appendices removed.

Two very important factors make a study of this type difficult to plan. The main one is that, after removal of a normal appendix, good clinical results are known to be the rule rather than the exception. Difficulty arises in finding a sufficiently sensitive clinical index of a satisfactory or

unsatisfactory result to allow recognition of whether small groups are closer to normal or abnormal in their follow-up characteristics. Even in a series as large as this one, some subdivisions proved too small to be readily subjected to realistic statistical analysis.

Secondly, it is also extremely important that all histological groupings - test and control - should be as homogeneous as possible, because even a small number of false inclusions will be liable to mask the true results.

The clinical follow-up of patients in this study was done by post. This was preferred to direct interview for several reasons. Firstly, in a subject where suggestion is of so much importance, a postal survey removes the risk of the interviewer's introducing bias to the answers. If postal questionnaires are carefully worded, interpretation of the result is likely to be highly objective. Secondly, the time required for one observer to visit or interview a large enough portion of the 1312 patients who had had appendicectomy for suspected appendicitis was not available.

Thirdly, the number of patients who might attend an interview in the hospital would be much influenced by people leaving the district, the weather on the day concerned, and what was on television that night! Added objections were the possibility

of patients requiring to be paid travelling and other expenses and their possible inclination to have advice on related or unrelated medical problems.

The main objections to a postal follow-up are the risk of low returns and the difficulty of assessing the significance to be attached to the non-returned circulars. These objections can be overcome only by securing a high proportion of returns (Ilersic, 1964, page 298). In this series the proportion of returns was exceptionally high being 90.5% of those patients traced. This justifies the use of this method of follow-up as a valid basis for further study.

The circulars used in this study are shown in the Appendix. The interval between operation and follow-up ranged between 12 and 24 months being 24 months in 458 cases, 12 months in 100 cases, and an intermediate length of time in the remaining 754 cases. If no reply was received a reminder was sent from at between 2 and 4 weeks after the original circular. About 60% of the people receiving each circular replied. In 50 cases a third circular was sent to those failing to answer two circulars but this produced very few extra replies and was soon abandoned.

Where the patient was not traceable at the original address attempts were made to find the patient's current address through

TABLE 5.

Results of postal follow-up of 1312 patients between 12 and 24 months after appendicectomy.

	Class A patients	Class B patients	Class C patients	Total
Circular complete	967	109	26	1,102
Deaths	11	-	2	13
Total followed up	978	109	28	1,115
Not traced	77	10	-	87
No reply	105	5	-	110
Total lost to follow up	182	15	-	197
Total	1,160	124	28	1,312

% followed up = 84.5%

% not traced = 6.5%

% followed up of total traced = 90.5%

the Ministry of Pensions and National Insurance, the Income Tax Authorities, and the City Housing Offices, but these methods gave very few extra results in relation to the considerable effort necessary.

Table 5 shows the distribution of cases in the main clinical groups and the results of sending circulars to the patients in these groups. It may be seen that follow-up information was obtained in 84.5% of cases (1115 of the 1312 in Classes A, B and C who had had appendicectomy for possible appendicitis) and that 6.5% (87 of 1312) of patients could not be traced. Therefore only 9.5% (110 of 1225) of those who apparently received circulars failed to answer. Although not all the patients answered all the questions satisfactorily only four of the replies were totally useless.

The questions in the circular which were relevant to this chapter were those numbered C1, C2 and D5.

"C1 Have you had any more pain in the abdomen since being declared fit? YES/NO

"C2 If "YES", was the pain ANSWER

a) the same as you had your operation for?

b) worse than you had before your operation?

c) less severe than you had before your operation?

d) quite different from that before your operation?

"D5 As a result of your operation, do you feel — ANSWER

a) no more pain

b) less pain than before

c) the same pain as before

d) more pain than before

e) don't know

These questions were framed so as to have a double-check on patients' satisfaction or dissatisfaction at their progress since operation.

CURED Only patients answering "NO" to C1, leaving C2 blank and answering "a" to D5 were accepted as being cured. These patients, having declined two opportunities to give indications that they had had further trouble, might reasonably be judged to be totally satisfied and thus classed as cured.

NOT BETTER Patients giving any permutation containing one of C2 "a" or "b" or one of D5 "c" or "d" were classed as "not better."

Only half of the patients in this group gave consistent answers indicating a clear opinion that they had not been helped by the operation, while the other half of this group, although stating they had again had the same pain in question C2, stated in D5 that they had no more pain or less pain than before. Also some patients answering "c" to question D5, gave "c" or "d" as their answers to C2. In all these cases however, it appears that these patients have had recurrence of their original symptoms and cannot be accepted as being organically cured or improved because of operation.

IMPROVED Patients not already included under the above classifications who gave any permutation of replies including C2, "c" or "d" or D5, "a" or "b" were classed as "improved." Again only half the patients in this category gave the consistent answer of C2, "c" with D5 "b". This shows that in many cases patients felt able to answer one of the two questions in a way suggesting they believed they had been cured. The significance of this important middle group is difficult to assess and is discussed below.

OTHER SITUATIONS Patients answering only one of the questions C2 or D5 were allocated to the most appropriate group. If this

TABLE 6

Distribution of cases to histological classes for each clinical presentation.

Class	Clinical presentation.	Total cases	Histological class								
			Complete acute appendicitis	Limited acute appendicitis	Normal	Atypical					
						Total	a	b	c	d	e
A	Emergency appendicectomy	1160	709	83	310	58	14	19	9	4	12
B	Planned appendicectomy	124	2	18	82	22	5	6	2	5	4
C	Interval appendicectomy after appendix abscess	28 *	6	-	9	12	-	-	10	-	2
D	Appendicectomy at unrelated operation	100	1	6	76	17	6	1	1	2	7
	All cases	1,412 *	718	107	477	109	25	26	22	11	25

a = unrelated inflammation
b = pre-acute appendicitis
c = resolving appendicitis
d = subacute/chronic appendicitis
e = obliterated lumen

* = includes one case where specimen contained no appendix

was in doubt, the patient was excluded. Patients answering "e" to D5 were classed as "improved" if they answered "c" or "d" to C2, or as "not better" if they answered "a" or "b" to C2; if C1 was answered "NO" or if C1 was answered "YES" but C2 left blank, the case was excluded.

We have thus objective classifications for each case for:

(1) the results of the operation;

(2) the histological diagnosis of the appendix removed; and

(3) the clinical circumstances under which each operation was done.

In total 1115 cases were successfully followed up and available for study.

The significance of limited acute appendicitis

Table 6 shows the allocation of appendices to histological and clinical categories.

Table 7 shows, for patients having emergency operations (class A), the number and percentage of cases in each of the four main histological categories who were cured, improved, or not better as a result of their operation. Cases showing "Atypical Appearances" were regarded at this stage as forming a homogeneous group. The exceptions to this generalisation are

TABLE 7

Number and percentage of patients in different histological categories who were cured, improved and not-better after emergency appendicectomy.

Histological category	Cured		Improved		Not-better		Total
	No.	%	No.	%	No.	%	
Normal appendix	153	(64)	51	(22)	31	(14)	235
Atypical appendix	29	(69)	6	(14)	6	(14)	41
Limited acute appendicitis	48	(71)	18	(27.5)	1	(1.5)	67
Complete acute appendicitis	517	(87)	64	(12)	11	(2)	592
Total	747	(80)	159	(15)	49	(5)	935

discussed later. The number of cases in Table 7 (935) differs from the total number of emergency operations in Table 6 (1160) by the number of people from whom no replies were received (182), whose replies were inadequate for this study (32) or who had died (11).

The features of note in Table 7 are:-

(1) The percentage of cures in histological groups "normal" "atypical" and "limited acute appendicitis" are not significantly different statistically.

(2) The groups "normal" and "atypical" are identical as regards incidences of "cured" "improved" and "not better."

(3) The incidence of "not better" for "limited acute appendicitis" and "complete acute appendicitis" is identical.

(4) The incidence of "not better" for each of the two groups of limited and complete acute appendicitis (1.5% and 2.0%) is significantly lower than that for each of the two groups of normal and atypical (14% and 14%).

(5) If the category of "improved" is discarded and "cured" and "not better" compared, "limited acute appendicitis" differs to a strongly significant degree from the "normal" and "atypical" groups ($P < 0.02$).

It appears, in summary, that "normal" and "atypical" appearances

may be regarded as one group which can be called "normal" for purposes of further discussion. Crucial to this and future chapters is the significance of the patients described as "improved."

If this category is omitted or regarded as a variation of cure, "limited acute appendicitis" can be regarded as a bona fide histological abnormality. If it is regarded as a variation of "not better," "limited acute appendicitis" becomes a further variant of "normal."

It has become clear to me, after speaking personally to many people who have had appendicectomy, that those who had very severe pre-operative pain tend to ignore trivial post-operative discomfort and talk of being cured, whereas patients who had relatively mild pre-operative pain take more notice of what is probably similarly trivial post-operative pain. This is in keeping with the observation that nearly half the patients who talk of being improved gave answers suggesting cure to one of the two relevant questions. It is also in keeping with the reasonable assumption that those with severe pain tend to have had complete acute appendicitis and those with less severe pain to have had less extensive histological changes, possibly only limited acute appendicitis.

TABLE 8

Number and percentage of patients in different histological categories who were cured, improved or not better after planned appendicectomy for recurrent R.I.F. pain.

Histological category	Cure		Improved		Not better		Total
	No.	%	No.	%	No.	%	
Normal	33	47	16	23	21	30	70
Atypical	11	55	4	20	5	25	20
Limited acute appendicitis	8	57	5	36	1	7	14
Complete acute appendicitis	1	-	-	-	1	-	2
Total	53	5	25	24	28	26	106

Clinical common sense backed by informed statistical advice thus permits limited acute appendicitis to be regarded as associated with a clinical abnormality differing in degree of severity from complete acute appendicitis.

Table 8 shows the distribution of patients cured, improved and not better in each histological group, after planned operations for recurrent right iliac fossa pain (Class B). Although the numbers available are comparatively small, it can again be seen that "normal" and "atypical" have the same distributions to the follow-up categories. The number of cases of limited acute appendicitis is also small but only one of 14 was regarded as not better (7%) compared with 26 of 90 in the normal and atypical classes (29%). Therefore, limited acute appendicitis once more appears to be a different entity from normal.

Differences of Sex and Method of Presentation

Table 9 shows the follow-up results for male and female patients after both emergency and planned procedures. The higher incidences of "not better" for both emergency and planned procedures in females as compared with males may be noted. The point of greatest importance however, is the higher incidence of patients "not better" after planned operations as compared

TABLE 9

Incidence of patients cured, improved and not better after subdivision into sex, histological group and clinical presentation.

Sex	Histology & follow-up / Clinical presentation	Normal appendix (including "Atypical appendix")			Limited acute appendicitis.			Complete acute appendicitis			Total
		Cure	Improved	Not better	Cure	Improved	Not better	Cure	Improved	Not better	
Female	Emergency operation (Class A)	108	42	33(18%)	26	13	1	244	40	4	511
	Planned operation (Class B)	30	14	21(31%)	6	5	1	1	0	0	78
Male	Emergency Operation (Class A)	74	15	4(4.5%)	22	5	0	273	24	7	424
	Planned operation (Class B)	14	6	5(20%)	2	0	0	0	0	1	28
	Total	226	77	63	56	23	2	518	64	12	1,041

Emergency removal of normal appendix gives 37 "not better" out of 276 operations
Planned removal of normal appendix gives 26 "not better" out of 90 operations
$\chi^2 = 27$ $P < 0.01$

For female patients separately $\chi^2 = 5.7$ $(P < 0.05)$
For male patients separately $\chi^2 = 3.6$ $(P \leq 0.05)$

with emergency operations. This applies to both sexes. It thus appears that the emergency removal of a normal appendix is more likely to be curative than the removal of the same appendix in planned, non-urgent circumstances.

It is of interest to study these results with two previous comparable investigations. McLennan and Watt (1934) in a 5-year postal and direct-interview follow-up of 563 cases of "chronic appendicitis" traced 73% of the patients and found that 83.5% of females and 74.2% of males were "cured" by their operation. These figures include an incidence of about 15% of cases described as "improved." This is no doubt a series broadly comparable to my cases described as class B (planned operation for recurrent right iliac fossa pain) with the advantage of a larger total of cases and the disadvantage of no histological sub-divisions. Thus the percentage of all patients failing to be cured is closely similar in the two series.

The second work of interest is that of Shelley (1938) who studied 887 cases of chronic appendicitis and found that where non-inflamed appendices were removed the cure rate was highest (95%) for patients whose symptoms were recurrent and had lasted less than 1 year. He reported a cure rate of between 65% and 70% for normal appendicectomy where there was no history

TABLE 10

Comparison for each sex of histological distribution of appendices removed as planned procedures in patients with R.I.F. pain as against appendices removed as incidental procedures in patients with unrelated illnesses.

Sex	Histology / Presentation	Normal + Atypical	Limited acute appendicitis	Complete acute appendicitis	Total
Female	Planned operation - for R.I.F.pain	62 + 13 = 75	15	1	91 (1)
	Incidental operation - no pain	54 + 12 = 66	5	0	71 (2)
Male	Planned operation - for R.I.F.pain	20 + 9 = 29	3	1	33 (3)
	Incidental operation - no pain	22 + 5 = 27	1	1	29 (4)

The incidence of abnormal appendices and normal appendices in lines 1 and 2 differs to the level: $X^2 = 3.0$ $P > 0.05$

of past attacks, or where recurrent episodes had lasted over 1 year. The histological criteria in Shelley's study were not clearly enough defined to be usefully discussed and there is no discussion of the criteria used to assess "cure."

Comparison of Planned and Incidental Appendicectomy

It was argued by Thackray (1959) that appendices removed in circumstances equivalent to my clinical class D (vide supra and table 6, facing page 43) do not differ from those removed from patients with "chronic" appendicitis (my class B). Thackray's evidence was presented on the basis of studying 50 patients with chronic appendicitis and 50 control cases. The controls were all females. The sex of the patients with chronic appendicitis was not stated.

In table 10, I have divided my incidental and planned appendicectomy cases into groups by sex and it can be seen that the proportions of normal appendices removed from patients in each sub-division of sex and presentation are broadly similar.

In females, however, the incidence of appendices showing acute appendicitis in patients who have complained of symptoms is higher to a level just below that normally accepted as being statistically significant ($X = 3.0$ $P<0.1$). This difference

is almost entirely composed of cases of limited acute appendicitis.

Some of the appendices removed at incidental operation were removed because the surgeon thought the appendix was "not quite right" and consequently the correctness of using material obtained in this way as a proper control is open to considerable doubt.

The class D operations in my series also came from a much older age group than the test material, comprising mainly patients having cholecystectomy, resection of tumours, or hysterectomy.

Thackray's series is smaller than mine and it is possible that his criteria of normality and abnormality, though broadly correct, were not sensitive enough to recognise real differences in a limited study of only 50 cases and 50 controls.

Although my figures are not conclusive I believe that incidentally removed appendices differ from those removed from patients with recurrent right iliac fossa pain in that the number of cases of limited acute appendicitis is higher in the second group. Otherwise, the classes appear to be closely similar.

This supports the impression that limited acute appendicitis although on occasions present without causing symptoms, may be a cause of mild right-sided abdominal pain. When it is found in a patient with abdominal pain and no other gross lesion is present to explain the pain the limited acute appendicitis may thus be

TABLE 11

Distribution of iron positive and negative appendices in each sex in various groups of histological changes and follow-up results.

Group			Female				Male				Total			
Class	Histology	Follow-up	Iron +	Iron −	Cases	%+	Iron +	Iron −	Cases	%+	Iron +	Iron −	Cases	+%
A	Normal	Cure/Improved	41	109	150	27	49	40	89	55	90	149	*239	36
		Not better	6	27	33	18	0	4	4	-	6	31	* 37	17
A	Limited	Cure/Improved	23	16	39	57	17	10	27	63	40	26	66	60
		Not better	0	1	1	-	0	0	0	-	0	1	1	-
A	Complete	Cure/Improved	55	229	284	20	131	166	297	44	186	395	581	31
		Not better	1	3	4	-	5	2	7	-	6	5	11	-
B	Normal	Cure/Improved	7	37	44	13	9	11	20	45	16	48	†64	25
		Not better	8	13	21	40	4	1	5	-	12	14	†26	47
B	Limited	Cure/Improved	8	3	11	72	2	0	2	-	10	3	13	75
		Not better	1	0	1	-	0	0	0	-	1	0	1	-
A & B	Normal	Cure/Improved	48	146	194	23	58	51	109	53	106	197	303	31
		Not better	14	40	54	26	4	5	9	-	18	45	73	25
D	Normal	-	17	49	66	25	15	12	27	57	32	61	93	34
A & B	Limited	Cure/Improved	31	19	50	62	19	10	29	65	50	29	79	62
		Not better	1	1	2	-	0	0	0	-	1	1	2	-
All A + B + C + D cases			217	593	810	25%	297	305	602	49%	504	898	1412	35%

* $X^2 = 4.9$ $P < 0.05$ (Significant)

† $X^2 = 2.9$ $P = 0.1$ (not significant).

regarded as the cause of the pain.

The significance of the prussian-blue reaction

It has already been shown in Chapter 2 that the presence of a positive prussian-blue reaction is indicative of a recent episode of appendicitis or of the early stages of a present episode. It appears that the test is a quantitative one. Apart from the diagnostic value of the test in individual cases it has been applied to a number of follow-up categories for males and females and the results are shown in table 11.

No attempt has been made in this analysis to exclude patients with a past history of appendicitis from any group.

The features of note are:-

(1) Female patients have on average 25% of positive cases as against nearly 50% for males. The total overall incidence of 35% for two years of study is the same as that reported previously for a single year's study (Howie, 1966).

(2) For both sexes patients having appendices removed which show complete acute appendicitis have a lower incidence of iron-positive cases than do patients in any other major histological group. This may be due to heavy infiltrates of pus cells obscuring small deposits of iron which would be visible

in the non-inflamed organ.

(3) The highest incidence of iron-positive cases is in patients with limited acute appendicitis and this is most markedly so in patients who have a history of recurring pain, although the number of cases available is small.

(4) The incidence of iron-positive cases in patients having normal appendices removed during planned operations for recurrent pain is closely similar to that in those having incidental appendicectomy suggesting again that the groups are closely similar, if cases of limited acute appendicitis are excluded.

(5) No group of patients other than those with limited acute appendicitis has a significantly higher incidence of iron-positive cases than the average for that particular sex.

The two conclusions which emerge are:

(1) that females are less likely to have iron in appendices removed at operation than are males; and

(2) that limited acute appendicitis appears to be a continuing or recurring process in both sexes.

The theoretical possibility of iron being deposited as a result of recurrent episodes of appendicular congestion is an attractive one which would explain why removal of normal appendices is so often accompanied by cure (if the appendix only was

congested) or improvement (if the appendix was congested together with other pelvic viscera). If this view was correct patients with normal appendices being removed should show higher incidences of iron-positives in the cure and improved groups than in the not better groups. Differences of this type cannot be demonstrated and the hypothesis thus does not appear to be tenable.

The difference between sex incidence can be explained in two ways. Either:-

(1) the female iron turnover rate is very much higher than that for males; or

(2) females complain of symptoms which lead to removal of the appendix when the appendix shows histological abnormalities of mild extent which in males would pass as a symptom-free episode and would lead to the deposition of a small quantity of stainable iron.

Both explanations are reasonable and probably contribute to the findings. Support for the second is given in this study by finding limited acute appendicitis in 52 females with symptoms but only in 29 males with symptoms. This is not a significant difference if considered in relation to all appendices removed but if only abnormal appendices are studied the difference is

statistically significant ($X = 8.5$ $P<0.01$).

It is of interest to note that the number of acutely inflamed appendices removed from patients with symptoms over the two years was exactly the same for each sex - 329. This suggests that, contrary to the views of other authorities, (Wilkie, 1914; Lee, 1961) the sex incidence of the disease is equal.

The significance of Atypical appearances and Class C cases

Finally in this review of the significance of histological appearances, I wish to consider the individual subgroups of the class labelled atypical appearances, and the group of patients having appendices removed some weeks after the diagnosis of an appendix abscess (Class C).

Post appendix-abscess cases (Class C)

There were 28 cases in this group, for one of which the pathological specimen was not classifiable as it contained no appendicular material. Of the other 27, 24 were iron-positive and three iron-negative. Of the three iron-negative cases, one had complete obliteration of the lumen and was not available for follow-up due to death unrelated to the original operation. One

appendix was in fact a mucocoele and this may originally have been mistakenly thought to be an abscess. The third appendix was entirely normal. The original clinical diagnosis in this last case was not a confident one.

Only one of the 24 cases with stainable iron was "not better" after surgery. In this case (a female of 32 years of age) the iron present was scanty and not of the usual post-abscess distribution. Haematuria was detected twice after this operation in association with right iliac fossa pain and a diagnosis of urinary tract disease was finally made.

Of the 10 patients allocated to the histological division of "resolving appendicitis" all had appendices which were strongly positive for stainable iron. Six were cured by operation; three were improved; and one died a year after operation from a "heart attack."

In this group the diagnostic abnormality is a strongly-positive iron reaction. The histological appearance described as "resolving appendicitis" in Chapter 1 is, as would be expected unusually common in this class.

Fibrous obliteration of the lumen

In Chapter 2, it was stated that this change was generally

taken to be the result of past inflammation and not to be a cause of symptoms.

25 of the total series of 1412 appendices studied histologically (1.75%) were in this category. 23 were iron-negative, and seven of these were removed at incidental operations. Of 13 patients followed-up, nine were cured, three improved, and one not better.

Of the two positive cases, one was removed two months after an appendix abscess (although the fibrous obliteration of the lumen appeared to be of long standing) and the other came from a patient having a laparotomy for carcinoma of the ascending colon who had originally presented with right-sided abdominal pain. The iron in this case was of post-abscess type and this may in fact have been the cause of original symptoms.

Although obliteration of the lumen is most often found in elderly patients - this is reflected in the 7% incidence in incidentally removed appendices - this, as has been correctly stated previously, (Faber, 1902, cited by Muller, 1959b) is in no way support for the view that obliteration is a function of ageing and is not post-inflammatory.

The absence of iron from all but two cases of this group suggests that fibrous obliteration is rarely a sequel to recent inflammation and also suggests that in the absence of mucosal

elements iron is not normally found in the submucosa. This second feature supports the belief that a mucosal abnormality - inflammation - is the cause of deposits of stainable iron.

Another feature of note is that in none of the many cases where the terminal 1 to 2 cm. of the appendix had been obliterated was iron to be found in the obliterated portion even if present in a more proximal part where mucosa was still present. Cases where lumenal obliteration appeared very recent - that is, where lymphoid follicles were still intact - were also notable for the absence of iron. These facts, together with the histological impression that the mucosa is strangled evenly out of existence by fibrous replacement of lymphoid and glandular structures, rather than irregularly replaced by scar tissue, raise considerable doubts as to how often fibrous obliteration of the lumen is a sequel to acute inflammation.

Pre-acute appendicitis

Of 26 cases in this group (1.8% of the whole series) 12 cases were iron-positive and 14 were iron-negative. Of these 16 patients followed-up nine were cured, four improved and three not better. These findings suggest that "pre-acute appendicitis" is a variation of normal and not a variation of limited acute appendicitis.

Unrelated inflammation

This was noted in 25 cases (1.75% of the whole series). Seven of these cases were from patients in the incidental operation group where other acute abdominal lesions were present as the main diagnosis. 11 cases were iron-positive and 14 iron-negative. Of the 17 patients followed-up eight were cured, five improved and four not better. This group is again indistinguishable from normal.

Resolving appendicitis

There were 22 cases of this description, 10 in post-appendix abscess cases, nine removed in acute emergency circumstances two as planned procedures for recurrent abdominal pain, and one removed at an operation for suspected carcinoma of the ascending colon. The 10 post-abscess cases were discussed above and shown to be abnormal. Of the 12 remaining cases 10 were iron-positive and two iron-negative. All seven patients who replied to the follow-up questions had been cured by their operations.

This histological appearance cannot be accepted as normal; but when it is found in a patient with acute symptoms, account must be taken of the non-acute nature of the histological appearances. The changes may in fact, represent the healing of

a recent asymptomatic episode of limited acute appendicitis of the type suggested to be common earlier in the chapter and bear no relation to the patient's present illness.

Subacute and Chronic appendicitis

Only 11 cases (0.77% of the total series) showed changes of this type. Seven were iron-positive, four iron-negative. The 10 cases available for follow-up showed eight cures and two improved.

The significance of this group must unfortunately remain "not proven" on the basis of the present study because too few cases are available. The indications tend to suggest that such changes may be responsible for symptoms of right iliac fossa pain.

Thus in patients presenting with acute symptoms, this combined class of atypical appearances may be regarded as synonymous with normal, bearing in mind the dubious status of chronic and subacute appendicitis.

In patients with no symptoms at the time of operation, resolving appendicitis may be accepted as a diagnostic abnormality, in particular when associated with stainable iron; all other

atypical appearances should again be regarded as normal with the possible exceptions of chronic and subacute appendicitis.

Conclusions

The normal appendix

This is as defined in Chapter 1 of this section but includes those appearances described as atypical appearances subject to the modifications noted immediately above.

Limited acute appendicitis

This condition represents a true abnormality and differs in degree of severity from complete acute appendicitis. It may or may not be associated with symptoms which, when present, will usually be less severe than those in complete appendicitis. If a patient with acute symptoms is found to have limited acute appendicitis, this can be reasonably accepted as the explanation of the patient's illness.

Stainable iron

The presence of stainable iron in large quantities is diagnostic of recent appendicitis, but small quantities of iron are present too often (especially in males) to be of diagnostic clinical value on their own.

These small deposits of iron suggest that the appendix may often be the site of mild asymptomatic appendicitis. These minor episodes probably predispose to major attacks; this view is supported by the finding of mucosal iron around foci which are apparently the starting point of complete acute appendicitis.

There is no evidence in this study to support the belief that fibrous obliteration of the lumen is a closely related sequel to acute inflammation.

There appear to be two stages in the development of acute appendicitis. The first - perhaps local trauma - causes a minor inflammatory lesion in the mucosa. This lesion will frequently be asymptomatic and heal spontaneously.

Secondly, under certain circumstances of altered haemodynamics (obstruction by faecoliths etc.) or diminished mucosal tissue resistance (perhaps due to adenovirus or enterovirus infection) mild lesions fail to heal and spread to become more severe.

The high incidence of iron in appendices and the not infrequent finding of asymptomatic limited acute appendicitis suggests that the appendix mucosa is often involved in the first of these states of abnormality and the high clinical incidence of appendicitis in the community can easily be explained by

the occasional addition of the second promoting factor.

There seems every reason from the Pathologist's viewpoint for advising removal of as many appendices as possible from persons who complain of right iliac fossa pain.

CHAPTER 4

MESENTERIC ADENITIS

Perhaps the most common differential diagnosis which must be considered in the patient with possible appendicitis is mesenteric adenitis. Mesenteric adenitis has been well described by Aird (1945) and Ward-McQuaid (1951) has given a detailed breakdown of findings and prognosis in a series of 500 operations for possible appendicitis in children under 14 years of age. He found mesenteric adenitis to be present in 15.4% of patients and suggested that mesenteric adenitis could be:

(1) allergic;

(2) of bacterial, viral or parasitic origin; or

(3) secondary to generalised or localised infection.

Various authors have suggested more definite aetiological agents. Bell and Steyn (1962) have demonstrated adenovirus types 1, 2, 3, 4, 5 and 6 in the nodes of children suffering from mesenteric adenitis. Mair et al. (1960) and Randall and Mair (1962) have demonstrated Pasteurella pseudotuberculosis apparently acting as causal agent in 4 cases of mesenteric adenitis. The now familiar relationship of abdominal pain to upper respiratory infection was first published by Brennermann

in 1927. Jones (1951) suggested that secondary glandular involvement might follow non-specific serous peritonitis and Raftery et al. (1950, quoted by Ward-McQuaid, 1951) claimed that histoplasmosis was present in 43% of cases of mesenteric adenitis, a finding not likely to be confirmed.

The possible relationship between acute regional ileitis and non-specific mesenteric adenitis was also discussed and Rosenberg (1937), Jackson (1937), and Stephens (1938) suggested a relationship existed.

Aird (1945) believed that if mesenteric adenitis was secondary to an infective agent, the appendix was not likely to be the portal of infection because the juxta-ileal glands - the first to be involved in mesenteric adenitis - were not enlarged in non-complicated acute appendicitis. Wilensky and Hahn (1926) supported this view strongly and stated with some confidence that "appendicular inflammation does not precede mesenteric lymphadenitis and that there are no clinical relationships between the two." Similarly, Ger (1954) stated that although appendicitis and adenitis might co-exist they were not related.

Steele (1945) on the other hand, believed mesenteric glands were related to the appendix in the same way as the

tonsillar glands to the tonsil; and Foster (1938 and 1939) in two papers stressed the same relationship, finding evidence of present or past appendicular disease in 95% of cases of mesenteric adenitis. No histological criteria, however, were given to allow this claim to be examined.

Objective assessment of mesenteric adenitis is again hampered by the natural tendency of the condition to be self-curative and by the high cure rate associated with removal of normal appendices. The state of understanding of mesenteric adenitis was summed up recently by the British Medical Journal (1965b) as follows:- "In fact, the whole condition is based on supposition apart from the fact of the enlarged glands so frequently found in these cases of abdominal pain mimicking appendicitis in childhood."

The purpose of this chapter is to present evidence suggesting that some - not all - cases of mesenteric adenitis are related to appendicitis either as a sequel to appendicitis or by their sharing the same histological agent (Howie, 1965).

Materials and Methods

The case records of the 1284 patients described in the previous chapter as being in clinical classes A and B (that is,

TABLE 12

Distribution of cases in classes A and B to sub-divisions related to presence or absence of mesenteric lymphadenopathy.

		Histological class			Total
		Normal	Limited acute appendicitis.	Complete acute appendicitis.	
Mesenteric nodes present	As diagnostic abnormality.	56	9	3	66
	With surgeon's appendicitis	6	1	14	21
	Not inferred to be important	24	5	3	32
	Total	84	15	20	119
Mesenteric nodes stated to be absent		93	20	24	137
Mesenteric nodes inferred to be absent		91	19	35	145
Total		268 †	54 ‡	79 *	401

* This represents 11% of all cases in this histological class

† This represents 68% of all cases in this histological class

‡ This represents 54% of all cases in this histological class

patients operated on for acute or recurrent abdominal pain) formed the basis of study. In all these cases the surgeon's operation notes were reviewed. The presence of enlarged or inflamed mesenteric nodes was described in 119 cases; the absence of such changes was positively stated in 137 cases and inferred in a further 145 cases where details of negative laparotomy findings were given.

The 119 cases where mesenteric nodes were described were divided into three sub-groups according to whether the surgeon's operative diagnosis was:-

(1) a positive one of mesenteric adenitis;

(2) one of acute appendicitis with mesenteric nodes enlarged as a secondary finding; or

(3) essentially negative, the presence of nodes being noted but not regarded as a diagnostic abnormality.

This allocation to sub-groups was done without prior knowledge of histological findings, follow-up results, or pre-operative history.

Other terms used in this chapter are used as previously defined; the histological class "normal" includes cases listed previously as "atypical appearances."

TABLE 13

Distribution of patients with enlarged mesenteric nodes to subdivisions of sex, follow-up results and presence of prussian blue positive material in the appendix.

Type of mesenteric adenopathy	Sex F : M	Follow-up (where answered)			Prussian blue in appendix		Total
		Cured	Improved	Not better	+ve	- ve	
Diagnostic abnormality	48 : 18	30	18	7	34	32	66
Co-existing with acute appendicitis	10 : 11	14	2	1	12	9	21
Significance not stated	21 : 11	17	5	3	13	19	32
Total	79 : 40	61	25	11	59	60	119

If the appendices were all normal and any past history of pain was not related to recent disease of the appendix, on the expected basis of 25% of females and 50% of males having iron positive appendices, the number of iron +ve appendices would be:

50% of 40 males	=	20	40
+ 25% of 79 females	=	20	
Observed total =			59
		χ^2 =	9
		P =	< 0.01

Results

Table 12 shows the number of cases in each of the main classes described above. It can be seen that "mesenteric adenitis" was present to a sufficient degree to be regarded as the principal diagnosis in 66 cases (5% of the total series).

Table 13 shows the sex distribution, follow-up results and prussian-blue reactions in the 119 patients found to have mesenteric nodes present. The features of note are:-

(1) The incidence of patients "not better" as a result of their operation is closely similar to that expected after removal of normal appendices;

(2) On the assumption that 25% of females with normal appendices and 50% of males with normal appendices should show stainable iron it would be expected that 40 appendices in the series of 119 would be iron positive. In fact 59 appendices were iron positive, a statistically significant excess over the expected figure ($X^2=9$; $P<0.01$). The largest part of this difference is contributed by these patients with enlarged nodes regarded as being diagnostic of mesenteric adenitis.

Table 14 shows the relationship of stainable iron in the

TABLE 14

Relationship between recent past abdominal pain and stainable iron in the appendix in patients diagnosed at operation as having mesenteric adenitis

	Past history + ve	Past history - ve	Total
Iron +ve	25 ✣	9	34
Iron -ve	15 †	17	32
Total	40	26	66

X^2 = 3.47

P = 0.05

If appendices were normal and not related to recent appendicitis number of iron positive cases would be:

25% of 48 female patients = 12
\+ 50% of 18 male patients = 9
} = 21

Observed = 34

X^2 = 8

P = <0.01

✣ One of 25 cases not better following operation (4% = prognosis following removal of abnormal appendix)

† Six of 15 cases not better following operation (40% = poorer prognosis than usual following removal of a normal appendix)

appendix to previous history of recent abdominal pain in the 66 patients with a surgical operative diagnosis of mesenteric adenitis. The correlation between past abdominal pain and stainable iron in the appendix is just short of that normally accepted as significant in biological work ($X^2 = 3.47$ $P \fallingdotseq 0.05$). The seven cases "not better" after operation all had recurrent pain before operation but only one of the seven was iron positive.

Discussion

By using the prussian-blue technique it can be demonstrated that appendices removed from patients with enlarged mesenteric nodes differ from normal appendices in containing more stainable iron than might be expected. This is particularly so where a definite operative diagnosis of mesenteric adenitis is made. This, by deduction from chapters two and three, implies that these appendices include an excess number which have recently been the site of appendicitis, probably in a mild form.

This is in fact confirmed by the correlation of the iron-positive cases with a past history of recent abdominal pain in cases diagnosed as mesenteric adenitis (table 14). If the past episodes of pain had been due to mesenteric

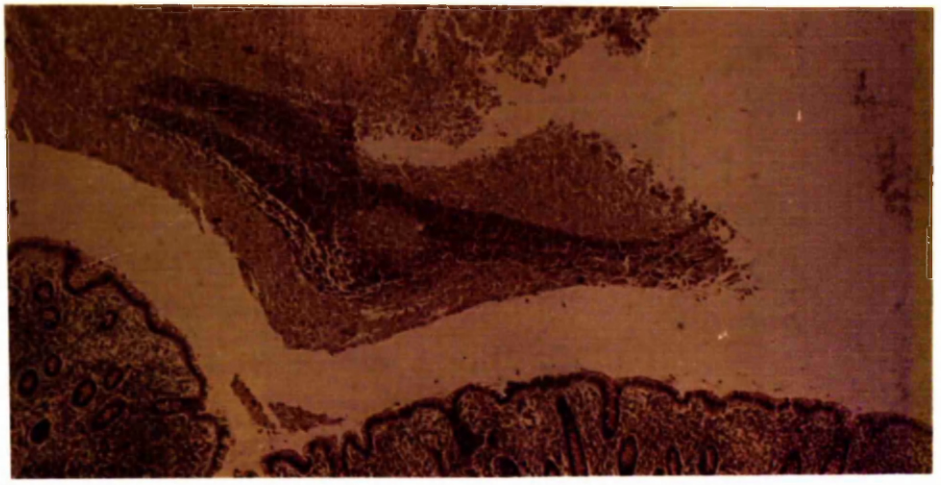


fig. 34

Figure 34 Longitudinal section from terminal portion of grossly normal appendix removed at an emergency operation from a male patient aged 17 years. Present episode of 12 hours duration. Similar episode two weeks previously.

Note apparently normal mucosa but fairly numerous pus cells in lumen of appendix (Haemalum and Eosin, x125).

adenitis which was quite unrelated to disease of the appendix, no correlation of this type should exist.

It is also notable that although removal of this group of appendices is associated with the same "not better" rate as normal appendices, six of the seven patients not improved had recurrent abdominal pain which was not associated with a prussian-blue positive appendix. These patients may thus be regarded as different from the rest of the group and without evidence of associated appendicitis.

The clear implication is that when mesenteric adenitis is found associated with an appendix containing deposits of stainable iron, the two findings should be regarded as related.

Figs. 33 - 35 illustrate a typical case which may be explained on this basis. A 17-year-old boy with mild abdominal pain of 12 hours' duration was admitted to hospital as a case of suspected appendicitis. Two weeks previously he had been seen in a different unit at the hospital with a similar mild pain but had been sent home.

At operation the surgeon's diagnosis was mesenteric adenitis with a normal appendix.

Low power examination of the appendix (fig. 34) showed pus in the lumen but no foci of active appendicitis were seen

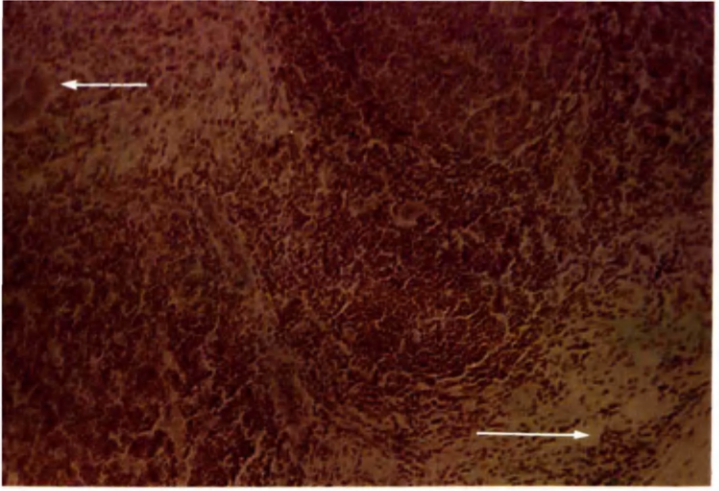


fig. 35

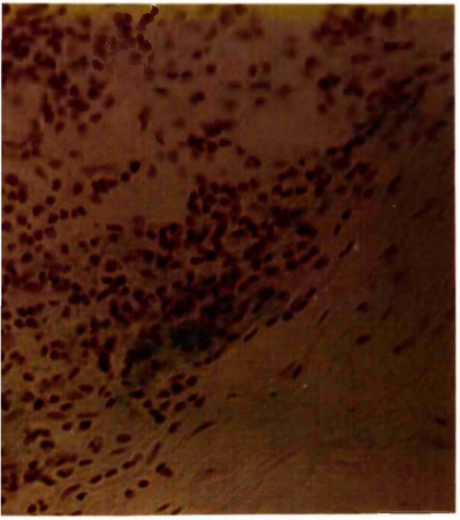


fig. 36

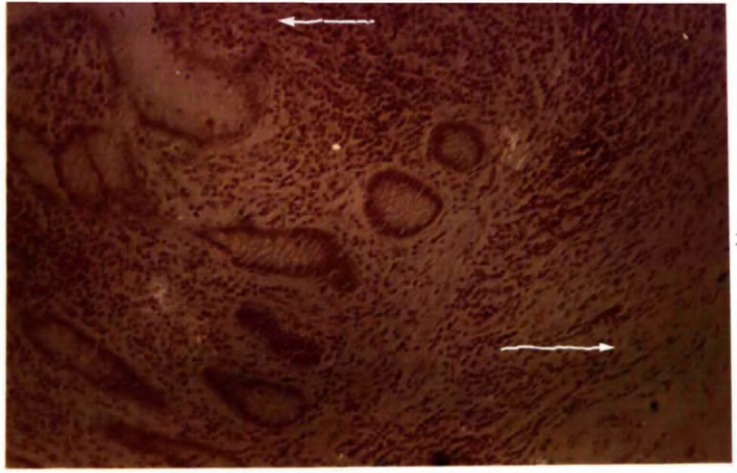


fig. 37

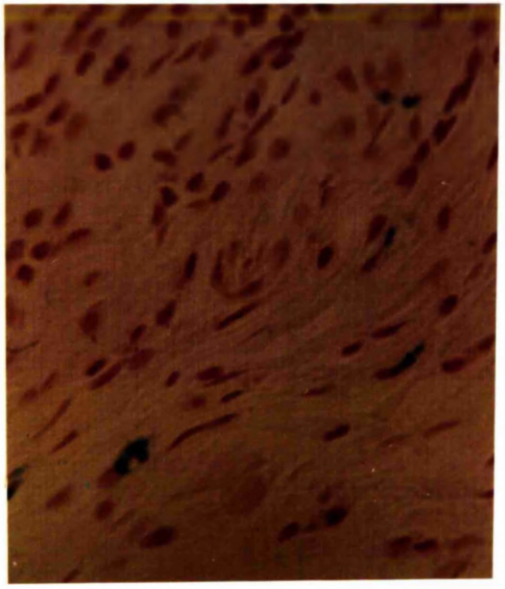


fig. 38

Figure 35 Section from area close to that shown in fig. 34. Some pus cells (not sufficient to allow a diagnosis of appendicitis to be made) are present around gland arrowed at top left. Some stainable iron (arrowed) is seen in submucosa, bottom right (Perls' prussian-blue, x135).

Figure 36 Higher magnification of area arrowed at bottom right of fig. 35 showing stainable iron (P.P.B., x390).

Figure 37 Adjacent section to that shown in fig. 35, also showing pus cells in mucosa (arrowed top left) and stainable iron in submucosa (arrowed bottom right) (P.P.B., x135).

Figure 38 Higher magnification of area arrowed at bottom right of fig. 37 (P.P.B., x480).

despite a thorough search. A few areas with scanty aggregates of pus cells in the mucosa were noted but these were insufficient to support a diagnosis of appendicitis. Figs. 35 - 38 show prussian-blue positive material in the submucosa adjoining two of the areas which showed pus cells in the mucosa. The whole picture strongly suggests a recent mild episode of appendicitis.

The patient has been well since operation.

This case illustrates how the techniques described in the earlier chapters may be used to increase our understanding of one of the problems related to the pathology of abdominal pain. In this example correlation of the clinical history and operative findings with histological abnormalities in the appendix demonstrates a relationship between mesenteric adenitis and recent or continuing appendicitis.

Whether the two lesions share a common aetiology or are related as cause and effect is not easily provable, but in either case an apparently abnormal appendix is being removed.

This example together with the other evidence discussed in this chapter suggests that the frequently curative effect of appendicectomy in mesenteric adenitis can be explained in many cases on the basis of the pathological changes which I

have demonstrated and evaluated in the previous chapters of this section.

Summary

The literature on mesenteric adenitis is revieved. Use is made of the techniques already described for clinico-pathological study of the appendix in relation to abdominal pain to demonstrate a relationship between appendicular disease and some cases of mesenteric adenitis.

CHAPTER 5

OTHER PATHOLOGY OF THE APPENDIX

No discussion of the pathology of the appendix would be complete without reference to some of the many interesting non-inflammatory lesions which may be found there. To be able to study any of these abnormalities in detail would require the collection of larger numbers of specimens than are available in this study. This review is based only on the present series and does not claim to consider all abnormalities which may be found. Nevertheless, as a by-product of the main study, it forms a small but relevant and illustrative sample of the abnormalities which may be found. The largest numerical collection of miscellaneous minor pathology is that of Collins (1955) who reviewed 50,000 appendices examined over 32 years in 11 different hospitals. The incidence of each abnormality described depends greatly upon the diligence of the examiner and upon the sources from which the material is drawn. This is well shown in the first sub-heading below.

fig. 39

Figure 39 Oxyuris vermacularis burrowing into lymphoid follicle. Appendix otherwise normal (Haemalum and Eosin, x45).

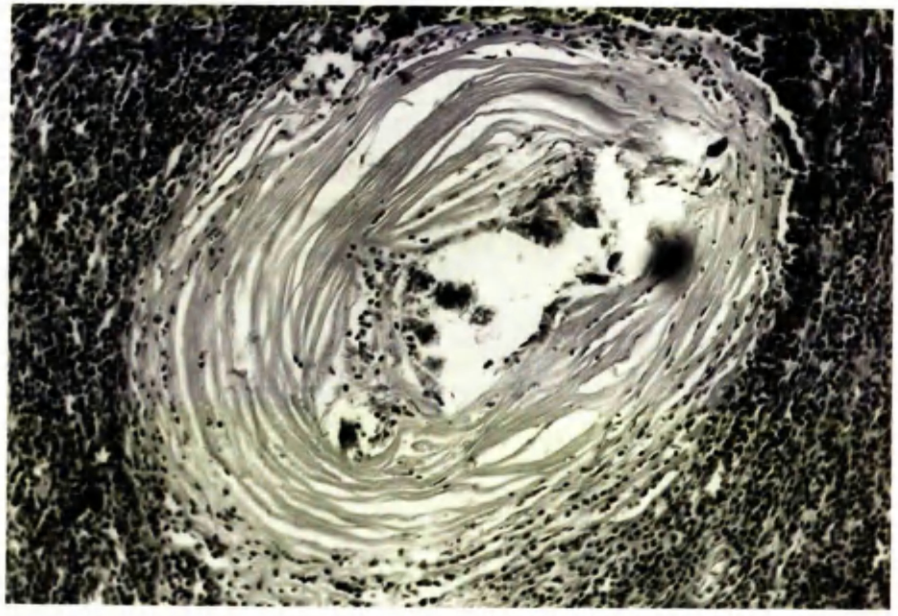


fig. 40

Figure 40 Worm granuloma in lymphoid follicle of otherwise normal appendix (H & E, x150).

Worms and Worm Granulomas

The most complete recent review of the subject is that of Richmond and Guthrie (1964). By serial sectioning of appendices they found infestation by Oxyuris vermicularis in 14% of patients under 21 and in 10% of all patients. This is higher than usually found in routine examination of appendices. The ease with which worms may be overlooked is demonstrated by two examples in my own series where worms were seen in only one of a pair of duplicate sections cut for different staining techniques. The threadworm granuloma was also reviewed by Richmond and Guthrie who found this lesion in six of 45 appendices infested by worms but in none of 32 non-infested normal appendices. They concluded that these granulomas, probably formed by worms entering the submucosa and there dying and becoming encysted, might be present for only a short period after infestation. Figs. 39 and 40 show typical appearances of a worm in the wall of the appendix and a worm granuloma respectively.

Apart from the lower incidence of worms to be expected where serial sectioning is not used, I believe that if inflamed appendices form a high proportion of any series under study, a lower incidence will result due to the contents of the lumen of the appendix being apparently emptied early in the

TABLE 15

Incidence of worms and worm granulomas found in routine histological examination of 1412 appendices

		Worms	Worm granulomas
Histology of appendix	Normal	38 of 586 (6.5%)	5
	Limited acute app.	7 of 107 (6.8%)	1
	Complete acute app.	3 of 718 (0.25%)	5
		48 of 1411 (3.3%)	11
Sex:	Female	31	4
	Male	17	7
Cure rate after operation:	Cured	18	6
	Improved	12	1
	Not better	4	1
	Not known	14	3
Iron:	+ ve	19	4
	- ve	29	7
	* Expected + ve	17	4
Total cases		48	11

* Assessed on basis of 25% +ve in females
50% +ve in males

acute episode.

In the present series of 1412 cases, worms were found in 48 cases and worm granulomas in 11 cases. In no cases were the two lesions found to co-exist but when one lesion was present serial sectioning was not done to look for the other. Table 15 summarises some of the findings in the series.

The difficulties of drawing conclusions due to sampling errors of the type referred to above are obvious. Patients whose appendices contained worms had the same cure rate following operation as appropriate for their main histological group and had the same iron incidence as their main histological group. Thus while some patients may have pain due to worms actively invading the mucosa the presence neither of worms in the lumen nor of worm granulomas in the submucosa can be regarded as a satisfactory explanation for a patient's abdominal pain.

Tumours of the Appendix

Carcinoid (Argentaffinoma) and Carcinoma

Although pathologists usually expect to find one carcinoid tumour in about every 100 appendices examined, Aird (1957, page 864) quoted an incidence of one in 1000 cases and Ackerman

(1959, page 377) an incidence of 1 in 500 cases. At the other end of the scale Vicary (1954) described 9 cases out of 377 (2.5%) whereas Boyd suggested an incidence of 0.2 - 0.4% (Boyd, 1942, page 298). The nature of carcinoid tumours is well discussed by Willis (1960, page 428) and the largest series of carcinoid tumours reported recently is that of Wilson et al. (1963). Appendicular carcinoid is acknowledged to be usually a non-metastasizing tumour but Wilson's figures showed 5 metastasizing carcinoids in a series of 36.

Even if a 15% incidence of metastases be allowed it is noteworthy that Thorsen (1958) in a very thorough study of the carcinoid syndrome could find only one example of carcinoid syndrome due to metastasizing appendicular carcinoid. Latham et al. (1961) also doubted the benign nature of appendicular carcinoid but did not produce facts to support their impressions.

In summary, carcinoid tumours of the appendix are capable of local aggression and of giving rise to hepatic deposits. They rarely appear to have been implicated in causing carcinoid syndrome and for this reason have been regarded as clinically benign despite the morphological evidence of spread.

Primary adenocarcinoma arising in the appendix (as distinct from that extending to the appendix from the caecum) is very

fig. 41

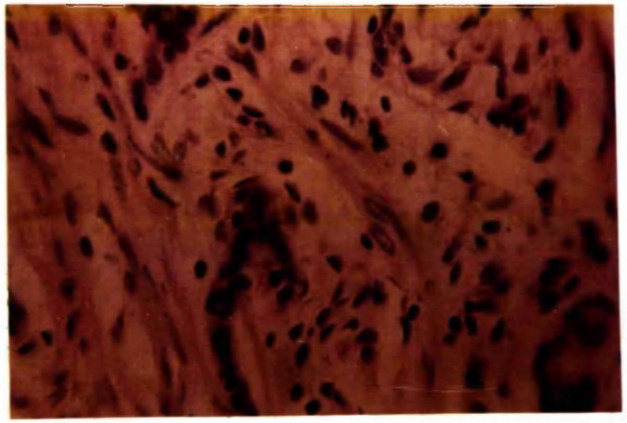


fig. 42

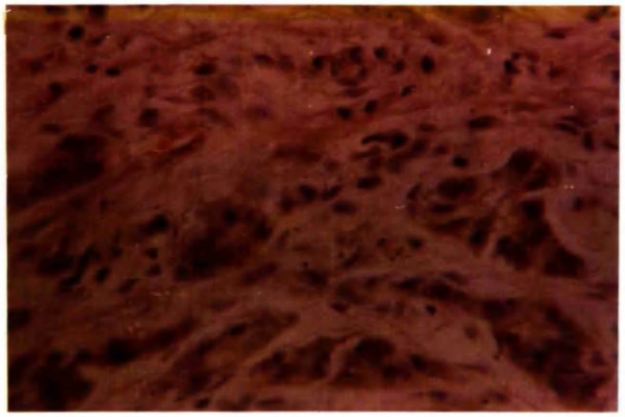


fig. 43

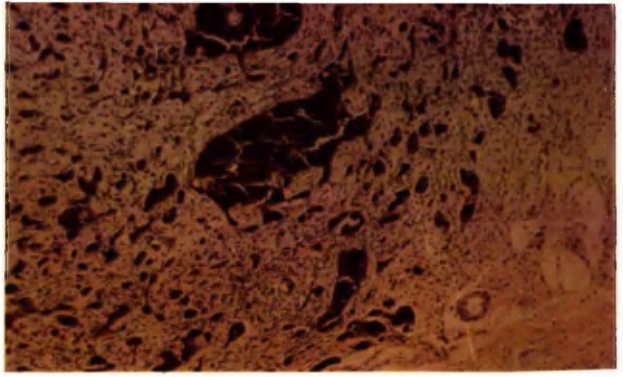


fig. 44

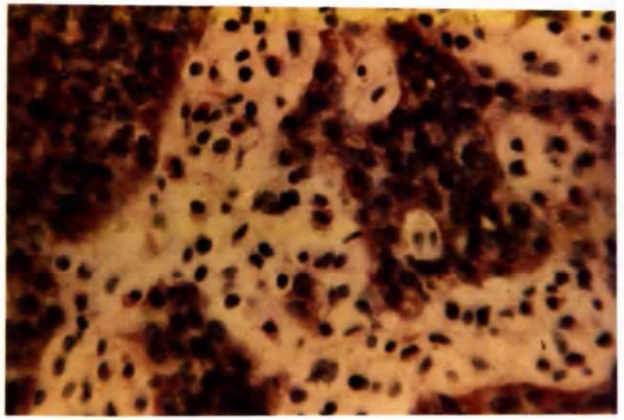


fig. 45

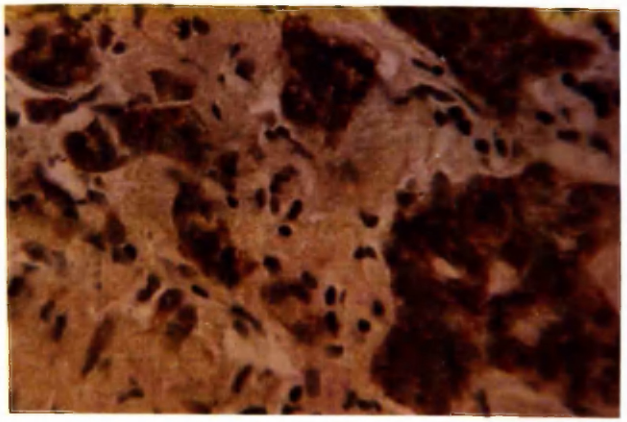


fig. 46

Figure 41 Low power, showing clumps of tumour cells near tip of appendix (Haemalum and Eosin, x40).

Figure 42 High power, showing clumps of tumour cells with no granules visible (H & E, x240).

Figure 43 High power, showing absence of argentaffin cells (diazo, x240).

CARCINOMA OF THE APPENDIX

Figure 44 Low power, showing clumps of tumour cells near tip of appendix (H & E, x40).

Figure 45 High power, showing clumps of cells many of which appear granular (H & E, x240).

Figure 46 High power, showing presence of brown-staining argentaffin cells (diazo, x240).

CARCINOID TUMOUR OF THE APPENDIX

uncommon. In cases of difficulty it may be distinguished from carcinoid tumour by diazo and other stains. Figs. 41 - 46 show typical pictures of carcinoid and carcinoma using haemalum and eosin, and diazo stains.

Pseudomyxoma peritonei and hyperplastic mucocoele are also potentially malignant tumours and are discussed below.

In the present series of 1412 cases, 12 cases of carcinoid tumour and one undoubted case of adenocarcinoma were seen. A second case of apparent primary carcinoma was noted in a 76-year-old female with a previously treated adenocarcinoma of rectum and a co-existent mucinous cystadenocarcinoma of ovary. There was no gross evidence of direct spread to the appendix from other sources and serial sections of the appendix showed no evidence of the appendicular tumour being other than a primary lesion. Whether this is an example of double or treble primary carcinoma is of course uncertain. The case has been reported elsewhere (Howie, 1963).

Of the 12 carcinoid tumours in this series six were found to be associated with acute appendicitis and six with otherwise normal appendices. Eight patients were female and four male. The carcinoma was found in a 27-year-old female who had a history of recurrent symptoms and who did in fact have acute appendicitis

at operation. Only four patients with carcinoid tumours had previously had medical advice concerning abdominal pain.

Mucocoele; Pseudomyxoma peritonei:

Mucocoeles of the appendix were well described in excellent articles by Woodruff and McDonald (1940) and Johnston (1954). Woodruff and McDonald described two varieties of mucocoele. The obstructive type was due to partial obliteration of the appendix proximally and continued secretion of mucus distally with resulting distension of the organ and flattening of the mucosa. The second variety was characterised by proliferation of mucus-secreting epithelium and is not associated with obstruction of the lumen. This was regarded as pre-invasive adenocarcinoma. Woodruff and McDonald found an incidence of 0.3% of mucocoeles out of 45,000 appendices. Only 6% of these mucocoeles were of the premalignant variety (10 cases out of 45,000).

Rupture of an appendix showing either type of mucocoele may result in formation of pseudomyxoma peritonei analagous to that following rupture of an ovarian mucinous cystadenoma. The prognosis of this condition is not favourable (Boyd, 1942, page 301) although removal of the appendix may arrest the process.

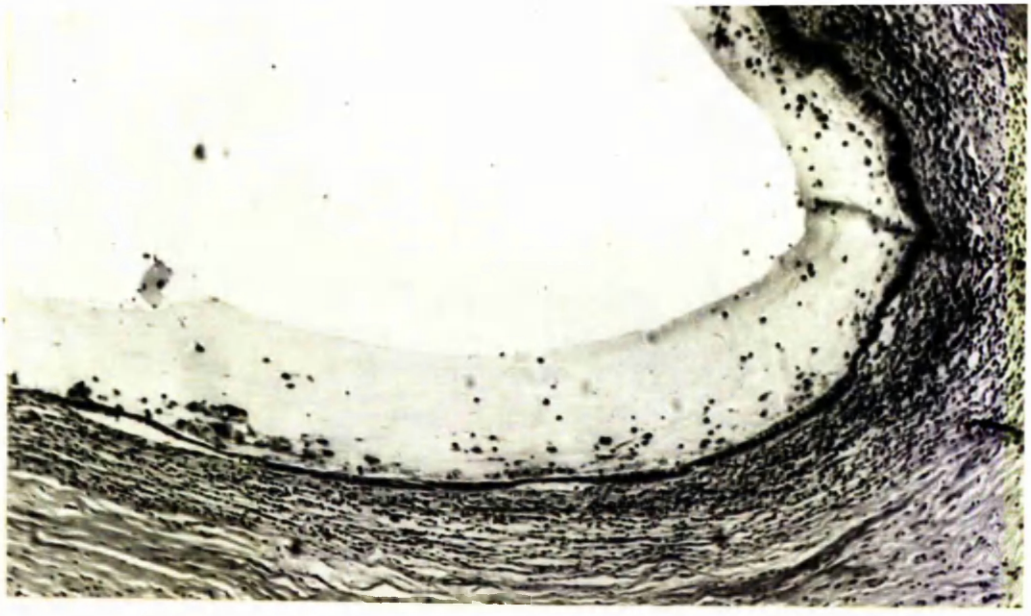


fig. 47

fig. 48

Figure 47 "Obstructive" mucocoele showing compression of mucosal lining due to increased intraluminal pressure resulting from sub-total fibrous obliteration of the lumen near the base of the appendix (Haemalum and Eosin, x75).

Figure 48 "Hyperplastic" mucocoele showing marked increase in the mucus-secreting glands of the appendix mucosa (H & E, x300).

In the present series 15 cases falling into one or other of the above categories were noted. Nine were simple obstructive mucoceles (see fig. 47). In seven of these cases there was a past history of abdominal pain and all eight patients followed-up were cured or improved by operation. Two cases of the hyperplastic mucocoele were seen (see fig. 48). One was an incidental finding in a patient with rectal cancer; the other was removed from a patient of 67 who complained of one year's recurrent pain leading to an alleged appendix abscess. The appendix removed two months later was not the site of previous abscess formation and was iron-negative.

Four patients had pseudomyxoma peritonei. One was a 47-year-old male with ruptured diverticulitis of the appendix; this man was an alcoholic and developed delirium tremens on his third post-operative day. Death resulted from inhalation of vomitus. The clinical history was not a detailed one and unfortunately no reference was made to presence or absence of previous abdominal pain.

The second patient was a 49-year-old female operated on for suspected carcinoma of rectum and found to have an adherent mass involving ileum, caecum and appendix associated with a ruptured diverticulum of the appendix. This patient had been in hospital

one month previously with low central abdominal pain described as due to "urinary infection" on the basis of a light growth of coliforms obtained from a mid-stream specimen of urine.

The third patient, a female of 17, with recurrent right iliac fossa pain over one year, was found to have a ruptured diverticulum with pseudomyxoma. She has been symptom-free since operation.

The fourth patient, a 32-year-old female presented a most interesting problem. She was first admitted to hospital two years before operation with low right iliac fossa pain diagnosed as cystitis, again on the basis of a bacteriological report of doubtful significance. Coliforms but no pus cells were noted in a mid-stream specimen of urine. She was treated conservatively. Soon after she was investigated for a history of seven years' infertility and found to have blockage of the right Fallopian tube. Two years after the first admission to hospital she was again admitted as a surgical emergency with relatively mild right iliac fossa pain but this time was taken to theatre. The operative finding was of multiple areas of adhesions including some between the right Fallopian tube and the tip of the appendix. The whole appearance suggested tuberculosis to the surgeon operating. Histological examination however, showed endometriosis

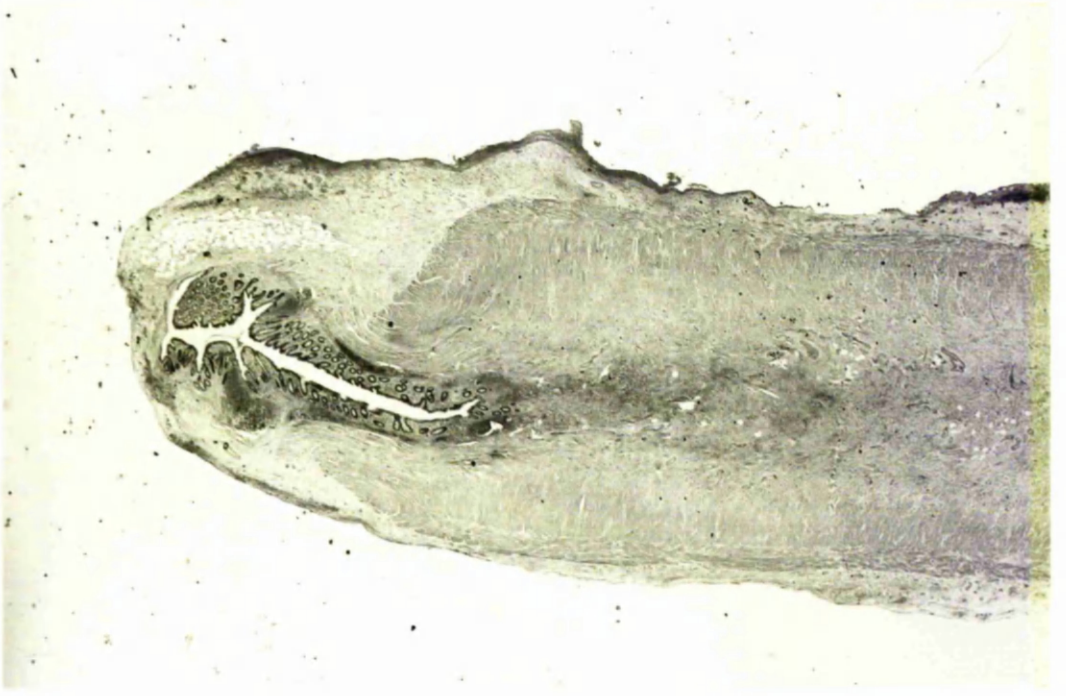


fig. 49

Figure 49 Ruptured diverticulum at the tip of the appendix. Mucin was demonstrated histochemically on the serosal lining but no glandular elements were identified beyond those seen in this figure (Haemalum and Eosin, x6).

of the appendix and pseudomyxoma peritonei. The pseudomyxoma may well have caused the obliteration of the right Fallopian tube to which it was adherent. Whether the sterility was due to this, or to endometriosis or the supposed abdominal tuberculosis - which has not been confirmed - is an open but interesting question.

Diverticulae of the Appendix

Wilson (1950) in his detailed contribution to this subject was notably cautious in discussing the aetiology of diverticulae of the appendix and believed that if infection contributed to their formation it was most likely to be by causing luminal constriction with rise of intraluminal pressure.

In the present series, diverticulae were seen in 39 of 1412 cases, an incidence of 2.7%. 19 patients were females and 20 males. A ruptured diverticulum is shown in fig.49. The main clinical implication of a diverticulum is the risk of pseudomyxoma developing after its rupture. Only two of the cases in the series were associated with a normal appendix, the other 37 being acutely inflamed. Over half (22 of 39) the patients gave a history of previous abdominal pain similar to that for which they were operated on and a striking feature was

fig. 50

Figure 50 Endometriosis of the appendix, showing endometrial glands in subserosa. There was no evidence of recent or active bleeding related to the endometriosis. The appendix was otherwise normal. There was no gross evidence of pelvic endometriosis (Haemalum and Eosin, x75).

the number of diverticulae which were positive for stainable iron (27 of the total of 39 or 68%, but 16 out of 22 appendices (95%) where the patient had a positive past history of abdominal pain). This simply confirms the obvious likelihood that diverticulae, however they be formed, will be particularly likely to be the starting point for attacks of mild or serious appendicitis and thus prone to erosion of their walls and rupture.

Endometriosis

The most recent review of endometriosis is that of Lane (1960) who discussed 30 cases collected during a period of 36 years. He states that haemorrhage rarely occurs into the lesion. Sutton and Hardy (1952) describe endometriosis as occuring in 0.02% of female patients. In my series I have seen four cases in 810 female appendices, only one of which was associated with positive prussian-blue reaction indicitive of recent haemorrhage. This lesion (fig.50) is not likely to be of clinical significance. A fifth patient in my series had a glandular structure on the serosa which was thought to be a Mullerian rest.

fig. 51

Figure 51 Pseudomelanosis of the appendix, showing typical deposits of pseudomelanin in the mucosa of an otherwise normal appendix (Haemalum and Eosin, x240).

Pseudomelanosis

This lesion is of interest to the histologist more for its staining properties than because of any pathological significance. These properties and possible aetiological factors are discussed fully by Pearse (1960, page 668). The two theories put forward are:-

(1) that aromatic protein degradation products are absorbed from the large intestine and converted into melanin in the connective tissue and

(2) that pseudomelanin is associated with chronic medication with anthracene purgatives such as cascara sagrada.

I noted 18 cases of this condition in my series of 1412 cases and in all of them a blue-green pigmentation of the affected area was obtained with the prussian-blue reaction. It may be only a chance finding that worms were present in three cases and a worm granuloma noted in a fourth case. The typical appearances of this condition are shown in fig. 51.

Other Findings

One case presented all the appearances of Crohn's disease (regional ileitis). After operation the patient continued to

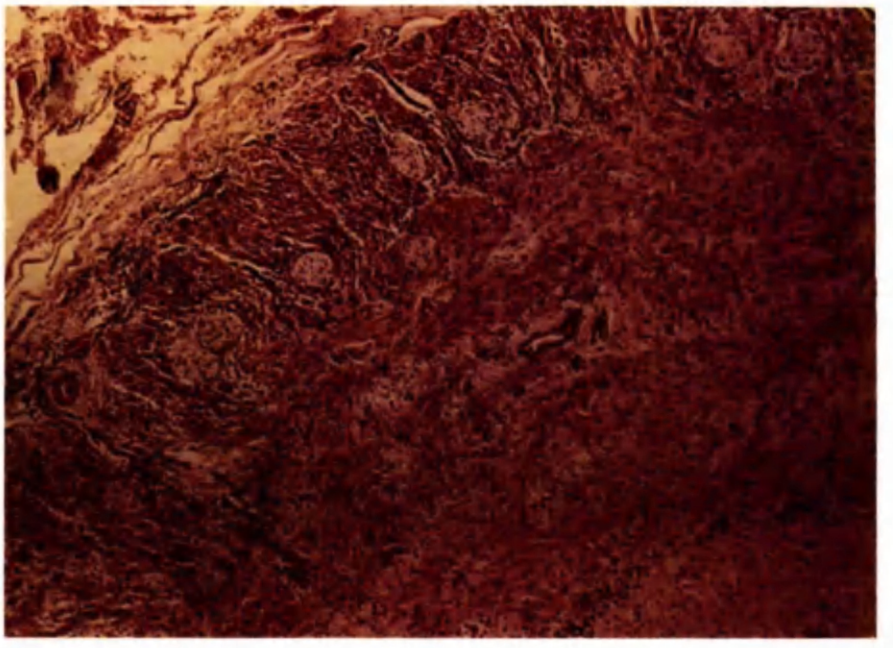


fig. 52

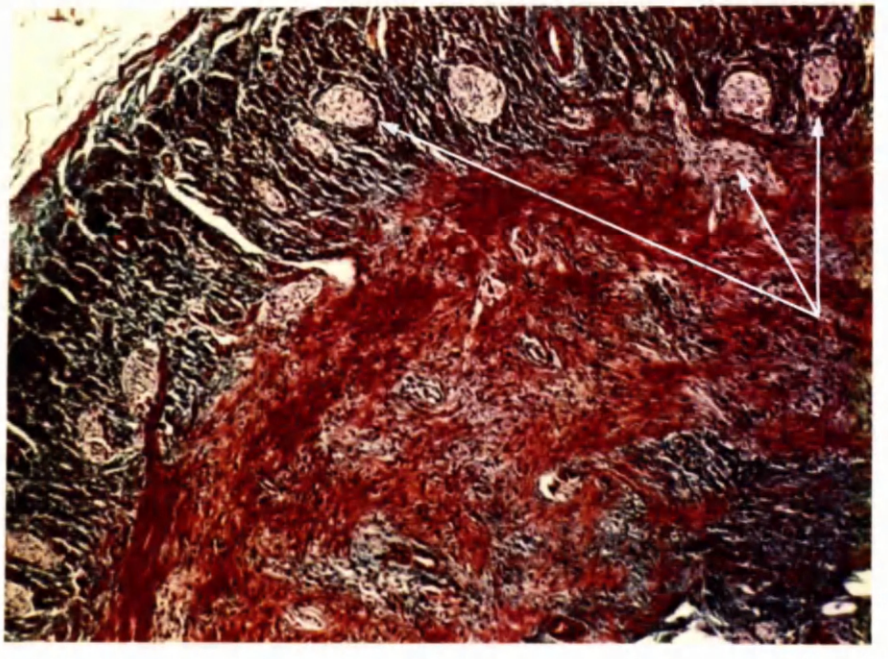


fig. 53

Figure 52 Segment of transverse section of appendix removed from 42-year-old male patient, 2 months after a clinical diagnosis of appendicitis had been made. Note bundles of neural tissue in muscularis and submucosa (Haemalum and Eosin, x75).

Figure 53 Same section as fig. 52 with neural bundles arrowed (Masson, x75).

have symptoms, as he had done for nine months before operation, and subsequently had a resection of another area of Crohn's disease of the small intestine with complete relief of symptoms after a fairly stormy convalescence.

One case was normal apart from an isolated arteritis at the tip of the organ. Arteritis has frequently been described in the past although its significance has never been established. The interesting feature in this case was that the patient was suffering from retroperitoneal fibrosis involving, amongst other viscera, the appendix. The patient has remained well since operation and no manifestations of any connective tissue disease have been seen.

One patient was observed to have what appeared to be a renal tubule at the tip of the appendix. Further inquiry showed that the appendix had in fact been adherent to the upper pole of the right kidney at operation but subsequent intravenous pyelogram examination gave no further information.

The final case is shown in figs. 52 and 53. The patient had his appendix removed 2 months following an appendix abscess and the striking neuromatous bundles were seen as demonstrated in the photographs. Whether this represents merely the neuromas described by Masson (1930) as a sequel to appendicitis or the

rare von Recklinghausen's disease of the appendix reported by Russell and Rubenstein (1963, page 270) in their textbook of tumours of the nervous system is of theoretical rather than practical importance.

Summary

In this study of 1412 appendices, a pathological change in addition to, or apart from inflammation was seen in 154 cases, or 10.5% of cases. These lesions are discussed briefly.

CHAPTER 6

CLASSIFICATION OF APPENDICES FOR CLINICAL STUDY AND EXAMINATION OF ACCURACY OF HISTOLOGICAL CRITERIA

Having claimed in the introductory section of this study that one of the inherent advantages of this particular study over other investigations of appendicitis lay in the histological classifications being used, I must now demonstrate that the criteria I use are:

(1) reproducible;

(2) superior to a simple clinical classification based on the surgical operative findings; and

(3) superior to other histological systems of classification.

At the same time as claiming basic advantages for my histological definitions of normal appendices and for the mild forms of appendicitis I am prepared to accept the claim of Barnes et al. (1962) for the superiority of surgical findings as a basis for classification in cases of severe appendicitis and to accept the surgical terms "gangrenous appendicitis" and "perforated appendicitis" as individual groups. The complete classification

to be used in the primarily clinical study which follows in the next section is defined and discussed later in the chapter.

Reproducibility of Results

A histological report was made to the surgeon on all appendices in this study shortly after their removal. These reports were based on the assumption that limited acute appendicitis was a variant of an abnormal appendix and that histological changes of inflammation short of limited acute appendicitis could not be accepted as diagnostic of abnormality.

We shall consider in this chapter the 1284 consecutive appendices removed from patients in clinical presentation classes A and B (patients operated on for acute or recurrent abdominal pain). All of the first 500 of these appendices were re-examined two years after the original report was given with no knowledge of the original findings and the results compared with that of the original report. Only in three cases was a difference of opinion found which involved gross errors of diagnosis, two appendices showing complete acute appendicitis having been reported as normal and one case vice versa. Most errors involved the separation of normal appendices with atypical appearances (which should have been reported as normal) from those with limited

acute appendicitis. Therefore, all of the 784 remaining appendices showing either atypical appearances or limited acute appendicitis on their original examination were re-examined. Although these cases were known by the observer to have been selected in this way, their exact diagnoses on the first examination were unknown. Altogether 41 cases of the 1284 were interpretated differently on the second examination, an incidence of error of objective interpretation of 3.2%. In six of these cases appendicitis had not been diagnosed on the first examination when it in fact was present, and in 35 cases appendicitis had been diagnosed wrongly on the first occasion. Most of the errors took place in the early months of the study, before the significance of traumatic artefact had been fully appreciated.

In summary, an experienced observer should have an accuracy of overall classification, using the criteria defined in Chapters 1 and 3, of about 96%. Where the material has been re-examined as in this study, the accuracy of classification must be well above that frequently accepted as satisfactory for clinical study.

Comparison with Surgical Findings

The operation notes of the 1284 patients with Class A and Class B type of clinical history were studied and the

surgeon's diagnoses were recorded. These were compared with the final histological findings and disagreement noted in 172 cases. Where the surgical diagnosis was stated to be doubtful or could not be inferred, it was regarded as being in agreement with the histological report. This total of 172 cases is composed of 88 cases diagnosed as histologically normal but regarded by the surgeon as showing appendicitis and 84 diagnosed histologically as appendicitis (17 as complete acute appendicitis, 67 as limited acute appendicitis) but regarded by the surgeon as normal. The percentage of cases in which disagreement as to classification exists is thus 13.5% or 1 case in 7. As the errors almost balance the difference is not obvious on superficial examination of proportions of normal and abnormal cases.

It is of interest that the tendency to overdiagnose appendicitis on operative grounds is most marked in units advocating operative treatment for doubtful cases of clinical appendicitis, whereas the tendency to underdiagnose appendicitis is mainly shown by conservatively-minded surgeons. Both groups of surgeons overdiagnose appendicitis in colleagues, members of the families of colleagues, or members of the nursing staff.

It is, of course, obvious that none of the surgical opinions are capable of re-examination by the same or a second observer

TABLE 16

Analysis of follow-up results in patients about whom disagreement of diagnosis exists between histologist and surgeon.

Follow-up	Histology = normal but surgery = appendicitis	Histology = appendicitis but surgery = normal	Total
Cured	40	42	82
Improved	14	20	34
Not better	8 +	3 †	11
Not followed-up	26	19	45
T O T A L	88	84	172

+ Percentage not better of those followed up = 13% (= follow-up of normal appendicectomy)

† Percentage not better of those followed up = 4.5%(= follow-up of abnormal appendicectomy)

and that their objectivity must therefore be still further doubted.

A distressing feature of the study was the discovery that in 52 of the cases where difference existed and the pathology report was available to the surgeon before the discharge letter was sent, no mention was made in the letter to the general practitioner of this doubt. In 35 cases this has led to a false impression being given that an acute appendix had been removed and in 17 cases a false impression has been given suggesting that a normal appendix has been removed.

Whatever the surgeons may believe about the value of histological opinions, to ignore them when disagreement exists cannot be regarded as indicating objectivity or desire for objectivity on their part.

All that the previous paragraphs have demonstrated is that disagreement is common. In an attempt to establish one system of classification as superior, the clinical follow-up results for the 172 patients about whom there is disagreement have been analysed (see table 16). Although the figures are small, it will be seen that the proportions of persons "not better" after operation in the two groups suggest that the histological classifications are the more useful prognostic indices. Two of

the patients "not better" in the group with histological appendicitis had limited acute appendicitis. The third patient had complete acute appendicitis.

In summary, histological criteria are superior to operative criteria where differentiation is required between normal and abnormal. Their superiority is shown in their prognostic value and is inherent in their being available for re-examination by one or more observers.

Comparison with other Histological Criteria

The present series cannot be discussed in this context but reference may be made to two other histological studies, in one of which I personally participated.

The first study is that reported by Campbell et al. (1961) and referred to in Chapter 1 of this section. They divided material into "normal" "superficial appendicitis" and "acute appendicitis." Their "superficial appendicitis" though not defined exactly, is probably equivalent to my limited acute appendicitis. In a retrospective study they made this diagnosis in 28 of 422 incidentally removed appendices (my clinical class D) and in 36 of 578 appendices removed from patients with appendicitis.

In a second prospective study they found superficial

TABLE 17

Agreement on diagnosis found when 3 pathologists examined one group of 165 slides from patients having appendicectomy.

		Howie		
		-1	0	+1
Dr. "A"	+1	14	7	73
	0	15	8	9
	-1	29	6	6

Complete agreement 110 cases.
Complete disagreement 20 cases.

		Howie		
		-1	0	+1
Dr. "B"	+1	13	16	85
	0	15	4	1
	-1	29	1	1

Complete agreement 118 cases.
Complete disagreement 14 cases.

		Dr. "B"		
		-1	0	+1
Dr. "A"	+1	6	6	81
	0	12	5	15
	-1	13	9	18

Complete agreement 99 cases
Complete disagreement 24 cases.

Overall agreement in 57% of cases)
2 pathologists agree in 93% of cases)

Key: +1 = appendicitis
-1 = normal appendix
0 = doubtful

appendicitis in 24 of 68 incidentally removed appendices and 27 of 141 appendices from patients with appendicitis. Thus the incidence of superficial appendicitis rose in the two series from 7% to 36% for incidental appendicectomies and from 6% to 19% for patients with appendicitis. The implication of this is that for histological criteria to be of value their upper and lower limits must be carefully defined. The criteria of Campbell et al. have apparently been basically reasonable but not exact enough to meet the requirements of objectivity required for a full-scale investigation.

The second study is of interest in that three pathologists (including myself) examined one set of histological material and the diagnoses have been compared. The full details will be published shortly (Barraclough et al. in preparation). Table 17 shows the breakdown of opinions of the three histologists. It will be noted:

(1) that complete agreement is found in only 57% of cases;

(2) that in the pair of opinions with fewest agreements and most disagreements, neither pathologist has made a particular study of the problems of appendicitis; and

(3) that in the most favourable pair of opinions (Howie versus "B") there is disagreement in 14 of 132 cases (10%) a figure not much

different from the 13.5% disagreement shown between surgeon and histologist given under the preceding heading.

It is difficult to compare these figures with others as no indications were given to the histologists taking part in the study of the circumstances of removal. In some cases the material was not of good histological quality and in some cases of difficulty only one or two sections were available for study, this being short of the best possible standards. Because of these difficulties, cases have been described as"doubtful" by myself when examination of more material might have made a definite diagnosis possible; no doubt the other histologists experienced the same problems.

However, excluding doubtful cases ("0" in table 17) from each pair of analyses, untested histological criteria compare unfavourably in objectivity and reproducibility with tested histological criteria but appear broadly comparable to surgical operative findings in their usefulness.

Summary

The difficulties of comparing different methods of classification are considerable. The histological criteria I have defined and tested appear to be more objective than any other criteria available and appear to give the most accurate prognostic help.

They are thus superior to other criteria for separating normal appendices from mild and severe acutely inflamed appendices.

This is clearly a fundamental and important division to make in any study of appendicitis and abdominal pain and its practical value has already been demonstrated. The other important features in a clinical study depend on the onset of advanced inflammatory changes more easily described at operation.

The classification of cases I propose to use for the clinical studies which follow is:-

1.	NORMAL APPENDIX	BASED ON HISTOLOGICAL CRITERIA DEFINED
2.	LIMITED ACUTE APPENDICITIS	
3.	COMPLETE ACUTE APPENDICITIS	
4.	GANGRENOUS APPENDICITIS	BASED ON SURGICAL FINDINGS
5.	PERFORATED APPENDICITIS	
6.	INTERVAL OPERATION	BASED ON A HISTORY OF A RECENT CLINICALLY DIAGNOSED APPENDIX ABSCESS

Class 1 will be divided on the basis of operative findings into cases where acute extra-appendicular pathology co-exists. Acute extra-appendicular pathology does not include mesenteric

TABLE 18

Distribution of appendices to tested clinico-pathological groups for future studies of abdominal pain.

Main classification	Sub-classification	Cases	
1. Normal appendix	No other acute lesion	396	(32.5%)
	Non-acute ovarian lesion	29	
	Acute ovarian lesion	13	(3.5%)
	Acute extra-appendicular lesion	34	
	Total	472	(36%)
2. Limited acute appendicitis	-	101	(7.5%)
3. Complete acute appendicitis	-	568	711 (54%)
4. Gangrenous appendicitis	-	78	
5. Perforated appendicitis	-	65	
6. Interval appendicectomy after appendix abscess	-	28	(2%)
Total	-	1312	(100%)

adenitis or ovarian lesions unless the latter are accompanied by rupture, bleeding or torsion. Patients who have abscesses found at emergency operation are placed in Class 5. Those having interval appendicectomy for recent appendix abscess are classed separately (Class 6).

This classification has the advantage of greater objectivity and simplicity over the Grey-Turner (1938) and MRC (1944) classifications. The distribution of cases to each class is shown in table 18.

Barnes and his colleagues (1962) have apparently been correct in their belief that histological criteria have not in the past formed a particularly useful foundation for the study of appendicitis. This, however, has been due more to the absence of good histological criteria than to any particularly satisfactory substitute being available.

This omission appears to have been rectified by the introduction of the histological criteria described and examined in this section.

The next section uses them to help examine the problems involved in deciding the treatment of the patient who presents to the general practitioner or surgeon as a possible case of appendicitis.

SECTION 2

A

STUDY OF THE MORBIDITY AND MORTALITY

RESULTING FROM DIFFERENT

APPROACHES TO THE TREATMENT

OF APPENDICITIS

CHAPTER 1

CRITERIA OF MORBIDITY

This section deals with a study of those patients admitted to hospital with abdominal pain where the fear of appendicitis is one of the reasons for their admission. The aim of the study is to determine whether operative or non-operative treatment causes the lower morbidity.

Any clinical trial of two methods of treatment entails difficulties of observer bias and definition of criteria but if these are properly catered for useful comparisons can be made. Four problems of design complicate this particular experiment. Firstly, one of the two treatments involves the unique physical and mental trauma of operation, and the principal morbidity will be short-term. In the non-operative treatment, on the other hand, the principal morbidity is in the introspective attitude developed by patients to their abdominal pain with the long-term risk of appendicectomy or appendicitis still present.

Secondly, although the test group is defined in the opening sentence of this chapter, patients are selected for

the two treatments by ill-defined criteria many of which are personal to the surgeon, and the two treatments are not superficially capable of direct comparison.

Thirdly, only about two-thirds of the patients selected for operative treatment indeed suffer from the disease for which they are being treated, and there is room for doubt - as has been demonstrated in the previous chapters - even about which patients these are. On the other hand, the number of patients selected for non-operative treatment who actually have appendicitis can be calculated only by inspired guesswork.

Fourthly, the risk of mortality inherent in the two treatments must be a major consideration. Failure to treat a patient with genuine but atypical or mild appendicitis may lead to a fatality from advanced appendicitis at a later date - appendicitis appears to be a recurrent disease - and even the removal of a normal appendix will, on simple rules of chance, save some people from being included in the class of those who die of advanced appendicitis in later life. On the other hand, by the same rule of chance, some people having this operation for removal of a normal appendix will die as a result of the operation and not from their original abdominal pain. On the surface this is the greater tragedy as the few people in this

group are usually in the prime of their lives and, if they did not in fact have appendicitis, their illness would have been self-limiting.

These difficulties preclude a simple comparison and a neat answer; but it is possible, nevertheless, by using patients as their own controls (Leak, 1954) to find the proportion in each group who are likely to have the ideal result of cure with no complications. It is also possible to analyse the risk and nature of those complications which are likely to arise and thus to present an overall picture of the probable course of events if one or other type of clinical management is employed.

The main subdivisions of patients used in this study are

(1) age;

(2) mode of clinical presentation; and

(3) degree of abnormality of the appendix.

The third of these divisions is the one which most influences short-term post-operative complications, and thus mortality. The clinico-pathological classification defined in Chapter 6 of the first section is the basis for this subdivision (see page 92).

The second of the above items was shown earlier to influence the rate of cure following removal of a normal appendix (Chapter 3 Section 1).

For the purposes of this study four distinct age groups can be recognised. The first is that of childhood. In the very early ages death is usually due to late diagnosis and the problem of obtaining a history is different from that in the adult. Because the bulk of the material in this study was collected in a hospital without paediatric practice, the first group is defined as from birth to 11 years. The second group of patients is that aged between 12 and 29 years. Most patients whose treatment is in doubt are found in this age group, and it is the study of the different forms of management available to those patients which forms the main subject of the present investigation. These patients are normally physically fit for operation. The third group of patients aged between 30 and 49 years, contains fewer diagnostic problems and these patients are usually also fit for operation, even if less certainly so than those in the previous group. The last group of patients, those over 50 years of age, carries an appreciable mortality, much of which is due to late diagnosis, although the general fitness of the patient is decisive in many cases.

Different problems influence the management of male and female patients. In females the problem is mainly that of differential diagnosis from pain of gynaecological origin. In

males the problem is the greater risk of morbidity and mortality likely to result from the delayed diagnosis of true appendicitis. This is reflected in the higher incidence of advanced changes found at operation, and possibly follows on the failure of mild appendicitis to produce warning pain sufficiently early or frequently in males (Chapter 3 Section 1). Where appropriate, male and female patients are considered separately.

Morbidity for operative and non-operative management of possible appendicitis is discussed in the two succeeding chapters under the main headings of short-term, intermediate, and long term morbidity.

The mortality caused by the respective methods of treatment is dealt with at greater length in the fourth chapter of this section.

Using the results of these studies, the probable consequences of advising operative or non-operative treatment for an individual patient have been calculated; and an estimate has been made of the way in which widespread acceptance of either the radical or conservative approach to treatment would influence the pattern of morbidity from abdominal pain and appendicitis in the community at large.

CHAPTER 2

MORBIDITY OF APPENDICECTOMY

This will be considered under four headings - namely, short-term, intermediate, long-term, and general. Short-term considerations are based on the period before the patient returns to normal employment. Intermediate complications fall within the period from 12 - 24 months after operation, for which time careful follow-up studies have been carried out. The long-term considerations are estimated on the basis of retrospective studies of appendicectomy. The "general" considerations are those related to cure, mortality, and psychological factors.

Short-term Morbidity

This can be measured in terms of days of hospital in-patient care, of weeks absent from normal employment, or of incidence of various complications. To a large extent the three are related although length of absence from normal employment also depends on non-medical factors. Separate consideration of the individual complications of appendicectomy was given in great detail in the monographs of Boyce (1949) and Love (1947). A more concise account of the morbidity from appendicitis was recently produced

by Wright (1963). Most previous studies of morbidity have been composed of cases collected over a wide span of years and thus subject to variables other than clinical severity of illness (new anaesthetics and antibiotics for example). The present series has the advantage of studying a large number of patients (1312) operated on over a period of only 2 years.

A points system has been devised for the purpose of this study to make the assessment of operative morbidity realistic and objective. A patient scores nil points only if in hospital for 10 days or less after operation and having absolutely no post-operative complications. Morbidity points are scored on the following basis:-

General

For each day in hospital beyond 10.	$\frac{1}{3}$ point
For each visit to hospital as an out-patient for wound dressing.	
For each home visit for wound dressing by family doctor or district nurse.	

Minor complications

A pyrexia of uncertain origin. Minor respiratory upset. Wound discharge.	2 - 4 points depending on severity.

Straightforward complications

Wound infection with pus or requiring antibiotic therapy.	5 points

Severe complications

Severe wound infection. Pneumonia.	6 - 8 points depending on severity.

Potentially dangerous complications

Adhesions; ileus. Pulmonary embolism; deep venous thrombosis. Pelvic abscess.	10 points

Any administration of a general anaesthetic - 5 points.

Other situations not described above scored as appropriate.

TABLE 19

Distribution of short-term post-operative morbidity for 1,312 patients subdivided into clinico-pathological groups as described in Section I.

	No morbidity	Trivial morbidity	Potentially serious morbidity	Serious morbidity	Potentially dangerous morbidity	Dangerous morbidity	Total
Normal appendix — Other acute lesion present	21	8	6	4	6	2 +	47
Normal appendix — No acute abdominal pathology	333 (78%)	60 (14%)	23	6	1	2 (0.5%)	425
Limited acute appendicitis	76 (76%)	8 (8%)	11	4	0	2 (2%)	101
Complete acute appendicitis	401 (69%)	74 (13%)	56	20	11	6 (1%) +	568
Gangrenous appendicitis	27 (34%)	14 (17%)	16	13	7	1 (1.3%) +	78
Perforated appendicitis	5 (7.5%)	12 (18%)	25	10	8	5 (7.5%) +++	65
Interval appendicectomy post-abscess	12	5	5	1	2	3	28
Total	875 (66.6%)	181 (13.5%)	142	58	35	21 (15%)	1,312

+ = death. Total = 6.

Mortality from appendicectomy is discussed in a later chapter.

A total score of 1 - 5 points is regarded as equivalent to the clinical description of "trivial" morbidity; a score of 6 - 10 points as "potentially serious" morbidity; a score of 11 - 15 points as "serious" morbidity; a score of 16 - 25 points as "potentially dangerous" morbidity; and a score of over 25 points as "dangerous" morbidity. As more severe forms of any complication usually differ from milder forms by the length of time the patient is kept under hospital supervision, so the morbidity score for that complication will be modified appropriately. It is found that by applying these criteria of morbidity-scoring to some typical cases realistic and objective results may be produced. These enable an overall picture of morbidity to be produced which is simpler to comprehend than that composed of long tables showing the breakdown of patients with chest infections, wound infections and so on.

Table 19 shows the distribution of short-term post-operative morbidity of cases in each of the clinico-pathological classes defined in Chapter 6 of Section 1 (table 18 facing page 93). As expected, morbidity rises with the advancement of the inflammatory

TABLE 20

Morbidity score for 377 male patients between 12 and 29 years of age in each clinico-pathological group described in Section I

	No morbidity	Trivial morbidity	Potentially serious morbidity	Serious morbidity	Potentially dangerous morbidity	Dangerous morbidity	Total
Normal appendix. Other acute lesion present	4	1	0	0	0	1	6
Normal appendix. No acute abdominal pathology	85 (82%)	12 (11%)	6	1	0	0	104
Limited acute appendicitis	20 (73%)	3 (11%)	2	2	0	0	27
Complete acute appendicitis	147 (73%)	25 (12%)	13	6	5	1 +	197
Gangrenous appendicitis	7 (33%)	5 (21%)	5	5	0	0	22
Perforated appendicitis	2 (10%)	1 (5%)	11	3	1	1	19
Interval appendicectomy post-abscess	1	1	0	0	0	0	2
Total	266 (71%)	48 (12%)	37	17	6	3	377

+ Indicates one death.

process. The prospects of a patient having what would be generally accepted as "an uneventful recovery" - equivalent to a morbidity score of up to 5 points - were 92% where a normal appendix was removed, 84% where limited acute appendicitis was present, 82% where complete acute appendicitis was present, but only 51% for a gangrenous appendix and 25% where perforation had occured. Tables 20 and 21 show the same findings for those male and female patients in this series whose ages were between 12 and 29 years inclusive.

The percentage of patients having "uneventful recoveries" after removal of appendices with limited or complete acute appendicitis was 89% in patients under 30 years of age but 70% in patients over 30 years of age. (Calculated on basis of totals in table 19, less the combined totals of tables 20 and 21). Where a gangrenous or perforated appendix was removed the incidence of uncomplicated recoveries was not significantly different in patients under 30 years of age (27 of 61 = 44%) from that in patients over 30 years of age (31 of 82 = 38%).

In patients under 30 years of age, only 11% of abnormal appendices were perforated (61 of 532) compared with 29% in patients above 30 years of age (82 of 280). This difference is highly significant ($X^2 = 45$ $P<0.01$).

TABLE 21

Distribution of short-term post-operative morbidity (as defined in text) for 520 female patients between 12 and 29 years of age subdivided into clinico-pathological groups as described in Section I.

		No morbidity	Trivial morbidity	Potentially serious morbidity	Serious morbidity	Potentially dangerous morbidity	Dangerous morbidity	Total
Normal appendix.	Other acute lesion present	11	0	0	2	1	0	15
	No acute abdominal pathology	182 (78%)	34 (14%)	11	5	2	1	234
Limited acute appendicitis		43 (86%)	2 (4%)	2	1	0	1	49
Complete acute appendicitis		162 (81%)	18 (9%)	9	3	4	2	198
Gangrenous appendicitis		4 (40%)	4 (40%)	1	1	0	0	10
Perforated appendicitis		2 (20%)	2 (20%)	2	3	1	0	10
Interval appendicectomy-post-abscess		2	0	0	0	0	2	4
Total		406 (78%)	60 (11%)	25	15	8	6	520

There were no deaths in this group of patients.
Figures in parenthesis refer to percentage of total cases in appropriate clinico-pathological group.

The higher morbidity from appendicitis which is found in elderly patients thus appears to be due more to late diagnosis than to the age of the patient.

No significant differences in morbidity between male and female patients were demonstrated in any main age group, but the number of patients with complications was small and this finding is not conclusive.

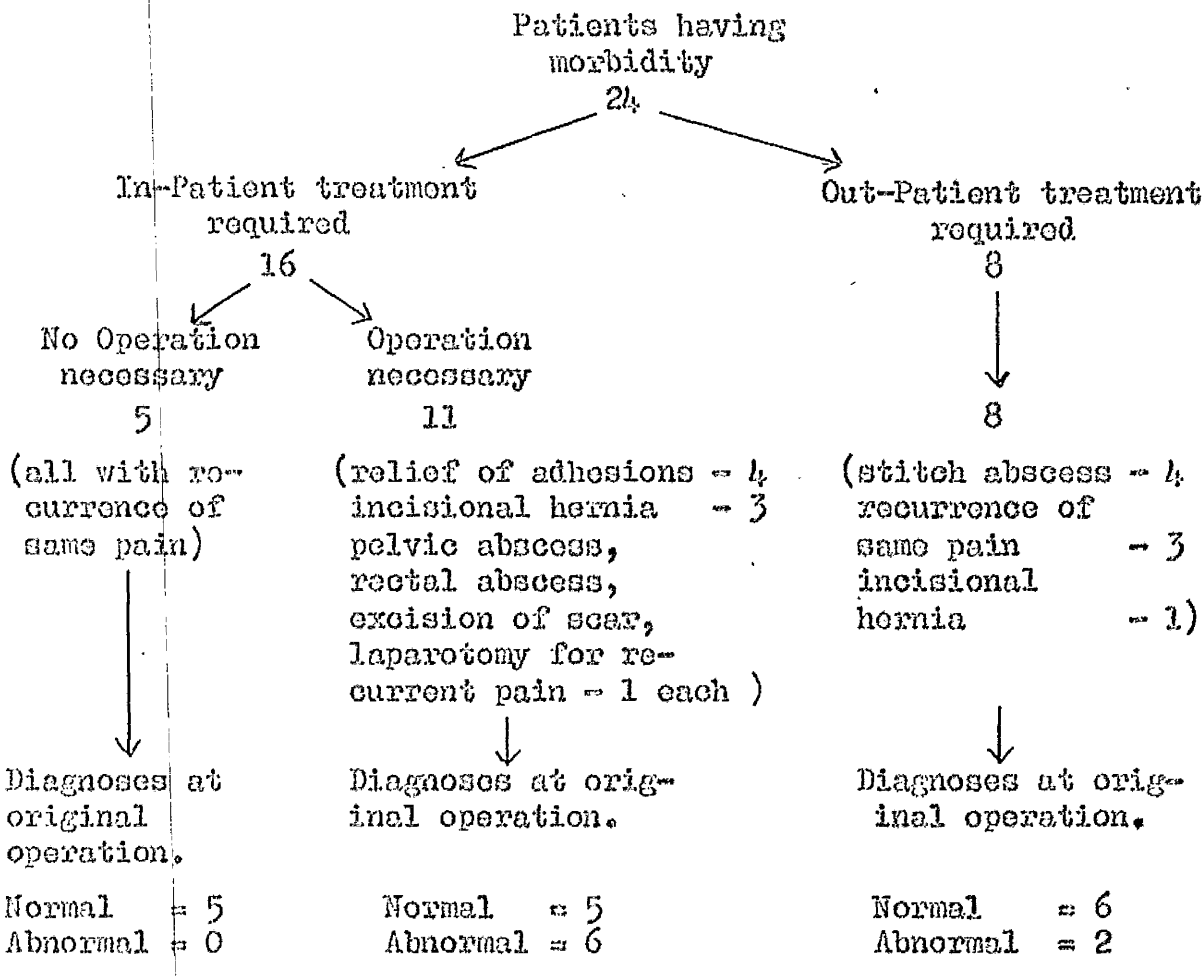
I confirmed Wilkie's observation (1914) that cases of perforated and gangrenous appendicitis are more common in males than females but the preponderance of cases of limited acute appendicitis in females in my series made the overall sex incidence of appendicitis equal. Both Wilkie and Lee have previously found a preponderance of cases of appendicitis in males. My findings confirmed the impression I discussed earlier, (page 52-3) based on the histological and prussian-blue studies, that inflammatory changes appear to produce symptoms more readily in females than in males.

Intermediate Morbidity

For the purpose of objective study this was defined as any side effect of the operation for which hospital advice was requested or where a clearly defined lesion was treated by the

TABLE 22.

Intermediate morbidity in 1,265 patients having appendicectomy for appendicitis or abdominal pain.



Total appendices removed	= 1,265
Further operations necessary	= 11
Intermediate morbidity	= 1%
Total normal appendices removed	= 425
Further operations necessary	= 5
Intermediate morbidity	= approx. 1%
Total abnormal appendices removed	= 840
Further operation necessary	= 6
Intermediate morbidity	= approx. 1%

For patients aged 12-29 years, normal appendices removed = 338
Further operation necessary = 5 (3 adhesions, 1 excision of scar, 1 laparotomy).
Intermpdiate morbidity = approx. 1%.

patient's family doctor within 2 years of operation. Excluding the 47 cases where an extra-appendicular acute pathology was the cause of the patient's illness, 1265 cases were studied and morbidity noted in 24 cases (2%). The findings are listed in table 22.

Following removal of a normal appendix from a young patient it appears that 1% of patients will be operated on again within two years, the main reason being adhesions. A further 1% are again admitted with the same pain as they had before their original operation and 1% each are treated for similar pain or for stitch abscess as outpatients. The intermediate morbidity is thus 4% of which 1% is serious.

Following removal of abnormal appendices under 1% of patients have a second operation within two years (6 patients of 840) of whom half have incisional hernias and the other half lesions perhaps related to septic complications. Only one patient in this series developed adhesions and a second had an intestinal obstruction due to a residual pelvic abscess. The patients developing incisional hernias were all over 30 years of age and had had advanced appendicitis with high post-operative morbidity.

Too few complications were recorded in this series to make

statistical analysis of individual complications possible, but it appears that the risk of a second operation being required within two years of returning to work following appendicectomy is in the region of 1%, and the risk of being again admitted to hospital without requiring operation is a farther 1%.

Long-term Morbidity

This refers to the risk of patients developing morbidity beyond two years after operation. The only complications likely to appear at this stage are intestinal obstruction due to adhesions, and possibly incisional hernia. Incisional hernia generally follows wound infection and patients developing this lesion appear to do so soon after operation. Generally they have had a high operative morbidity. They will thus have already been included in the list of imperfect results.

The long-term risk of developing adhesions cannot be assessed prospectively for this study at the present stage. National and regional statistics are not available to calculate accurately the risks involved and it is necessary to estimate these by rather artificial methods.

All patients admitted to the Western Infirmary, Glasgow with abdominal pain or adhesion obstruction during the year 1963

TABLE 23.

Long-term morbidity in 1,265 patients having appendicectomy for appendicitis or abdominal pain.

Patients admitted in 1963 with:
a) Adhesion obstruction = 75
b) Abdominal pain = 393

Number with previous appendicectomy
a) = 17
b) = 37

Present admission not related to past appendicectomy
a) = 5
b) = 28

Present admission related to past appendicectomy
a) = 12
b) = 9

Previous operation within 2 years of this admission
a) = 4
b) = 9
13

Previous operation outwith 2 years of this admission
a) = 8
b) = 0
8

Now requiring operation
a) = 4
b) = 2
6

Now requiring operation
a) = 8
b) = 0
8

Total appendicectomies in 1963 = 650

∴ Estimated intermediate morbidity = 6 of 650 = approx 1%
(= that estimated in Table 22)

∴ Estimated long-term morbidity = 8 of 650 = approx. 1%

were studied for past history of appendicectomy and an attempt was made to discover:

(1) what proportion of these complaints were due to previous appendicectomy; and

(2) what portion of these fell on either side of the two-year interval which would already have been covered by the studies in the paragraph above.

The results are summarised in table 23. 17 patients with proven adhesions had had previous appendicectomy and in 12 of these this was the most recent and apparently relevant operation. Of these 12, four had been operated on within two years and eight had been operated on outwith two years. Of these eight patients, six had clearly had operations for severe appendicitis; four of the eight operations had been done in childhood.

Of 393 patients admitted with the diagnosis of abdominal pain 37 had had previous appendicectomy; nine of these admissions were related to the past operation or to the same pain for which the operation had been done. All nine cases had in fact undergone the operation within the previous two years. Of the 28 cases of abdominal pain not apparently related to past appendicectomy, 25 had been operated on more than two years before.

Thus 13 patients were admitted to hospital over a period

of one year with complaints related to appendicectomy within the previous two years. On the basis of 650 operations per year this represents an intermediate morbidity of about 2% receiving inpatient treatment about half having a further operation. This is a similar conclusion to that arrived at by different reasoning in the preceding part of this chapter.

If one is allowed to use a parallel arguement for long-term complications, eight patients in 650 would be expected to develop adhesions at some time beyond two years after appendicectomy.

The apparent downward annual incidence of appendicectomy (Section 2 Chapter 4) and the differing risks of appendicectomy in past years when post-operative infection was more serious than now, must be recognised as hazards in making assumptions of this kind. No more realistic alternative, however, appears to be available.

It thus appears reasonable to forecast a late morbidity of about 1% for appendicectomy, this being composed almost entirely of patients with adhesion obstruction.

No deaths from this complication were noted in this small series of cases.

General Considerations of Morbidity

As mentioned in the introductory notes for this chapter, consideration of morbidity is incomplete without study of cure rates, mortality rates and psychological factors.

Cure rates have already been discussed at length in Chapter 3 of Section 1 and it will be recalled that just over 98% of those operated on for acute appendicitis - limited or complete - are improved or cured by operation. Removal of a normal appendix in emergency conditions will result in cure or improvement in 86% of cases whereas the same operation in non-emergency circumstances cures only 71% of cases. Although consideration of cure rates must be made when studying the management of patients who may not have appendicitis, serious morbidity or mortality is no exchange for probability of quick cure in what is usually a self-limiting condition. This consideration can only influence the choice of treatment if morbidity and mortality risks for two different managements are closely similar.

In this thesis mortality rates from appendicectomy have been referred to in passing on several occasions. This is a topic of fundamental importance to the clinical problems involved.

Only six deaths took place in my series of 1312 cases, all following removal of obviously abnormal organs. This is too small a number from which to draw useful conclusions and an intensive investigation of death rates from appendicitis and appendicectomy at different age groups is presented in Chapter 4 of this section.

The final consideration is that of the psychological factors involved in removal of the appendix. That these are important is widely accepted but surgeons often appear reluctant to make allowances for their existence and unwilling to use them as an aid to obtaining a cure for the patient. I wish to refer in this study to three features. The first is that removal of a normal appendix is a more effective treatment in "emergency" than "cold" conditions. This has already been referred to in this chapter. This can easily be explained on the basis of the drama of receiving night surgery making an operation more "glamorous" and exciting than a routine waiting-list operation; also the feeling exists that the patient is being treated for a complaint that is actively present as against one that is a past event and seems less important as the day and hour of operation slowly draw near. Post-operative discomforts are also more happily accepted by a patient who feels the operation was an emergency one and who suffered acute pain before it. By the time a patient

TABLE 24.

Work loss after removal of a normal appendix in emergency and planned circumstances.

(All patients between 12 and 29 years of age; each group contains 66% females, 33% males).

	Patients studied	Time off work				Average weeks off work
		3 weeks or less	4 weeks	5 weeks	Over 5 weeks	
Emergency operation	196	60 (30%)	44 (22%)	22 (11%)	70 (36%)	4.8
Planned operation	63	9 (14%)	14 (22%)	7 (11%)	33 (52%)	5.5

is operated from the waiting-list, there is generally a background of recurrent visits to hospital and of growing impatience and dissatisfaction, not a good basis for carrying out an operation of doubtful pathological necessity and associated with a certain inevitable degree of post-operative discomfort. There is no evidence that the actual operative morbidity of a receiving-day operation is any greater than that associated with appendicectomy at the end of a long routine list.

Work loss is also less after emergency normal appendicectomy than planned normal appendicectomy (table 24). A good case may be based on these psychological considerations for treating patients who have recurrent pain without operation until a further acute attack takes place on the understanding that when this happens, the general practitioner will have access to a surgeon who understands the problems of the situation and is prepared to operate. Unfortunately surgeons prepared to increase their proportion of diagnostic error from about 27% to 33% (see Section 2 Chapter 6) by this realistic procedure lay themselves open to charges of carrying out unnecessary and unjustified operations. Even if these surgeons are not able to quote statistical support for their action, it is certain that their opponents are equally unable to produce any statistical

support for theirs. There is equally little doubt which action, appears constructive from the general practitioner's point of view. The justification of this action is in fact the problem being studied in detail in this section.

The second psychological factor to be borne in mind is the influence of a family history of appendicectomy. Chapter 1 of Section 3 deals with this problem in greater detail. At this stage it is sufficient to say that there is evidence that although appendicitis does not run in families to a greater degree than would be expected in a common complaint, there is a tendency for appendicectomy to run in families. Thus the patient whose parents or brothers or sisters have had their appendix removed is more likely eventually to have the operation than the patient with no such background. When a family history of appendicectomy is present it should be realised that this tendency exists and this would appear to be a positive psychological indication for immediate treatment as against indecisive non-operative management.

The third psychological consideration is the effect on the individual concerned of being in hospital. There is evidence that many patients, especially the younger ones, are very badly informed about their proposed or completed treatment, and it would

be a very serious form of late morbidity of operation if the experience of being in hospital was so bad that it made patients reluctant to be admitted again on a later occasion. The effect of appendicectomy as an experience is discussed in Chapter 2 of Section 3. The conclusions are salutory.

Summary

The potentially serious morbidity, (short-term, intermediate and long-term) involved in removal of a normal appendix is 8% + 1% + 1% or 10%. Following removal of an uncomplicated acute appendix it is 17% + 1% + 1% or 19%. Following removal of a gangrenous or perforated appendix it totals about 50% and 75% respectively. Probably a further 3% of all patients will have intermediate morbidity of a non-serious nature and a further 15% have trivial short-term post-operative complications which are discovered only on carrying out a follow-up study and are not of serious significance.

The degree of pathological change appears to have more influence on the morbidity to be expected than does the age or sex of the patient.

CHAPTER 3

MORBIDITY OF NON-OPERATIVE TREATMENT OF POSSIBLE APPENDICITIS

As in the previous chapter the morbidity of conservative treatment of patients with possible appendicitis is considered under the headings of short-term, intermediate and long-term morbidity.

Patients were included in the study if they were admitted to hospital between 1st February, 1963 and 31st January, 1964 and their discharge classification number was 785.5 (abdominal pain) 468.1 (mesenteric adenitis) or 550-553 (appendicitis) provided that while in hospital they neither had appendicectomy, nor were given a date to return for "interval" appendicectomy. Also excluded were those patients who had previously had their appendices removed.

This left a total of 359 patients, but in 150 of these there was sufficient evidence in the case-record to make it clear that appendicitis was not considered a possible diagnosis and appendicectomy was not a possible form of treatment. These 150 patients had such lesions as peptic ulcers (with x-ray confirmation)

cholecystitis (with x-ray confirmation) salpingitis (where accompanied by typical signs and symptoms) and renal tract disease (but only where accompanied by clinical and laboratory results which provide a fully reliable diagnosis).

Thus 209 patients remained in whom the risk of missing an acute appendicitis was one of the reasons for admission and therefore in whom appendicectomy might have been carried out if the circumstances of the patient's illness had been even slightly different.

Follow-up of all patients two years after their admission to hospital was carried out on a postal basis using the questionnaire shown in the Appendix. As in the follow-up of patients who had had operative treatment, reminders were sent to those who did not reply and various efforts were made to trace patients who had left their original address. 32 of the total of 209 patients were not traced (15%). Only 17 of 177 patients whose addresses were traced (10%) did not reply to the follow-up circular. The proportion of patients followed-up is thus sufficiently high to subject the results to detailed analysis.

The results for male and female patients aged between 12 and 29 years inclusive - which form more than three-quarters of the total - were calculated separately.

Short-term Morbidity

There is no short-term morbidity comparable with that after operation. None of the complications, other than failing to make a diagnosis of appendicitis, could be regarded as potentially serious and this risk is assessed below.

The only feature of interest is the length of time off work after non-operative treatment of possible appendicitis. 32 of 129 patients who answered this question were off work for two weeks or more, and 22 of these were off for three weeks or more. The seven patients who were off work for a month or more would almost certainly not have been absent from work any longer had they undergone operation.

The average number of days off work for patients who subsequently have "no more pain," "less pain than before" and "the same pain as before" is 7, 10 and 16 days respectively. If a patient is to be treated non-operatively it would appear essential to advise early return to work to avoid the patient becoming introspective about his or her symptoms, with the consequent liklihood of a recurrence of pain.

Intermediate Morbidity

This can be assessed objectively for comparison with the

TABLE 25.

Two year clinical follow-up of 209 patients admitted to hospital with possible appendicitis over a period of one year and treated non-operatively.

	All cases		Aged 12-29		
			Female	Male	Total
Total studied	209		102	65	167
Not traced	32		19	7	26
Available for follow-up	177		83	58	141
Subsequent operation	32	68	11	14	25
Same or worse pain	36		21	10	31	56
Less severe	46	92	25	15	40
No more pain	46		19	14	33	73
No reply	17		7	5	12
+ % operations	18		13	24	17.5
+ % not better	20		25	16	21.5
† % cured/improved	57.5		58	55	56.5

+ Calculated on basis of patients available for follow-up

† Calculated on basis of replies received.

intermediated morbidity of operative treatment in two ways. The first is by studying the cure rate and the second is by finding the number of patients who are re-admitted to hospital during this period of two years and who undergo appendicectomy on the subsequent admission. Table 25 summarises the results of non-operative treatment of possible appendicitis for the complete series of 209 patients and for the young females and males separately.

It will be noted that the cure rate of 57.5% is poorer than that achieved by operative treatment of patients who had normal appendices removed. (When compared with the 86% cure of emergency normal appendicectomy the difference is highly significant. Compared with the 71% cure rate after planned appendicectomy the difference is at the borderline of statistical significance; $X^2 = 3.85$ $P = 0.05$).

It will also be noted that 32 patients in fact had their appendices removed during this time. This represents 17.5% of all patients in the group studied and must be regarded as the intermediate morbidity of conservative treatment.

Of these 32 patients, one had a gangrenous appendicitis, six had complete acute appendicitis, five had limited acute appendicitis and 20 had normal appendices. All but three of the

patients were operated on in the same hospital as they had been admitted to originally.

Clinical features of conservatively treated patients

The case records of all 209 patients in this part of the study were examined to attempt to find common factors in the cases of patients who came to subsequent operation or who were not relieved of their symptoms by non-operative treatment.

Other than the length of time off work (which has been discussed above) the outstanding feature was that 31 of 36 patients who continued to have the same pain had already a past history of the same pain when they were originally admitted to hospital; this compared with only 15 of 46 patients who had no more pain after leaving hospital. (The 32 patients who eventually underwent appendicectomy were asked to complete the circular related to operative treatment and are thus not eligible for discussion under this sub-heading).

It is also of interest that 32 of the 36 patients who continued to have the same pain after leaving hospital had been told either by their family doctor or by the hospital staff that they had appendicitis. This compares with 26 of the 46 patients who had no more pain after leaving hospital.

No significant differences were discovered on studying:

(a) marital status;

(b) white cell counts;

(c) the code number used in diagnostic classification;

(d) whether or not admission followed a referral by the general practitioner; or

(e) whether or not it seemed from the terms of the case-sheet and discharge summary that appendicectomy had been "very unlikely," "unlikely" or "possible" as the form of treatment.

Of the 82 patients who again had pain following discharge from hospital, 49 were subsequently absent from work because of this within the two year period of follow-up. One of these patients was off for 2 weeks, three for 3 weeks and the others for lesser intervals.

Long-term Morbidity

In the same way as the long-term morbidity of operative treatment was inferred from studies of patients re-admitted with relevant sequels of appendicectomy, so the long-term morbidity of conservative treatment must - in the absence of an unrealistically long prospective study - be inferred by finding the number of patients having appendicectomy who had been

TABLE 26.

Past history of non-operative treatment in 1,284 patients having appendicectomy for right iliac fossa pain.

Histology of appendix	Previous In-Patient Treatment				Total
	In this hospital		In a different hospital		
	Within 2 yrs.	Outwith 2 yrs.	Within 2 yrs.	Outwith 2 yrs.	
Normal	44	8	7 (2)	15 (5)	74
Limited acute appendicitis	10	2	0	2 (2)	14
Complete acute appendicitis	15	6	3	7 (3)	31
Perforated or gangrenous appendicitis	1	1	0	1	3
Total	70	+17	10 (2)	+25 (10)	122

Figures in brackets refer to previous admission to hospital when the patient was aged 11 or younger.

(+ explanation in text, p. 120-1.)

treated conservatively more than two years previously.

For this purpose the past history of the 1284 patients who formed the main portion of the study of patients who underwent appendicectomy for right iliac fossa pain have been examined. The results are shown in table 26. It will be noted that nearly 10% of patients having appendicectomy (122 of 1284) had previously been treated conservatively for the same pain, and that 40% of these patients were subsequently found to have genuine acute appendicitis (48 of 122).

Over the two year period covered by table 26, 70 patients who had been treated conservatively in this hospital and 10 who had been similarly treated elsewhere had their appendices removed. Division by 2 gives figures for one year of 35 and 5 which are closely similar to the figures of 29 and 3 found in the prospective follow-up study which formed the basis of the discussion on intermediate morbidity.

If the patients whose earlier admissions occured when they were under the age of 12 are omitted, (figures in brackets in table 26) we are left with totals referring to management of patients of the age groups covered by this study. We may now infer that 17 + (25-10) would be the number of patients who would be expected to come to operation at a period later than two years

following previous conservative treatment (see asterisks in table 26). Half of this total would thus be the late morbidity in the present series which covers only one year as against the two years covered by table 26.

This figure of 16 out of 209 would give a late morbidity of non-operative treatment of approximately 8%.

The intermediate morbidity which was noted to be lower in young females than in the total series appears to be compensated by a higher late morbidity.

Summary

No attempt has previously been made to assess the morbidity of non-operative treatment of possible appendicitis. There is thus no established method to use as a guide. This chapter uses new techniques to assess this morbidity. Appendicectomy at a later date is taken as the primary index of potentially serious morbidity, and is found to involve 25% of patients.

This is based on a study of some 200 patients. The results appear to apply broadly to patients of any age and either sex.

It appears that, in addition, the intermediate cure rate is only 57.5% as against 86% with emergency operation in the

same circumstances.

The presence of a past history of similar pain appears to prejudice unfavourably the results of conservative treatment and it appears that if patients are to be treated conservatively and gain favourable results they should be encouraged to return to work as soon as possible after leaving hospital and should not be allowed to think that they have had appendicitis.

The short-term or permanent risk of mis-diagnosis and the subsequent development of genuine appendicitis which may proceed untreated to perforation of the appendix must also be accepted when advising non-operative treatment. Thus this estimate of 25% morbidity for non-operation makes no allowance for any of those subsequent operations being other than straight-forward.

The 10% of patients off work for three weeks or more after conservative treatment may be regarded as suffering the equivalent of what was regarded as trivial short-term morbidity after appendicectomy.

CHAPTER 4

DEATH FROM APPENDICITIS AND APPENDICECTOMY

Previous analyses of deaths from appendicitis have explained the poor prognosis in advanced appendicitis in the very young and very old and have noted successive improvements in prognosis attributable to improved anaesthetic techniques, antibiotic treatment, and resuscitive measures (Rees, 1952; Moloney et al, 1950; Pleves and Foskey, 1955; Christenson, 1958). No precise estimates have been made of the risks involved in removing normal or abnormal appendices in defined age groups or of the risks from conservative treatment of the patient with mild appendicitis. These are the main aims of this chapter.

The suggestion of Lee et al. (1957) that mortality from appendicitis was higher in non-teaching hospitals than in teaching hospitals was denied by Cunningham and Leask (1957) who suggested the reverse to be true. This chapter also examines this question.

Finally an attempt is made to test the views of Castleton et al (1959) and Trvelsen (1961) both of whom have reported a decrease in the incidence of appendicitis in recent years.

Materials and Methods

The Registrar-General for Scotland's records were searched for deaths from appendicitis or appendicectomy during the 10-year period 1954-63. 870 such deaths were found. I visited 21 hospitals throughout Scotland and examined personally the records of 616 of the deceased patients. The Senior Surgeon or Medical Superintendent of 55 small or inaccessible hospitals was asked to supply information concerning a total of 191 patients on the form shown in the Appendix. 29 patients who had died at home and 34 who died in Institutions or Private Nursing Homes were not studied further. All hospitals except one where more than 10 deaths had taken place during the period of study were visited personally.

65 of the original 870 deaths were not due to appendicitis and were excluded on the ground of incorrect certification. Of the remaining 805 patients, details were collected concerning 650, 523 of these personally and 127 through the co-operation of colleagues. 56 case-records could not be traced by the hospitals concerned. No replies were received from eight hospitals covering a total of 36 deaths.

Each of the 76 hospitals was also asked to give the number of appendicectomies carried out annually from 1954-1963; and

33 hospitals - only two of which were teaching hospitals - provided this information.

The number of appendicectomies done annually in each Scottish Hospital from 1961-1964 was computed from the Morbidity Statistics collected by the Scottish Home and Health Department. The codings searched for appendicectomy were those for appendicitis, mesenteric adenitis, abdominal pain and ovarian cyst. Overall, this gave totals which approximated closely to those given by individual hospitals for the number of appendicectomies each year. The 33 hospitals which had supplied totals as described above accounted for 33%, 32% and 32% of the annual totals for Scotland for 1961, 1962 and 1963 respectively. The total number of appendicectomies from 1954-60 inclusive was therefore calculated on the assumption that the figures collected by the 33 hospitals also represented 32% of the total operations done annually from 1954-1960.

From the study of case-records, patients were diagnosed as having had acute appendicitis, gangrenous appendicitis, perforated appendicitis, appendix abscess with or without drainage, or no appendicitis. Histological reports were rarely available. Therefore all appendices not clearly abnormal were classed as normal. The combined clinical descriptions of early appendicitis,

TABLE 27.

Death-rate from appendicitis each year from 1954-63.

Year	Operations carried out by 33 hospitals	Total operations for Scotland.	Deaths	Deaths/Operation	Deaths from removal of "normal" appendices
1954	5,529	† 17,270	93	1:185	8
1955	4,990	† 15,590	84	1:185	2
1956	4,902	† 15,320	100	1:153	2
1957	5,009	† 15,650	101	1:155	6
1958	4,905	† 15,320	74	1:207	1
1959	4,736	† 14,510	89	1:163	3
1960	4,630	† 14,490	78	1:185	5
1961	4,344	÷ 13,300	76	1:175	4
1962	4,384	÷ 13,810	56	1:245	1
1963	4,038	÷ 12,670	54	1:234	2
Total	47,467	147,930	805	1:183	34

÷ Actual totals

† Estimated totals on basis of totals returned by 33 hospitals representing 32% of Scottish total as found for 1961, 1962 and 1963 (see text p.125 for basis of an justification for calculations).

mild appendicitis, chronic appendicitis, and normal have been regarded as equivalent in total to any cases defined in my personal series as limited acute appendicitis and no appendicitis.

Particular note was made of past history of possible appendicitis and of previous abdominal operations.

The proportions of operations in each major age group (childhood, 12-29 years, 30-49 years, and over 50 years) was also provided for 1961-4 by the Scottish Home and Health Department's analyses.

Excluding children, the Department's distribution of patients to the three adult groups was in the ratio 70 : 20 : 10 respectively. In my own series of 1284 patients treated operatively for possible appendicitis (see Chapter 2 of Section 2) the distribution to each of these age groups was 70 : 22 : 8. My series thus appeared to be representative of experience in Scotland generally and it thus appeared reasonable to regard the distribution of cases in my series to each degree of pathological change as also representative for Scotland in general.

Results

Table 27 shows the number of appendicectomies carried out annually by the 33 hospitals which were able to provide this

TABLE 28

Death rate for different degrees of severity of appendicitis at various ages.

Age & clinical presentation	Operations in personal series	*Estimated operations in Scotland 1954-63		Deaths	Death-rate
12-29 Normal appendix	359	32,669	39,585	8	1:5000
" Limited acute appendicitis	76	6,916			
" Complete acute appendicitis	395	35,945		14	1:2600
" Gangrenous appendicitis	32	2,912		20	1:1500
" Perforated appendicitis	29	2,639		35	1:750
Not traced	-	-		5	-
30-49 Normal appendix	74	6,734	8,005	7	1:1100
" Limited acute appendicitis	14	1,271			
" Complete acute appendicitis	111	10,101		7	1:1400
" Gangrenous appendicitis	19	1,729		11	1:160
" Perforated appendicitis	16	1,456		33	1:44
Not traced	-	-		7	-
50+ Normal appendix	39	3,549	4,650	19	1:250
" Limited acute appendicitis	11	1,001			
" Complete acute appendicitis	62	5,642		32	1:175
" Gangrenous appendicitis	27	2,457		79	1:30
" Perforated appendicitis	20	1,820		209	1:9
Not traced	-	-		71	-
Paediatric patients (1-11 yrs)	-	31,000		85	1:350
Nursing Home Patients	-	?		34	?
Deaths at home	-	-		29	-
Deaths from abscess + drainage	-	?		37	?
Deaths from abscess not drained	-	-		63	?
Total	1,284	147,841		805	1:183

	Aged 12-29	Aged 30-49	Aged 50+
*Age distribution excluding patients under 12 yrs. of age in Scottish Home and Health Dept. returns 1961-4:	70%	20%	10%
Distribution in my own series of 1,284 patients whose appendices were examined in 1963-4:	70%	18%	12%

Operations in children under 12 represented 21% in Scottish Home and Health Dept. Returns .'. for 1954-63 (estimated operations 148,000 in Table 27)

Estimated operations on children = 31,000
Estimated operations on adults = 117,000
Estimated operations on adults of 12-29 = 81,000

information together with the actual or estimated total number of operations each year, calculated as described above. The number of deaths and the death rate per annum are also shown as is the number of deaths resulting each year from appendicectomy where obvious acute appendicitis is not present.

Table 28 shows the number of operations in my own series in each main age and pathology group. Deducting the 21% of operations carried out on children from the total operations for Scotland calculated in table 26, 117,000 operations on adults were available for distribution. This was done in proportion to the findings in my own series. The number of deaths in each group is based on the results obtained by follow-up and the death rates calculated accordingly. The 83 patients listed as "not traced" are predominantly older patients and the death rates given for patients over 50 are thus slightly low; the proportionate differences in different pathological groups should not be affected.

Table 29 is calculated on the same basis as table 28 and shows the difference in death rates between males and females. It will be noted that 62% of patients dying from appendicitis are males whereas in all groups studied more females underwent operation. There thus appears to be a poorer prognosis for

TABLE 29.

Sex differences in death rates in appendicitis.

	Clinical classification	Operations in personal series	* Estimated total Scotland 1954-63	Deaths	Death-rate.
Males:	Normal appendix age 12-29	138	12,558	4	1:3200
	All patients age 12-29	375	34,124	51	1:650
	All patients age 30-49	104	9,464	59	1:160
	All patients age 50+	64	5,824	276	1:21
	Perforated appendicitis, age 50+	8	728	135	1:5
	Total patients (including children)	-	-	492	
Females:	Normal appendix age 12-29	249	27,118	4	1:6750
	All patients age 12-29	516	46,956	33	1:1400
	All patients age 30-49	130	11,828	19	1:625
	All patients age 50+	95	8,645	176	1:50
	Perforated appendicitis, age 50+	12	1,092	73	1:15
	Total patients (including children)	-	-	313	

* see table 28

appendicectomy in males in all main groups in the ratio of at least 2 :1.

Table 30 deals with any past history of possible appendicitis found in the 650 patients for whom follow-up details were available. 21 of the 650 deaths were from true appendicitis which had apparently been the subject of previous conservative treatment; a total of 3% of deaths may thus be regarded as preventable. 6 of these deaths were in patients aged 12-29 years and these represent the consequences of the failure of conservative treatment in this age group. As shown in table 30, the number of patients treated non-operatively in hospital for possible appendicitis over the same period was probably about 35,000 and of these between 14.5% and 40% probably had mild appendicitis.

The minimum figure is calculated on the basis of the number of extra appendices showing appendicitis which would be removed if all surgeons adopted the radical approach to appendicitis as discussed in Chapter 6 below. The maximum figure is based on 40% incidence of appendicitis in patients who have operation following previous conservative treatment for the same symptoms. On this basis the death rate for non-operative treatment of mild appendicitis lies between 1 : 850 and 1 : 2300. It should be emphasised that these figures do not refer to conservative treatment of appendix

TABLE 30

Past history of possible appendicitis in 650 patients dying from appendicitis or appendicectomy

Past History.	AGE				Pathology of Appendix				Total
	12 yrs	12-29 yrs.	30-49 yrs.	50yrs. +	Normal	Acute	Gang. Perf.	Abscess	
Admitted to hospital	1	6	2	15	3	1	14	6	24
Seen at hospital - not admitted	0	2	3	9	4	1	5	4	14
Seen by general practitioner only	3	3	4	19	4	1	19	5	29
Not seen by medical adviser	0	2	1	1	1	1	2	0	4
Total	4	13	10	44	12	4	40	15	71

For patients aged 12-29 years:-

Ratio of operative to non-operative treatment of possible appendicitis is 7:3 (table 34, facing page 145)

Operations carried out from 1954-1963 = 81,000 (table 28, facing page 127)

∴ patients treated non-operatively = 35,000

The percentage of this total (35,000) representing patients with mild acute appendicitis must lie between (1) that calculated on the basis of the extra 440 cases of appendicitis which would be removed using the radical approach to the treatment of the 3,020 patients at present treated non-operatively as shown in table 35, facing page 146 $\left(\frac{440}{3,020} = 14.5\%\right)$ and

(2) the 40% incidence of acute appendicitis found in patients having appendicectomy after earlier unsuccessful non-operative treatment for the same symptoms (table 26, facing page 120).

∴ Patients treated non-operatively for mild acute appendicitis in period 1954-1963 lies between 14.5% of 35,000 and 40% of 35,000, that is, between 5,000 and 14,000.

From the table above 6 deaths resulted; all were from advanced appendicitis

∴ death rate from non-operative treatment of mild appendicitis lies between $\frac{5,000}{6}$ and $\frac{14,000}{6}$

that is, between 1:850 and 1:2,300.

abscess and a past history of hospital admission is not included if, at that time, the patient was given an appointment for "interval" appendicectomy.

Table 31 examines the fate of patients in teaching and non-teaching hospitals. The non-teaching hospitals were divided into those in cities, large provincial centres, and small rural or outlying areas. The mortality rates lay between 1 : 220 in teaching hospitals and 1 : 250 in city non-teaching hospitals. The differences were not statistically significant.

Discussion

This study is the most intensive modern investigation of death from appendicitis. The work presented also represents the first attempt to define the risks of failing to remove an abnormal appendix from a patient with possible appendicitis.

The accuracy of the estimates I have made depends on a number of assumptions. The main ones are:-

(1) that my own series of appendicectomies is representative of experience on a national scale;

(2) that the total number of operations estimated for the ten year period is reasonably accurate; and

(3) that a representative proportion of the records of patients

TABLE 31.

Showing insignificant difference in death rates in teaching and non-teaching hospitals throughout Scotland from 1961-3 inclusive

	Teaching hospitals	Non-teaching hospitals			Total
		City	Provincial	Rural outlying	
Operations	14,123	4,565	15,933	5,243	39,864
Deaths	65	18	67	22	172
Death-rate	1:220	1:250	1:240	1:240	1:230

The total deaths of 172 differs from that of 186 in Table 27(1961-3) by those deaths taking place in patients' own homes or in Nursing Homes.

who have died have been re-examined objectively.

The accuracy of my own series is supported by finding a 70% incidence of operations in patients aged 12-29 both in my series and in the figures analysed by the Scottish Home and Health Department. The distribution to the other two adult age groups was also closely similar. The estimate of total number of operations cannot be improved upon without unrealistic searching of theatre records in the large city hospitals. The basis for the estimates has already been discussed.

The examination of 650 records out of 805 possible (81%) is itself suggestive that a representative portion of all deaths have been analysed. As 56 of the remainder were lost and as those deaths in Nursing Homes, Institutions, and patients' own homes are excluded from all calculations except the annual death rates, the only cases not studied are the 36 about which no replies were received. Thus 92 relevant records have not been studied - mainly because they were lost. The majority of these records belong to older patients and the estimates of the risks of death in these patients have thus been slightly underestimated in tables 28 and 29. The error should be equally distributed to the different degrees of pathological change.

With this exception it may thus be stated that the risks

calculated represent the most accurate assessment at present possible, of the death rates in the given circumstances.

The estimate of death due to conservative treatment of appendicitis is a particularly difficult one to make. The reasoning however is clearly stated and may be used as a basis for discussion by other workers of maximum or minimum risks of death. It appears clear, however, that if a patient has appendicitis, operation carries a lower mortality than conservative treatment. (This, of course, does not refer to patients with possible abscess formation).

It thus appears reasonable to accept the findings in this study as valid estimates of the death rates from appendicitis which have been studied. The following conclusions may be drawn:
(1) The absolute number of appendicectomies each year is declining as is the number of deaths from acute appendicitis. The annual death rate, however, remained constant until 1961, since when there appears to have been an improvement in prognosis. This may have been due to the introduction of the new penicillinase-resistant penicillin drugs. The evidence thus suggests that there has been a true decline in the incidence of appendicitis in recent years and suggests that there may recently have been an improvement in the prognosis of appendicitis;

(2) The mortality from appendicitis increases sharply within each age group with each successive advance in the abnormality of the appendix. The prognosis in elderly patients with perforated appendicitis is particularly grave. The prognosis for males appears to be poorer than for females in all categories;

(3) The mortality involved in treating young adults with mild appendicitis conservatively appears to be between 1 : 850 and 1 : 2300 whereas the death rate for operation in complete acute appendicitis is 1 : 2600 and for limited acute appendicitis and normal appendicectomy together is 1 : 5000; and

(4) There is no evidence to suggest that the prognosis of appendicitis and appendicectomy is better or worse in teaching hospitals compared with non-teaching hospitals be they large or small.

Summary

This chapter presents a detailed survey of the 805 deaths from appendicitis or appendicectomy in Scotland from 1954 - 1963. The death rates for appendicitis of different degrees of severity in adults at different ages are calculated and an estimate is made of the risk of death from non-operative treatment of mild appendicitis in the young adult.

Evidence is presented to support the belief that there has been a fall in the incidence of true appendicitis. No evidence is found to support the belief that teaching and non-teaching hospitals offer a different prognosis in their treatment of appendicitis.

CHAPTER 5

APPENDICECTOMY "EN PASSANT"

It appears relevant at this stage to review the evidence for and against appendicectomy during major abdominal operations.

Aschoff (1932, page 145) advised the removal of all accessible appendices from patients without symptoms of appendicitis. Since that time American surgeons and obstetricians have been more enthusiastic in following this advice than have their British counterparts. Larsson (1954) reviewed the literature and presented 20 personal cases of satisfactory results from appendicectomy at Caesarean section together with a considerable number of cases (764) collected from other obstetricians sharing the same belief in the correctness of the double operation. An interesting letter to the Editor of The Lancet by Hawkins (1956) illustrated that the majority of British obstetricians did not remove the appendix during hysterectomy and a number of cases of unfortunate results from the double operation were quoted along with some where later removal of the appendix had been required after simple hysterectomy.

The only published figures relating to death rates from hysterectomy and appendicectomy as against hysterectomy alone

(Proc. roy. Soc. Med., 1950) suggested that appendicectomy does not significantly add to the risk of mortality from hysterectomy although there were occasional exceptions to this general rule.

Apart from the risk of causing death from adhesions, faecal fistulae, and the like, appendicectomy involves opening the bowel and thus risking contamination of a clean operation. Hawkins suggested that this risk should be protected against by using suitable antibiotic cover.

Apart from at hysterectomy or Caesarean section, the appendix may also be removed at cholecystectomy or at operations for relief of peptic ulcer. The present work gives an opportunity to examine the consequences of not removing the appendix during these operations where this double procedure is theoretically possible.

Material and Methods

The basis of this chapter was the study of the case records of the 1512 patients having appendicectomy for actual or possible appendicitis in the Western Infirmary of Glasgow over the two year period February 1963 - January 1965 along with the study of 650 patients dying from appendicitis or appendicectomy in Scotland from 1954 - 63 inclusive whose case-sheets were available as

TABLE 32.

Incidence of previous abdominal operations in patients

a) dying from appendicitis or appendicectomy;
b) having appendicectomy for abdominal pain.

	a) Patients dying from appendicitis or appendicectomy.	b) Patients having appendicectomy for abdominal pain.
No. of patients at risk	650	1,312
No. of patients with past operation	25 (4%)	40 (3%)
No. of Operations carried out	27	47

Description and No. of Operations.

Hysterectomy	5	7	Hysterectomy/Myomectomy	12	20
Caesarean Section	0		Caesarean Section	3	
Major gynaecology	2		Major gynaecology	5	
Perforated duodenal ulcer	7		Perforated duodenal ulcer	9	
Gastrectomy/gastroenterostomy	6		Gastrectomy/gastroenterostomy	7	20
"Operation for duodenal ulcer"	2		"Operation for duodenal ulcer"	4	
Cholecystectomy	5		Cholecystectomy	3	
			Traumatic surgery	2	
			Others	2	

described in the previous chapter.

Details of any previous abdominal operation were noted and the results are as shown below.

Results

Patients dying from appendicitis

25 patients of 650 dying from appendicitis or appendicectomy had had previous abdominal operations. This represents 4% of all deaths from appendicitis. 18 of those 25 patients died from perforated appendicitis, three from gangrenous appendicitis and two from apparently straightforward acute appendicitis. Two had normal appendices removed. Two patients had had two previous abdominal operations. Of the 27 operations during which appendicectomy was not carried out, seven were hysterectomies or ovarian cystectomies, five were cholecystectomies, seven were straightforward repairs of perforated duodenal ulcers, five were gastroenterostomies, one was a partial gastrectomy and two were described as "operations for duodenal ulcer." These findings are shown in table 32.

Of the 25 patients who died, the youngest was 46 and eleven were aged under 65 and may thus be regarded as dying prematurely. Six could have previously had appendicectomy at 30-39 years of age and a further six between 40 and 49 years of age.

Patients having appendicectomy for abdominal pain

40 patients of 1312 having appendicectomy for abdominal pain had had previous abdominal operations. This represents 3% of all patients requiring appendicectomy in my own series. Of the 40 patients eight had normal appendices removed, eight had perforated or gangrenous appendices removed and 24 had straightforward acute appendicitis. Only five patients in the group were under 30; the others were divided equally between under 50's and over 50's. No evidence of excessive operative morbidity could be demonstrated for the group.

Eighteen of the 40 patients had previously had a major gynaecological or obstetric operation; nine of these were hysterectomies, three were described as fibroidectomies or as myomectomies and four were ovarian cystectomies. (One patient had had a hysterectomy as an emergency post-partum procedure and presumably would not have been a candidate for appendicectomy. One of the patients who had had ovarian cystectomy had also had a Caesarean section previously). Two further patients had had previous Caesarean sections; one of them also had had a right salpingo-oophorectomy for a ruptured tubal pregnancy. Three patients had previously had cholecystectomies; two had previously had laparotomies for traumatic lesions of liver or

spleen, one had had a negative laparotomy through a mid-line upper abdominal scar for abdominal pain, and one had had a previous operation for "relief of adhesions."

The remaining 15 patients had a past history of operation related to peptic ulceration. Two patients each had had previous gastrectomy and gastroenterectomy, three patients had had both repair of a perforation and a later definitive operation, four patients had a total of six perforations amongst them and four patients had had operations described as "for duodenal ulcer." The findings in this section are summarised in table 32.

Discussion

From the findings listed above 4% of deaths (25 of 650) and 3% of all appendicectomies (40 of 1312) could have been prevented by removing the appendix as a routine procedure at cholecystectomy, hysterectomy, gastroenterostomy and other similar abdominal operations.

It would thus appear to be the duty of those who reject the principle of "en passant" appendicectomy to present evidence to show that this additional procedure increases the morbidity and mortality of the primary operation concerned.

There must clearly be situations where the general condition

of the patient or the technical difficulty of appendicectomy rules out the double operation and this is one feature which makes accurate comparison of the evidence for and against the procedure difficult.

A carefully planned prospective study appears essential to assess the morbidity caused by the addition of appendicectomy to the basic operations in question.

When it is realised that probably about 10% of all people reaching the age for hysterectomy or cholecystectomy have already had an appendicectomy it may be appreciated that the figures presented in the results section underestimate the morbidity of not removing accessible appendices when possible.

Love (1947) has told of a gynaecologist who did not practice routine appendicectomy at hysterectomy nevertheless welcoming the fact that his own wife had, in the same circumstances, had her appendix removed. He regarded this as different because it was his wife.

This suggests that the arguments against doing appendicectomy during abdominal operations when possible cannot be strong. The evidence I have given shows that a small but definite number of appendicectomies and deaths from appendicitis could be prevented by this procedure.

Summary

4% of deaths from appendicitis and 3% of appendicectomies for abdominal pain could apparently be prevented by removing the appendix routinely while carrying out another intra-abdominal operation.

There is at present no evidence that this practice of double operation carries an equivalent risk of increase of mortality and morbidity over the individual operations carried out alone.

CHAPTER 6

RADICAL OR CONSERVATIVE?

The aim of treatment of a patient with possible appendicitis is to relieve symptoms with the lowest risk of morbidity or mortality.

For the young adult the cure or improvement rate after non-operative treatment is 56.5% (Section 2, Chapter 3) compared with 71% success after planned appendicectomy or 86% success after emergency appendicectomy even if the appendix removed is normal (Section 1, Chapter 3). The morbidity of non-operative treatment involves 25% of patients (Section 2, Chapter 3) whereas removal of a normal or straightforward acutely inflamed appendix causes morbidity to only 10% and 17% of patients respectively (Section 2, Chapter 2). The mortality due to failure to remove an abnormal appendix appears to lie between 1 : 850 and 1 : 2300 whereas that following removal of a normal or mildly inflamed appendix is 1 : 5000 and that for operation for complete acute appendicitis is 1 : 2600 (Section 2, Chapter 4). For the patient whose diagnosis is not certain it thus appears that removal of a normal appendix offers a better prognosis than non-removal of an abnormal appendix.

The final purpose of this section is to find the morbidity in the community arising from operative and non-operative treatment of young patients.

The two approaches to treatment which are compared are defined as "radical" and "conservative." The basic difference in these approaches is noted in the management of patients with mild symptoms and signs, often not typical of appendicitis, and often apparently settling without operative treatment. In these circumstances the "radical" treatment is more often appendicectomy and the "conservative" treatment more often observation with no operation.

"Radical" surgeons are influenced by tragedies they have seen after non-operative treatment of doubtful cases of appendicitis with later death or serious illness from advanced appendicitis. "Conservative" surgeons remember those tragedies after possibly unnecessary removal of a normal appendix with later adhesion-obstruction or fistula formation causing serious morbidity or even loss of life. The conservative surgeon's dislike of removing normal tissue for what is probably a self-curative condition (if he can be sure that appendicitis is not, in fact, present) is balanced by the radical surgeon's awareness of the facts that (1) surgical treatment gives the better cure rate even when

a normal appendix is removed and often relieves continuing anxiety on the part of the parents and general practitioners; and

(2) for a large number of patients treated non-operatively, appendicectomy will eventually be necessary because of continuation of the same symptoms.

Materials and Methods

This study was based mainly on patients treated in the Western Infirmary of Glasgow. The approach of senior surgical staff to treatment of possible appendicitis covered a wide spectrum of views from extreme conservatism to extreme radicalism. Three of the five surgical units were conservative, two radical. Each unit received emergency calls in rotation for 24 hours at a time. This part of the study deals with emergency admissions only and covers a period of 1 year (February 1st, 1963 to January 31st, 1964). Distribution of patients to each unit was thus a random one and the series was of sufficient size to reduce bias to a satisfactorily low level.

It is assumed that the overall handling of patients admitted to this hospital over the period of study was representative of that for Scotland in general and that the handling of patients

TABLE 33.

Treatment given to patients admitted to each of five surgical units with possible appendicitis over a period of one year.

		Conservative Units			Radical units		Average per unit			Total	
		I	II	III	IV	V	Conservative	Radical	X^2		
Operative treatment	Abnormal appendix removed	62	52	73	98	84	62	91	5.4*	369	536
	Normal appendix removed	26	22	18	60	41	22	50.5	11.2*	167	
Non-operative treatment	Recurrence of same symptoms	16	20	13	8	6	16	7	-	63	191
	No recurrence of same symptoms	29	34	27	18	20	30	19	-	128	
	Total	133	128	131	184	151	130	167.5	-	727	

* The population served by the hospital is about 250,000. Therefore the chances of a patient being operated on for suspected appendicitis within the period of time covered by the study are small and the absolute figures from which these calculations have been made may be treated as having come from Poisson populations; to test whether there is a significant difference between the two types of unit, the Poisson index of dispersion has been used and these figures of $X^2 = 5.4$ and 11.2 represent significant differences, $P < 0.05$.

by radical and conservative units in the Western Infirmary may be regarded as representative of what would result from universal adoption of either point of view.

From 1961-64 an average of 7000 patients aged 12-29 years had their appendices removed each year (Scottish Home and Health Dept. - quoted in Chapter 4 Section 2). I have shown that three people between 12 and 29 years are treated non-operatively for every seven undergoing appendicectomy (table 34). It thus appears that about 10,000 people aged 12-29 are admitted to hospital in Scotland each year with possible appendicitis. This figure forms the basis for the next part of this chapter.

Results

Table 33 shows the number of patients with possible appendicitis admitted as "emergencies" to the five general surgical units of the Western Infirmary of Glasgow over the period of study of one year.

The numbers of patients who had normal and abnormal appendices removed are shown separately. The number of patients treated non-operatively who subsequently had the same symptoms (including those who later required operation) is also shown, as is the number of patients satisfied by non-operative treatment.

The figures for the three conservative units and the two

TABLE 34.

Treatment given to patients aged 12-29 years admitted to each of five surgical units with possible appendicitis over a period of one year.

		Conservative units			Radical units		Average per unit			Total	
		I	II	III	IV	V	Conservative	Radical	X^2		
Operative treatment	Abnormal appendix removed	43	37	43	62	52	41	57	2.6*	237)	372
	Normal appendix removed	25	16	17	47	30	19	38	6.3*	135)	
Non-operative treatment	Recurrence of same symptoms	13	16	13	7	3	14	5	-	52)	161
	No recurrence of same symptoms	27	22	28	12	20	26	16	-	109)	
	Total	108	91	101	128	105	100	116	-		533

*Calculated on basis of Poisson population - see footnote to table 33

$X^2 = 2.6$ $P > 0.05$ = not significant

$X^2 = 6.3$ $P < 0.05$ = significant

Ratio of patients treated operatively:non-operatively

= 372 : 161

= 7 : 3

radical units are grouped together and the average figures for conservative and radical treatment are compared statistically.

It can be seen that radical units remove significantly more abnormal appendices than do conservative units. (91 against 62; $X^2 = 5.4$ $P<0.05$) but also significantly more normal appendices (50.5 against 22; $X^2 = 11.2$ $P<0.01$). Radical units treat only 15.5% of patients admitted to hospital non-operatively (26 of 168) whereas conservative units treat 35% of patients admitted to hospital non-operatively (46 of 130).

Table 34 shows that the same trends apply to the smaller group of patients aged from 12 to 29 years, although the number of abnormal appendices removed by radical and conservative units is not significantly different (57 against 41; $X^2 = 2.6$, $P>0.05$). In this age group, 10% of patients admitted to radical units and 40% of those admitted to conservative units are treated non-operatively.

From tables 33 and 34 it can be seen that whether a patient is admitted to a radical or conservative unit influences considerably the treatment given. Consequently the risks of morbidity and prospects of cure are also influenced by this chance allocation.

Table 35 shows the probable treatment of the 10,000 patients

TABLE 35

Estimated treatment of 10,000 patients aged 12-29 years admitted to hospital with possible appendicitis each year in Scotland

a) under present approach to treatment
b) using conservative approach to treatment
c) using radical approach to treatment.

		Number of patients		
		a. Present management.	b. Conservative management.	c. Radical management
Operative treatment	Abnormal appendix removed	4,460	4,100	4,900
	Normal appendix removed	2,520	1,900	3,300
	Total operations	6,980	6,000	8,200
Non-operative treatment	Recurrence of same symptoms	980	1,400	450
	No recurrence of symptoms	2,040	2,600	1,350
	Total	3,020	4,000	1,800
	TOTAL	10,000	10,000	10,000
	PATIENTS DISSATISFIED*	1,332	1,666	912

*Calculated as 14% having normal appendix removed + those with recurrent symptoms after non-operative treatment.

aged 12-29 years who, it was earlier estimated, are admitted to hospital each year in Scotland with possible appendicitis. This is based on the assumption that the present overall surgical treatment in the Western Infirmary of Glasgow is representative of that in Scotland in general. The table also shows how this distribution would be altered by widespread adoption of conservative or radical treatment, again assuming that the experience gained in the Western Infirmary is representative of each of these forms of treatment. The number of people dissatisfied by treatment is also shown, being calculated as 14% of patients who have a normal appendix removed (Section 1 Chapter 3) plus those patients who complain of recurrence of the same symptoms (this includes those who require later operation) after non-operative treatment. Comparing the figures for general use of conservative treatment with those for general use of radical treatment, the following are the conclusions:-

(1) use of the radical approach results in 2,200 more operations than use of the conservative approach, but 800 of these operations lead to removal of an acutely inflamed appendix. Thus the conservative surgeon although carrying out 1400 fewer unnecessary operations, fails to carry out 800 necessary operations;

(2) use of the radical approach results in 9.1% of patients being

TABLE 36

Estimated number of patients suffering morbidity out of a total of 10,000 patients aged 12-29 years admitted to hospital with possible appendicitis each year in Scotland.

a) using present approach to treatment
b) using conservative approach to treatment
c) using radical approach to treatment.

		Number of patients suffering morbidity		
		a Present management	b Conservative management	c Radical management
Operative treatment	Abnormal appendix removed +	758	697	833
	Normal appendix removed †	252	190	330
Non-operative treatment	Total patients ‡	755	1,000	450
	TOTAL	1,765	1,887	1,613

All figures based on appropriate figures in table 35

\+ Morbidity affects 17% of patients
† Morbidity affects 10% of patients
‡ Morbidity affects 25% of patients

} Explanations in text.

dissatisfied by their treatment whereas 16.6% of patients are dissatisfied by conservative treatment. There is thus a 7.5% advantage in probability of cure for patients treated by radical surgeons.

Table 36 estimates the morbidity which would result from the distributions of the 10,000 patients aged 12-29 which are shown in table 35. The morbidity of appendicectomy for acute appendicitis is taken as the average of the values for complete acute appendicitis in young males and females (shown in tables 20 and 21 facing pages 103 and 104) plus 1% each for intermediate and late morbidity. This gives a total figure of 17%. The morbidity of normal appendicectomy calculated on the same basis is 10%. The morbidity of non-operative treatment is the 25% estimated in Chapter 3 of this section. The morbidity from present treatment thus involves 17.6% of patients whereas widespread use of conservative or radical treatment would cause morbidity to 18.8% and 16.1% respectively. This represents a reduction of 2.7% in morbidity using radical treatment as against conservative treatment.

Table 37 shows how widespread adoption of either form of treatment would influence avoidable mortality. Avoidable mortality is that resulting from operative removal of a normal appendix

TABLE 37.

Estimated avoidable mortality in 10,000 patients aged 12-29 years admitted to hospital with possible appendicitis each year in Scotland,

a) using present approach to treatment
b) using conservative approach to treatment
c) using radical approach to treatment

		Number of deaths		
		a Present management	b Conservative management	c Radical management
Operative treatment	Normal appendix removed *	0.5	0.38	0.66
Non-operative treatment	Acute appendix not removed	0.6 †	0.75 ‡	0.41 ‡
Total	(number of patients out of 10,000)	1.1	1.13	1.07

This table is based on the figures in Table 35

* Mortality from removal of normal appendix = 1:5000 (Chapter 4, Section 2)

† 6 deaths found in 10 years
∴ 0.6 deaths found in 1 year

‡ calculated as above value of 0.6 ± difference in number of acute appendices removed each year by given form of management as against present management, assessed at death rate of 1:2300 (Chapter 4, Section 2).

or non-operative treatment of mild appendicitis with subsequent death from appendicitis. Table 37 is based on the death rates discussed in Chapter 4 of Section 2 and uses the minimum estimated risk of death from non-operative treatment of actual appendicitis of 1 : 2300.

The deaths due to removal of normal appendices are calculated on the basis of one death for every 5,000 normal appendices removed.

The six deaths found to have resulted from non-operative treatment of appendicitis over ten years, are used to give a base-line of 0.6 deaths per year for this treatment under the present management of abdominal pain. The increase or decrease in the number of abnormal appendices which would be removed by radical or conservative management is calculated from the top line of figures in table 35. The alteration in the death-rate is then calculated on the basis of one death in 2,300 patients treated non-operatively for actual appendicitis.

In absolute numbers, the influence of choice of management on avoidable deaths is small. Radical treatment, however, appears to reduce the avoidable mortality by about 6% as compared with conservative management. This is a minimum estimate of the advantage of radical treatment being based on the minimum risk

of death from non-operative treatment of mild appendicitis which was calculated in Chapter 4 of this section.

Discussion

In the age group of 12-29 years, where the problem of operating or not operating on a patient admitted to hospital with possible appendicitis arises most often, it appears that the surgeon who advocates the radical or mainly operative approach to treatment satisfies 7.5% more people than his conservative counterpart who avoids operation where possible. He does this with a concurrent reduction of 2.7% in the number of patients suffering morbidity from the treatment given and with no increase in the risk of loss of life.

On the debit side the only features would be the administrative problem caused by an extra 2000 operations per year and the unsatisfactory feeling that radical treatment is supporting operative treatment for non-physical illness. However, the errors of the conservative surgeon total 27% (table 35 shows 1900 normal appendices removed and apparently also 800 abnormal appendices not removed) against 33% of the radical surgeon (3,300 normal appendices removed) and it thus appears that until better clinical diagnostic criteria become available neither group of surgeons can claim a significant

advantage in diagnostic accuracy.

It must thus be concluded that when a patient aged from 12 to 29 years is admitted to hospital with a considered diagnosis of possible appendicitis, unless an alternative diagnosis can be positively established, appendicectomy during the acute phase of the illness is the treatment of choice.

This chapter has concentrated on the choice of treatment in the young adult because this represents a well-defined clinical problem, and the one which this work has been primarily designed to investigate.

In older age-groups diagnostic accuracy is considerably higher (Harding, 1962) and the factors influencing management - mainly concerned with risk to life rather than morbidity or cure rate - are not in dispute. The articles by Christensen (1958) and Glenn and Thorbjarnarson (1960) summarise well the problems of appendicitis in the aged. In this context my figures of morbidity and mortality confirm the risks of delay in treatment of acute appendicitis and assist to put the consequences of missed appendicitis in perspective when non-operative treatment is being considered in a doubtful case.

As stated before, the hospital in which the greater part of this work was done has no paediatric practice and study of

the problems of abdominal pain in childhood has thus not been possible. Apley's book "The Child with Abdominal Pains" (1959) and the recent works of Jackson (1963) and Vulliamy (1965) give excellent reviews of this branch of the subject.

Summary

The differences between the radical and conservative approach to treatment of possible appendicitis are discussed and an estimate made of the results of general adoption of each policy.

Radical treatment in the young adult produces a satisfactory result in 7.5% more cases than does conservative treatment and causes morbidity in excess of the ideal result of each treatment to 2.7% fewer patients. Mortality is not influenced significantly in terms of absolute numbers, but radical treatment results in a reduction of about 6% in the number of avoidable deaths resulting from conservative treatment. For the young adult admitted to hospital because of possible appendicitis, appendicectomy is thus concluded to be the treatment of choice.

ADDENDUM

When it became clear that the advantage in the management of the young adult with possible appendicitis lay with the operative or radical approach, all the criteria of morbidity and mortality were re-assessed to ensure that no bias in favour of this approach to treatment had been introduced. No bias was found and all inferences made have been calculated to give the minimum advantages to radical treatment. Any errors introduced by the new techniques of analysis used in this study will thus under-estimate rather than over-estimate the advantages of operation under the defined circumstances.

SECTION 3

A

STUDY OF SOME

SOCIAL AND EPIDEMIOLOGICAL

ASPECTS OF APPENDICECTOMY

CHAPTER 1

APPENDICITIS AND THE FAMILY HISTORY

Without some obvious advance in knowledge concerning the aetiology of appendicitis, it is difficult to imagine improvement on the monograph by Rendle-Short (1946) entitled "The Causation of Appendicitis." This book discusses the many hypotheses that have been advanced from time to time to explain the peculiar geographical and racial incidence of the disease and the apparent increase in its incidence during the present century. More recently Tobe (1965) advanced the view that a virus caused appendicitis but his arguments were not based on sound reasoning. I discussed the weakness of his argument elsewhere (Howie, 1965). The two main errors were:-

(1) accepting an alteration of one dilution in serological study of paired sera as indicative of virus infection and

(2) using control material from a greatly different age group than that of his test group.

Zbitnew (1959) also looked for evidence of viral disease in a small series of cases and failed to find an association.

Whatever cause or causes are eventually found, it is unlikely that they will be avoidable to an extent sufficient

to influence the pattern of this disease in the community.

One interesting aetiological aspect of appendicitis, however, appeared capable of investigation in the course of the work described in the previous sections. This was the commonly held view that appendicitis "runs in families." Nimeh (1960) has cited one family with 40 cases in its family tree (he does not state how many members did not have appendicitis) and Rendle-Short refers to a family which apparently had hereditary kinking of the appendix which predisposed to appendicitis. In a condition so common as appendicitis it would not be surprising if many patients in the same family were sometimes found to be affected. Undoubtedly a family which has once been involved with an episode of "appendicitis" becomes appendix-conscious (Thompson, 1962) but no study has ever been designed to see whether true appendicitis or merely appendicectomy or neither of these runs in families.

Materials and Methods

All patients receiving follow-up circulars were asked how many of:- (1) their parents; (2) their siblings; and (3) their children had had their appendices removed.

Every patient whose appendix was classed as histologically

normal and who supplied the information requested above was paired with the next patient in the series of the same sex, in the same age decade, having the same clinical presentation but having complete acute appendicitis.

All patients with limited acute appendicitis were also matched in this way with patients having complete acute appendicitis.

To test the reliability of using patients with complete acute appendicitis as controls the number of patients in each group who were only children or who had families was also noted.

A higher incidence of appendicectomy operations in the relatives of patients with complete acute appendicitis compared with the relatives of patients with histologically normal appendices could be used as support for the belief that appendicitis indeed runs in families. If the relatives of patients having normal appendices removed show an excess number of appendicectomies this would suggest that it is appendicectomy that runs in families. If the incidence of relatives with appendicectomy is the same in test and control groups it would appear that neither appendicitis nor appendicectomy run in families.

TABLE 38

Incidence of appendicectomy in relatives of patients in various clinico-pathological groups compared with that in relatives of patients matched for age by decade, sex and clinical presentation but having complete acute appendicitis

Test group	Patients in group	Relatives having appendicectomy			Number of patients with children	Number of only children
		Parents	Siblings	Children		
Females: Emergency operation	146	60 of 292+	58 of 339	6 of 70	28	44
Normal appendix		(37 of 292)	(41 of 282)	6 of 63	(25)	(44)
Females: planned operation	58	19 of 116	30 of 127‡	3 of 37	18	20
Normal appendix		(14 of 116)	(16 of 135)	(5 of 54)	(19)	(13)
Males: Emergency operation	71	20 of 142	19 of 146	1 of 24	14	25
Normal appendix		(22 of 142)	(14 of 151)	(2 of 36)	(17)	(18)
Males: planned operation	21	7 of 42	5 of 55	1 of 6	3	7
Normal appendix		(8 of 42)	(2 of 23)	(0 of 7)	(3)	(8)
Females: Limited acute appendicitis	36	11 of 72	15 of 67	3 of 15	7	12
		(10 of 72)	(12 of 52)	(6 of 30)	(10)	(12)
Males: Limited acute appendicitis	24	8 of 48	3 of 29	0 of 12	5	13
		(10 of 48)	(4 of 38)	(1 of 11)	(6)	(6)

Numbers in brackets represent incidence of appendicectomy in matched control families

\+ Test and control differ to a significant degree $X^2 = 6.6$ $P < 0.02$

‡ Test and control differ to a significant degree $X^2 = 6.2$ $P < 0.02$

Results

The results of the study are shown in table 38. Two significant differences were demonstrated between test and control groups. Both involve female patients who have normal appendices removed. Where this is done as an emergency the excess number of relatives involved is in the parents of the patients having appendicectomy but where the operation is a planned procedure the excess is in the siblings of the patients.

No other differences are seen between test and control groups. The close similarity in the numbers of patients who have families of their own or who are only children suggests that the test and control groups are basically similar in family distribution. Outside the differences discussed it will also be noted that the proportion of patients' relatives who have had appendicectomy remains fairly constant throughout the different groups tested, the only exception being the higher incidence in siblings of female patients with limited acute appendicitis. This number is based on a small sample and does not differ significantly from the control series.

Discussion

It would appear that the family history influences the

number of females who have normal appendices removed; this influence is exerted by the parents in emergency conditions but by brothers or sisters in planned circumstances.

It may easily be appreciated how pressure from anxious parents might tip the scales in favour of the general practitioner asking for a hospital opinion in a case of suspected acute appendicitis. It is also understandable that a young girl whose brother or sister has either gained freedom from symptoms or maybe become the focus of family attention by having an appendicectomy might feel that she required the same treatment.

That these familial influences exist should be remembered when deciding on treatment, because patients with a family history of this type will tend to be those who keep turning up at hospital or in the surgery with "my appendix" or "her appendix," and will continue to do so until some surgeon obliges by removing the appendix.

This truth, however unscientific, has been and will continue to be perpetuated by the belief that appendicitis "runs in the family." Although this short chapter appears to disprove this belief the conclusion to be drawn is the paradoxical one that a family history of appendicectomy is an indication for appendicectomy sooner rather than later.

Summary

On the basis of a study of the family history of 356 patients without complete acute appendicitis compared with the histories of matched patients with complete acute appendicitis I conclude:-

(1) that appendicitis does not run in families;

(2) that appendicectomy does run in families; and

(3) that this influences the ultimate management of female patients complaining of right iliac fossa pain.

CHAPTER 2

APPENDICECTOMY AS AN EXPERIENCE

The unique physical and mental discomforts of an operation can be fully appreciated only by those who have experienced them. It is a recurring complaint against hospitals and hospital medicine that too little consideration is given to patients as individuals and that clinicians are not prepared to give reasonable explanations of diagnosis and treatments to patients either spontaneously or - for the rare patient who has the courage to ask - on request.

Many features which influence the impact of a stay in hospital are difficult to assess but it appeared relatively easy to use the follow-up study of my series of patients to inquire about the effect of hospitalisation as an experience and also about the standard of explanations given to patients.

All patients were asked the following questions:-

(1) Was the operation

(a) less trouble to you than expected?

(b) more trouble to you than expected?

(c) about as troublesome as you expected?

(d) a dreadful experience?

TABLE 39

Hospitalization as an experience in 1,006 patients in different clinico-pathological groups undergoing appendicectomy.

	Less trouble than expected.	As troublesome as expected.	More trouble than expected.	A dreadful experience	Total
Normal appendix	187	60	51	24	322
Complete) Limited) acute appendicitis	356	115	58	17	546
Perforated) Gangrenous) acute appendicitis	61	21	20	10	112
Appendix abscess + interval operation	17	0	7	2	26
Total	621	196	136 †	53 *	1,006

* Includes 9 patients having planned appendicectomy for R.I.F. pain of recurrent type

† Includes 17 patients having planned appendicectomy for R.I.F. pain of recurrent type

} = 26 of 109 patients at risk or 24%

(2) Did the hospital staff explain to you what was wrong and what they were going to do?

(a) very well

(b) well

(c) badly

(d) not at all

Excluding patients who turned out to have acute extra-appendicular disease, 1278 patients were available for study and 1006 answered both questions satisfactorily.

Table 39 shows the distribution of patients in the main clinico-pathological groups answering question 1 and table 40 shows the replies to question 2. It will be noted that 5% of patients (53 of 1006) find appendicectomy a dreadful experience and 13.6% find it more trouble than had been expected. The distribution of their cases to the various clinico-pathological groups is of interest.

24% (26 of 109) of cases having planned appendicectomy for recurrent right iliac fossa pain have been unfavourably impressed by their experience. This compares with 14% so influenced after acute appendicectomy (75 of 546), 23% (75 of 322) after removal of a normal appendix and 28% (79 of 138) after removal of a complicated appendix. The high rate of unfavourable

TABLE 40

Explanation of treatment given to 1,006 patients in different clinico-pathological groups undergoing appendicectomy.

	Satisfactory explanation	Poor explanation	No explanation	Total
Normal appendix	262	8	52	322
Complete / Limited } acute appendicitis	456	5	85	546
Perforated / Gangrenous } appendicitis	95	1	16	112
Appendix abscess + interval operation	24	2	0	26
Planned operation for recurrent pain	73	0	36 (33%)	109 *
ALL PATIENTS	837	16	153	1,006

(* figures in this line also included elsewhere in table)

experiences after removal of complicated appendices is mainly attributable to high morbidity but the almost equally high rate for normal and planned appendicectomy contains very few cases of appreciable morbidity and this does not explain the distressingly high rate in these categories.

When the second table is examined, it can be seen that 153 of 1006 patients feel they have had no explanation and a further 16 feel the explanation has been poor. This represents nearly 17% of the total series. Some patients who received no explanation did feel that the emergency nature of their admission excused this omission whereas others added a note to the effect that although they had been given no explanation, they had not asked for one. The significant feature in this table is the 33% incidence of "no explanations" in patients having planned appendicectomy for recurrent right iliac fossa pain.

An equally salutory finding is that of the 53 patients who found appendicectomy "a dreadful experience" 19 (37%) stated that they had received no explanation of proposed or actual treatment.

A third distressing trend is that although only about 10% of all patients in the series are aged 14 or under, this age group includes 20% of the patients who received no explanation.

Although it appears that the explanation given influences the effect of being in hospital as an experience, there is no evidence to suggest that it influences the cure rate significantly.

Summary

Of 1006 patients undergoing appendicectomy 189 patients found the experience more trouble than anticipated or a dreadful experience and a further 121 considered that they did not receive a satisfactory explanation of their treatment. This group of 310 patients is nearly one-third of the total who had operations. Many of these unfortunate results are attributable to features outwith the control of the medical or nursing staff but 46 patients belong to both dissatisfied categories discussed above and in these patients (about 5% of the total) it appears that hospitalisation has been a needlessly unsettling experience. It is unfortunate also that younger patients should so be frequently involved as the experience may discourage them from seeking proper medical advice at an early stage of a later, more serious illness.

It is also worth reflecting that if this proportion of patients has been thus influenced by appendicitis and appendicectomy, the distress caused to patients with fear of

or actual malignant disease - where evasiveness by the medical staff is endemic - must be one of the most important of present-day iatrogenic disorders.

CHAPTER 3

CANCER AND APPENDICECTOMY

It has been assumed in all the preceding chapters that the appendix is a non-functioning organ and that appendicectomy carries no risks of loss of normal body function.

Recently Sutherland *et al.* in two papers (1964 and 1965) and Archer *et al.* in a third paper (1964) demonstrated that the appendix plays an important part in the immune mechanism of the rabbit. At about the same time McVay (1964) published an alarming article suggesting a relationship between appendicectomy and the subsequent development of cancers of colon and other organs in man. The possible theoretical relationship between Sutherland's and McVay's work is at once obvious. However, although the lymphoid tissue in the human appendix is certainly active in early adult life it appeared unlikely on morphological grounds that the appendix lymphoid could be of material importance to the human immune system. In the absence of a disease mechanism of this type it seemed hard to accept McVay's findings at their face value, but the practical and theoretical implications of this association were so great that it was deemed necessary to attempt to repeat McVay's work.

Accordingly, working with Dr. W. R. Timperley, then of the Bacteriology Department of the Western Infirmary of Glasgow, I carried out the study reproduced below, which was based on follow-up of live patients as against the study of post-mortem records used by McVay. This work has now been published (Howie and Timperley, 1966).

Materials and Methods

As test material, we used patients registered in the West of Scotland Cancer Register as having cancer of the breast, cervix uteri, colon or rectum. All patients had been first diagnosed as cases of cancer not more than two years previously. 1656 cases of cancer were included in the study: 588 cases of breast cancer, 500 cases of cervical cancer and 568 cases of colonic cancer. All patients known to have died were excluded. We recorded whether the notification was from a teaching or a non-teaching hospital. The circular shown in the appendix was posted with a stamped addressed envelope for reply.

The replies received were grouped for sex and for age by decades. 916 patients from a Glasgow General Practitioner's list served as a healthy control population, and received a similar circular. The number of circulars sent was calculated

TABLE 41.

Number of cases of appendicectomy, tonsillectomy and cholecystectomy in patients with cancer of breast, cervix uteri, colon and rectum, and with no cancer.

Description		Replies received	Appendicectomy No.	Appendicectomy %	Tonsillectomy No.	Tonsillectomy %	Cholecystectomy No.	Cholecystectomy %
Cancer of breast		420	54	(13)	54	(13)	6	(1.4)
Cancer of cervix		307	48	(16)	47	(16)	7	(2.2)
Cancer of colon	Female	140	12	(8)	13	(9)	11	(7.8)
	Male	152	9	(6)	11	(7)	2	(1.3)
	Total	292	21	(7)	24	(8)	13	(4.4)
All cancers	Female	867	114	(13)	114	(13)	24	(2.7)
	Male	152	9	(6)	11	(8)	2	(1.3)
	Total	1019	123	(12)	125	(12)	26	(2.5)
Controls	Female	478	63	(13)	117	(24)	15	(3.1)
	Male	145	28	(19)	24	(16)	1	(2.5)
	Total	623	91	(15)	141	(23)	16	(2.5)

TABLE 42.

Number of cases of appendicectomy, tonsillectomy and cholecystectomy in patients with cancer of breast, cervix uteri, colon and rectum compared with healthy controls matched for sex and for age by decade.

Description		Cases	Appendicectomy Test	Appendicectomy Control	≠ Tonsillectomy Test	≠ Tonsillectomy Control	‡ Cholecystectomy Test	‡ Cholecystectomy Control
Cancer of Breast		420	54	51	54	95	6	7
Cancer of Cervix		307	48	40	47	77	7	7
Cancer of Colon	Female	140	12	13	13	20	11	4
	Male	152	9*	28*	11	24	2	1
	Total	292	21	41	24	44	13	5
All cancers		1019	123	132	125	216	26	19

* $X^2 = 11.1$ P 0.01 highly significant

≠ Most of the test figures differ significantly from the control figures.

‡ None of the test figures differ significantly from the control figures.

on the assumption that one-third would not be returned.

Results

Table 41 shows the number of appendicectomies, tonsillectomies, and cholecystectomies previously carried out in patients later developing cancer of colon and rectum, cancer of breast and cancer of cervix together with the incidence of these operations in the control group. Significance values for the findings were not calculated as the series are not matched exactly for age.

Table 42 shows the numbers of appendicectomies, tonsillectomies, and cholecystectomies in each tumour group compared with controls matched for age and sex. Excluding tonsillectomy, which is discussed later, the only statistically significant finding is the incidence of appendicectomy in male patients, where the number in the control group (28 of 152) is significantly in excess of that in the cancer group (9 of 152).

Table 43 shows the response to the two circulars. The number of patients who received circulars was calculated on the basis of total letters sent, less those returned by the Post Office as wrongly addressed. From this total we deducted the number of cases where relatives replied to say that the patients had died. After making these deductions and noting the number

TABLE 43.

Fate of Circulars sent to Patients with Cancer and to Healthy Controls.

Description	Circulars sent	Fate of Circulars				% Receiving Circular who did not reply
		Patients No longer alive	Patients not traced	Replies Received	Not Accounted For	
Cancer of breast	588	31	29	420	108	20.4
Cancer of cervix	500	24	44	307	125	28.9
Cancer of colon	568	78	52	292	146	33.3
All cancers	1656	133	125	1019	379	27.1
Healthy Controls	916	5	215	623	74	10.6

Patients regarded as receiving circular = circulars sent-(patients dead + patients not traced).

of replies received, 379 cancer patients were still unaccounted for (27% of the series) as against 74 of the control series (10% of the series).

The incidences of the different operations are closely similar in cases from teaching and non-teaching hospitals (table 44).

The mean age of patients with breast cancer was 57.0 years, with cervical cancer 51.7, with colonic cancer 63.0 for females and 62.8 for males. The average age at which appendicectomy was carried out was 29.7 years, at which tonsillectomy was done was 16.1 in females and 21.1 in males and the mean age at which cholecystectomy was done was 50.6 years.

Discussion

The present series is open to criticism for two reasons: first the failure to account for 379 of the 1656 cases with cancer; and second the high incidence of tonsillectomy in the control group (23%) compared with the cancer group (12%). There are however several reasons why these criticisms should not be regarded as invalidating the general conclusions.

First, it seems unlikely that the people who failed to reply would have had a greater proportion of previous operations

TABLE 44.

Analysis of previous operations carried out on patients subsequently attending teaching and non-teaching hospitals with cancer of various organs.

Type of Hospital.	Cases	Previous Operations					
		Appendicectomy		Tonsillectomy		Cholecystectomy	
		Cases	%	Cases	%	Cases	%
Teaching Hospital	456	52	11.4	60	13.1	12	2.6
Non-teaching Hospital	563	71	12.6	65	11.5	14	2.4
Total	1019	123	12.0	125	12.2	26	2.5

than the people who did reply. Patients who have had none of the operations listed in the circular were more likely to think that a reply was not required than patients who had had one or more of the operations. It was in fact noted in each series that the patients who replied by return of post had had a closely similar number of operations to the patients whose replies were received last. It is also possible that a number of the 379 patients who were not accounted for had died.

The high incidence of tonsillectomy in the control series suggests either that tonsillectomy protects against subsequent development of cancer or that the control series was biased with respect to tonsillectomy. The second appears the more likely explanation.

The reasons for this assumption are as follows. Cancer patients attending teaching hospitals and non-teaching hospitals in this region had equal incidences for appendicectomy, tonsillectomy, and cholecystectomy (table 44). The teaching hospitals draw patients almost entirely from the City of Glasgow while the non-teaching hospitals draw patients from Glasgow, the surrounding industrial area and a further rural area. It therefore seemed that the incidence of the operations studied was not subject to variation within the West of Scotland area.

Consequently a population from one City Practitioner's list which includes some 3,500 patients representative of all social classes was expected to provide a suitable control. This has proved to be true for cholecystectomy.

However, forty years ago, when most of the tonsillectomies in the control series were done, the decision to remove tonsils was made by the family doctor who often then did the operation himself. The high incidence of tonsillectomy in the control series may therefore reflect only the preference of the doctor then in charge of the practice.

Appendicectomy, like cholecystectomy, is done in hospital and these two operations are thus more closely related in terms of general practitioner management than are tonsillectomy and appendicectomy.

If the control series is accepted as valid for appendicectomy and cholecystectomy, the only significant finding is the excess of appendicectomies in the male control group compared with the male cancer group. No explanation for this is evident, but it offers no support for the suggested relationship between previous appendicectomy and the subsequent development for cancer.

The study of McVay is open to criticism on two counts. First the appendix is positively stated to be present or absent

in the post-mortem notes of only 322 of the 820 cases (including controls) in his original series. This original series was later enlarged by the inclusion of 94 extra controls not present in the first eight tables of his report to give 416 out of 914 fully documented cases. Only 120 of the 322 cases referred to above had cancer of colon. The author made great efforts to make the figures of his total series accurate by study of the clinical records of the patients who came to autopsy. Nevertheless, the fact that the presence or absence of the appendices is only assumed and not observed in so many of the cases is a potential source of error. This was discussed by McVay, but not accepted as influencing his findings.

McVay correctly disregarded removal of the appendix after the definitive diagnosis of cancer had been made. However, if appendicectomy was done at the same time as removal of a rectal or colonic neoplasm and this was not recorded in the operation notes, it might appear at post mortem that this was a case of appendicectomy many years before. We have seen this error happen on previous occasions.

The second criticism is in the selection of controls with regard to time of death. The test patients died within the period 1947 to 1962, a scatter of 15 years, whereas the controls

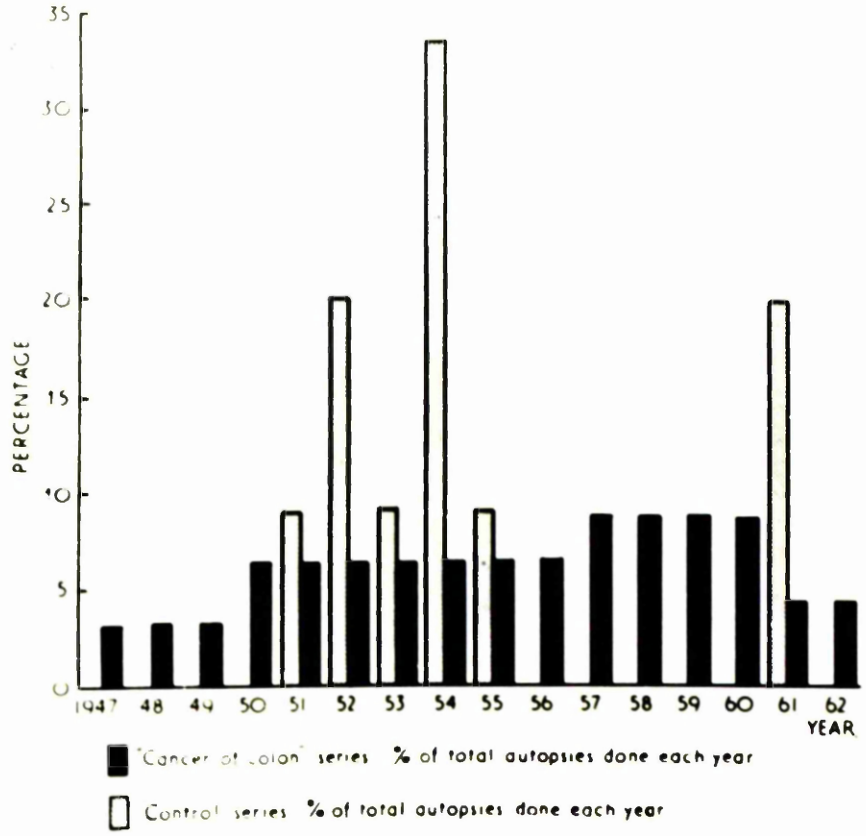


fig. 54

Figure 54 % of total "Cancer of Colon" and "Control" autopsies done each year in study reported by McVay (1964).

were collected predominantly in the period 1951 to 1955. Fig. 54 shows the approximate percentage of the test and control autopsies done in each year of McVay's study, calculated as closely as possible from details given in his report. Although the arithmetic mean year of death is closely similar for the test and control series, 60% of the cancer patients and only 30% of the controls came to autopsy in the second half of the period of the study.

If the mean age at death is taken as 60 years and the mean age at which appendicectomy was carried out was 30 (the mean age in our present series) the peak years at which the colon cancer group would have been liable to appendicectomy would have been 1927 to 1930 and the peak years for the control group would have been 1921 to 1925. The modal age for appendicectomy is certainly less than the mean age of 30 and brings the control series in particular into the period of time before appendicectomy was at its height of popularity. It is difficult to assess the importance of this, but the spread of time covered by the test series and the absence of exact time correlation of the control autopsies must cast doubt on the validity of comparisons between the two series - in particular as they are claimed to be matched for age.

Confirmation of this as a possible source of error is seen

by noting that in our series, the percentage of females who had had their appendices out falls as the average age rises. Cancer of cervix cases, average age 51.7 have 16% appendicectomies, cancer of breast, average age 57.0 have 13% appendicectomies and cancer of colon cases, average age 63.0 have 8% appendicectomies. The control series shows the same general trend.

On the evidence of our observations and in view of the possible errors of McVay's series which we have referred to, we conclude that there is insufficient evidence to support an association between previous appendicectomy and the subsequent development of cancer.

Summary

1656 cases of cancer of breast, cervix uteri, colon and rectum were studied by postal follow-up for incidence of appendicectomy, tonsillectomy and cholecystectomy. 916 healthy patients from a general practitioner's list were studied in the same way.

We find no evidence to support the suggestion made by McVay - which we discuss critically - that removal of the appendix predisposes to the subsequent development of cancer of colon or of other regions.

Although studies to investigate possible relationships between appendicectomy and auto-immune diseases may be in process, no results have been published and there is at present, nothing to suggest that any associations will be demonstrated.

The only other disease recently linked with the appendix is multiple sclerosis. In the continuing search for new features in the aetiology of this disease Poskanzer (1965) noted a weakly significant association between appendicectomy and multiple sclerosis in patients compared with their spouses. This part of Poskanzer's study is however a superficial one and much more detailed analysis of his material along the lines discussed in reference to McVay's work would be required before this relationship could be regarded as properly established. This possible association would be unlikely to influence the choice of operative or non-operative treatment in a patient with abdominal pain.

The decision to advise appendicectomy should thus not be influenced by the fear of this operation predisposing to the development of cancer or other diseases.

SUMMARY AND CONCLUSIONS

For many patients with abdominal pain, appendicitis is the obvious diagnosis and appendicectomy clearly the only correct treatment. For many other patients with abdominal pain appendicitis is a possible but less certain diagnosis and the treatment of these patients varies widely. The factors which decide whether operation will or will not be advised are often those of expediency and not based on tested clinical experience. Strongly believed and widely divergent views are held on the rights and wrongs of appendicectomy where appendicitis is a possible but doubtful diagnosis. The two extremes of view, no matter how sincerely held, cannot both be correct. No objectively collected evidence is at present available to allow comparison of the radical operative and conservative non-operative approach to this common clinical problem. This important deficiency is a direct consequence of the failure of surgeons and pathologists to agree within or between their specialities on what constitutes a normal appendix and when an appendix causes clinical symptoms.

This work is designed to present objective evidence to allow a choice to be made between operative and non-operative treatment of possible appendicitis, particularly in the young adult. A detailed objective study of the pathology of the appendix is an essential preliminary to the clinical part of the work. Section

1 thus deals with the pathology of appendicitis and Sections 2 and 3 with the mainly clinical aspects of the problem.

Section 1

(1) New and objective histological definitions of the normal appendix and of two grades of acute appendicitis (limited acute appendicitis and complete appendicitis) were presented on the basis of an extensive clinico-pathological study. This study involved (i) histological examination of 1412 appendices removed at operation over a period of two years (ii) examination of clinical records and operative findings from each operation and (iii) postal follow-up of the 1312 patients out of the above total whose appendices had been removed for possible appendicitis. The replies to the follow-up allowed objective assessment of cure rates from operative treatment. 1102 replies (85%) were received.

(2) A new test was described and evaluated for the diagnosis of recent appendicitis. This was dependent on demonstration, by the prussian-blue technique, of stainable iron in the wall of the appendix. This was assumed to be an indication of the recent presence of inflammatory exudate. Correlation of the clinical,

operative and histological findings of 669 cases showed that the presence of a positive prussian-blue reaction was the best index of recent appendicitis at present available.

(3) A study of mesenteric adenitis based on the above material and techniques showed that although many cases of mesenteric adenitis were not related to appendicular disease a relationship between the two diseases could frequently be demonstrated. It is not possible in these related cases to say whether mesenteric adenitis was a sequel to mild appendicitis or the two conditions shared one aetiology. The curative effect of appendicectomy in mesenteric adenitis may in appropriate circumstances be predicted on the basis of the histological findings discussed under the previous headings.

(4) Brief reviews of the significance of some of the less common lesions of the appendix were given.

(5) The histological criteria used as the basis for this part of the work were tested against other available histological criteria and against surgical opinion. My histological criteria were found to be more objective than any other histological or operative diagnostic criteria and to give greater accuracy in prediction of cure and failure of cure than surgical opinions did.

My criteria were thus assumed to be a suitable foundation for a meaningful clinico-pathological classification of appendicular pathology. This classification forms the foundation for the clinical Sections of the work.

Sections 2 and 3

(6) New criteria of morbidity were defined to allow objective assessment of post-operative complications of appendicectomy. Morbidity was calculated as short-term (from operation till return to work, including convalescence in hospital and at home) intermediate (up to two years after operation), or long-term (beyond two years after operation).

(7) On the basis of examination of clinical records and information collected by postal follow-up of 1102 of 1312 patients who had appendicectomy for possible appendicitis, short-term morbidity of potentially serious nature was found to involve 8% of patients who had a normal appendix removed; 16%, 20%, 50%, and 75% were the percentages of patients having potentially serious morbidity after appendicectomy for respectively limited acute appendicitis, complete acute appendicitis, gangrenous appendicitis, and perforated appendicitis.

Examinations of the above records together with retrospective studies of 75 patients with adhesion obstruction and 393 patients admitted to hospital with abdominal pain (both groups the total over a period of one year) allowed calculation of potentially serious intermediate and late morbidity of 1% each.

The potentially serious morbidity from appendicectomy for no appendicitis, acute appendicitis, gangrenous appendicitis, and perforated appendicitis thus affects approximately 10%, 20%, 50%, and 75% of patients involved.

A further 10 - 15% of patients have trivial short-term morbidity and a further 3% trivial intermediate morbidity. Morbidity is influenced more by degree of pathological change than by age or sex.

(8) The morbidity of conservative (non-operative) treatment of possible appendicitis was assessed from postal follow-up and examination of the clinical records of 206 patients treated conservatively over a period of one year. Follow-up was done after a two-year interval. 90% of patients traced replied to the questionnaire. There is no short-term morbidity comparable to that for patients having appendicectomy, and potentially serious morbidity is defined as the necessity for later appendicectomy. In the intermediate follow-up this was found to involve 17% of

patients treated conservatively, and by indirect studies a long-term morbidity of 8% was calculated. This represents a potentially serious morbidity from conservative treatment of 25%.

10% of patients were off work for 3 weeks or more after conservative treatment and this may be regarded as equivalent to the trivial short-term morbidity of appendicectomy.

(9) A family history of appendicectomy, a previous history of similar abdominal pain, or an earlier suggestion of a diagnosis of appendicitis increases the chances of later appendicectomy. 40% of patients who have subsequent appendicectomy are found to have true appendicitis.

(10) 805 deaths from appendicitis and appendicectomy over a 10-year period in Scotland were critically examined, full details being available in 650 cases. It was found that in all age groups mortality from appendicectomy rises sharply with advance of the pathological process. Similarly for any given degree of pathological change, mortality rises sharply with increase in age. For any given circumstances the mortality in males appears to be about twice that in females. The mortality from the conservative treatment of mild appendicitis in the young adult was estimated at between 1 : 850 and 1 : 2300 whereas, in the same age group,

mortality from appendicectomy lies between 1 : 2600 for complete acute appendicitis and 1 : 5000 for limited acute appendicitis together with normal appendicectomy.

(11) There appeared to be a slow but steady fall in the incidence of appendicitis from 1954 - 1963 and an improvement in the prognosis for appendicectomy in 1962 and 1963. This improvement coincided with and may have been related to the introduction of the new synthetic penicillinase-resistant penicillins.

(12) The mortality rates for appendicectomy in teaching and non-teaching hospitals do not differ significantly.

(13) Removal of a normal appendix during the acute phase of an attack of abdominal pain cured or improved 86% of patients. The same operation postponed to a later date as an "interval" operation cured or improved 71% of patients. Conservative treatment of mild abdominal pain of the type which might have been treated operatively if a different surgeon had been in charge resulted in cure or improvement in 57.5% of patients. These figures represent significant differences.

(14) Surgeons who adopted the radical approach to the treatment of possible appendicitis removed significantly more normal and

significantly more abnormal appendices over a period of one year, than did their conservative colleagues.

(15) If the radical approach to treatment was universally adopted for the treatment of young adults, 7.5% more patients would be satisfied by their treatment than if conservative treatment was universally adopted. At the same time potentially serious morbidity would affect 2.7% fewer patients and any extra deaths due to removal of additional normal appendices (this would total 0.28 deaths per year in Scotland) would be more than balanced by reduction in deaths from advanced appendicitis in patients who had previously been treated conservatively for the same symptoms.

(16) If patients having abdominal operations also had an appendicectomy carried out when possible, there would be a reduction of up to 4% in the number of appendicectomies required at a later date and a 3% reduction in the death rate from appendicitis.

(17) Appendicectomy appeared to run in families but there was no evidence to support the belief that appendicitis is a familial disease.

(18) The recently made suggestion that appendicectomy predisposed

to development of cancer was examined and work carried out to test the theory. No evidence was found to support the association.

On the basis of a critical re-examination of the pathology of the appendix and of the clinical management of abdominal pain it is therefore concluded that if a young adult patient is admitted to hospital because of possible appendicitis, unless an alternative diagnosis can be satisfactorily established the treatment of choice should be appendicectomy before the acute phase of the illness has passed.

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Dr. M. A. Heasman) and from the Western Regional Hospital Board's Cancer Registration Scheme could not readily have been collected elsewhere, and was quite essential for the completion of the work.

I received valuable technical assistance from the technicians in the Pathology Department of the Western Infirmary, in particular from Mr. L. Miller. Mr. G. Kerr took all the photomicrographs and the colour prints were processed by R. T. Evans Ltd. Mr. R. Callender prepared figure 54.

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Hertzler, A.E.	1926	Amer. J. Obstet. Gynec., 11, 155-70.
Ger, R.	1954	S. Afr. med. J., 28, 589-91.
Howie, J.G.R.	1963	Brit. med. J., 2, 250.
Howie, J.G.R.	1964	Lancet, 1, 1240-2.
Howie, J.G.R.	1965	Lancet, 2, 182.
Howie, J.G.R.	1966	J. Path. Bact., 91, 85-92.
Howie, J.G.R., Timperley, W.R.	1966	Cancer (Philad.), 19, 1138-42.

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Hersic, A.R.	1964	"Statistics," 13th ed., H.F.L., London.
Ingram, P.W., Evans, G.	1965	Brit. med. J., 2, 149-51.
Jackson, A.S.	1937	Surg. Gynec. Obstet., 65, 1-10.
Jackson, R.H.	1963	Brit. med. J., 2, 277-81.
Jewers, J.	1959	Lancet, 2, 1164-7.
Johnston, J.H.	1954	Brit. med. J., 1, 135-6.
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Landsdown, R.G.P., Williamson, G.S.	1914	Brit. J. Surg., 2, 306-24.
Lane, R.E.	1960	Amer. J. Obstet. Gynec., 79, 372-7.
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Morley, J.	1928	Brit. med. J., 1, 887-90.
Muir, R., Niven, Janet S.F.	1935	J. Path. Bact., 41, 183-97.
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Muller, S.	1959b	Acta chir. scand., 118, 146-54.
Nimeh, W.	1960	Amer. J. Gastroent., 34, 513-23.
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Plewes, B., Teskey, L.	1955	Canad. med. Ass. J., 72, 175-8.
Poskanzer, D.C.	1965	Lancet, 2, 1264-6.
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Randall, K.J., Muir, N.S.	1962	Lancet, 1, 1042-3.
Rees, W.S.	1952	Lancet, 2, 1199-203.
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Richmond, H.G., Guthrie, W.	1964	J. Path. Bact., 87, 415-20.

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Rukstinat, G.T.	1963	Amer. J. Gastroent., 39, 389-94.
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Truelsen, F.	1961	Acta chir. scand., Supp. 283, 275-81.
Van Meurs, D.P.	1954	Brit. med. J., 2, 991.
Vicary, F.	1954	Arch. Surg., 68, 329-36.
Vulliamy, D.G.	1965	Brit. med. J., 1, 1113-5.
Ward-McQuaid, J.N.	1951	Lancet, 2, 524-7.
Wass, S.H.	1955	Brit. med. J., 1, 752-4.
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APPENDIX

SERIES NO.

SECTION C - SINCE YOUR OPERATION

1. Have you had any more pain in the abdomen since being declared fit? YES / NO

2. If "YES", was the pain ANSWER
   (a) the same as you had your operation for?
   (b) worse than you had before your operation?
   (c) less severe than you had before your operation?
   (d) quite different from that before your operation?

3. Please give details of these attacks of pain in the table below :-

Approx. date	No. of days off work, if any	No. of days in hospital, if any	Were you seen by family doctor?	Were you seen by hospital doctor?

4. Since being declared fit after your operation, have you had any trouble with your operation wound? YES / NO
   If "YES", please give details opposite. .....

5. Have you had any other trouble due to your operation? YES / NO
   If "YES", please describe the trouble you had. .....

SECTION D - GENERAL

1. Please show below the number of relatives you have, and how many of them have had their appendix out :-

   Parents ... out of ...2... have had their appendix out
   Brothers and sisters ... out of ... have had their appendix out
   Children ... out of ... have had their appendix out

2. Was the operation ANSWER
   (a) less trouble to you than expected?
   (b) more trouble to you than expected?
   (c) about as troublesome as you expected?
   (d) a dreadful experience

3. Did the hospital staff explain to you what was wrong and what they were going to do? ANSWER
   (a) Very well
   (b) Well
   (c) Badly
   (d) Not at all

4. Which member of staff told you? (if you know) .....

5. As a result of your operation, do you feel ANSWER
   (a) no more pain
   (b) less pain than before
   (c) the same pain as before
   (d) more pain than before
   (e) Don't know

NAME
ROUTINE NO.
SERIES NO.

SECTION A - YOUR OPERATION (This includes the time till you were fit for your normal job)

1. After the day of your operation, how long were you off work or unable to do your normal job? .....

2. Did you have any trouble from your operation wound after you left hospital? .....

3. If "YES", how long did your wound take to heal completely after you left hospital? .....

4. How many visits to your family doctor did you make after leaving hospital before you were declared fit? .....

5. How often did your family doctor visit you during this time? .....

6. Before you were declared fit, did you return to hospital as an outpatient for any of the following reasons :-

   (a) to have stitches out YES / NO
   (b) for wound dressing YES / NO If "YES", how often .....
   (c) for a check-up YES / NO If "YES", how often .....
   (d) for any other reason YES / NO If "YES", how often .....

SECTION B - BEFORE THE ILLNESS FOR WHICH YOU HAD YOUR OPERATION

1. Before the illness which led to your operation, did you ever have trouble from pain of a similar type? YES / NO

2. If "YES",

   (a) how many days have you been off work because of it? .....
   (b) when was the last attack before your operation? .....
   (c) did you see your family doctor about this pain? YES / NO
   (d) were you ever seen at a hospital because of this pain? YES / NO

3. If you were seen at a hospital ("YES" to (d) above)

   (a) which hospital did you attend? .....
   (b) what was the date or dates? .....
   (c) did you have to stay in hospital as a patient? .....
   (d) if so, for how long? .....

4. Had anyone before suggested you might have appendicitis? YES / NO

5. If "YES", who made the suggestion? .....

CIRCULARS USED TO COLLECT

INFORMATION USED AS BASIS FOR TEXT

1. The 1312 patients whose appendices were removed because of acute or recurrent right iliac fossa pain and were studied histologically, received the following letter together with the questionnaire facing this page, between 12 and 24 months after their operation.

Western Infirmary,

Glasgow, W.1.

Dear

It is now some time since you had your appendix taken out.

We are interested to know how you have been since leaving hospital and to have some extra information about your health before your operation. I shall be grateful if you will fill in the enclosed circular as well as you can and return it in the stamped, addressed envelope which is provided.

All the answers you give will, of course, be treated as confidential.

Thank you for your help.

Yours faithfully,

J. G. R. Howie, M.B., Ch.B.,
Registrar.

If no reply was received after two to four weeks, the questionnaire was again sent, this time with the covering letter shown below.

Western Infirmary,

Glasgow, W.1.

Dear

I recently sent you a form asking questions about your appendix operation some two years ago. I do not seem to have had a reply so far. In case you have lost the form, I enclose a second form with a second reply paid envelope.

It would be much appreciated if you could fill this up as soon as possible. More than half the people have now returned their forms and we are anxious to have as many answers as possible.

Yours faithfully,

J. G. R. Howie, M.B., Ch. B.
(Registrar)

NAME:-

CODE:-

SECTION A. When you were in hospital.

1. From the day you entered hospital, how long were you off work or unable to do your normal job? .....

SECTION B. Before you were in hospital.

2. Had you ever had the same sort of pain before you were in hospital? YES/NO.....

3. Had you ever been in hospital with any of these previous attacks? YES/NO.....

If YES when.....

which hospital.....

4. How many days have you been off from your normal job because of any pain described in (2) and (3) .....

SECTION C. After you were in hospital.

5. Since being in hospital have you had any more pain? YES/NO.....

6. If YES was it (a) the same pain

(b) worse pain

(c) less severe pain than you were in hospital for ANSWER.....

7. How many days have you been off from your normal job because of say pain described in (5) and (6)? .....

8. Have you had to go into hospital as a patient again? YES/NO.....

If Yes (a) how long were you in hospital? .....

(b) which hospital were you in? .....

(c) what date were you again in hospital.....

(d) did you have an operation? .....

(e) what operation did you have, if any? .....

SECTION D. At any time.

9. Has anyone at any time suggested that you might have appendicitis? YES/NO.....

10. If YES (a) who made the suggestion? .....

(b) when this made? .....

2. Patients who had been treated non-operatively for possible appendicitis and who did not receive the above circular as a result of subsequent appendicectomy within the period covered by the main part of this work, were sent the following letter and the questionnaire facing this page 24 months after the relevant admission to hospital.

Western Infirmary,

Glasgow, W.1.

Dear

It is now about two years since you were in the Western Infirmary with abdominal pain. We would like to know if you have had any further trouble since you were in hospital.

I would be very grateful if you could fill in the enclosed form as well as you can and return it to me using the stamped addressed envelope which is provided.

All answers will, of course, be treated as confidential.

Thank you for your help.

Yours faithfully,

J. G. R. Howie, M.B., Ch.B.
(Registrar)

If no reply was received after two to four weeks, the questionnaire was again sent, this time with the covering letter shown below.

Western Infirmary,

Glasgow, W.1.

Dear

I recently sent you a form asking questions about your stay in hospital some two years ago. I do not seem to have had a reply so far. In case you have lost the form, I enclose a second form with a second reply paid envelope.

It would be much appreciated if you could fill this up as soon as possible. More than half the people have now returned their forms and we are anxious to have as many answers as possible.

Yours faithfully,

J. G. R. Howie, M.B., Ch.B.
(Registrar).

In all letters shown in the appendix to this point, the date of sending and the patient's name were written in ink and the letter was signed by me personally. It was hoped that this would reduce to a minimum the impersonal atmosphere inevitable in this type of follow-up and therefore lead to a higher number of returns than might otherwise have resulted.

3. In the survey of death related to appendicitis and appendicectomy, the letter reproduced below was sent to the Medical Superintendent of each of the 21 hospitals which I hoped to be able to visit.

Western Infirmary,

Glasgow, W.1.

The Medical Superintendent, May, 1966.

Dear Sir,

With the aid of a grant from the Western Infirmary of Glasgow and with the co-operation of the Registrar General for Scotland, I am investigating some of the features related to deaths from appendicitis and appendicectomy in Scotland over the period 1954-63.

My object is to assess the risk of death following removal of a normal appendix, removal of abnormal appendices of different severity and, thirdly, the number of patients dying who have on an earlier occasion been in hospital with possible appendicitis. It is thus hoped to be able to compare the short and long-term risks of death involved in the conservative and operative management of doubtful appendicitis.

Nearly 1,000 people have died from appendicitis or the complications of appendicectomy in the period of the study and I enclose a list of those from your hospital, together with their date of death while in hospital. I would be most obliged if you could make available the case records of those patients for me to examine. If this can be arranged, I will gladly visit your hospital at a convenient time for this purpose. If possible, I would also like to know the approximate number of appendices removed in your hospital each year from 1954 - 1963 inclusive.

Your assistance in this project is essential for its success and will be most sincerely appreciated.

I look forward to hearing from you.

Yours sincerely,

(J. G. R. Howie).

In all cases arrangements were subsequently made for me to visit these hospitals.

In the case of 55 other hospitals, the letter which is shown below was sent:-

Western Infirmary,

Glasgow, W.1.

The Medical Superintendent, May, 1966.
or Chief Surgeon,

Dear Sir,

With the aid of a grant from the Western Infirmary of Glasgow and with the co-operation of the Registrar General for Scotland, I am investigating some of the features related to deaths from appendicitis and appendicectomy in Scotland over the period 1954-63.

My object is to assess the risk of death following removal of a normal appendix, removal of abnormal appendices of different severity and, thirdly, the number of patients dying who have on an earlier occasion been in hospital with possible appendicitis. It is thus hoped to be able to compare the short and long-term risks of death involved in the conservative and operative management of doubtful appendicitis.

Nearly 1,000 people have died from appendicitis or the complications of appendicectomy in the period of the study and I have made arrangements to visit all hospitals in Scotland where more than 10 deaths have occured during this period.

To gain an overall picture of appendicitis throughout the country it is particularly important to have details from smaller hospitals as well, and

some 200 of the deaths have been scattered amongst 55 of these. It is not possible to visit all the hospitals in the time available for this study and I would be most grateful if the information I require for this work could be given for each patient who has died in your hospital, on the enclosed form. If possible, I would also like to know the approximate number of appendices removed in your hospital each year from 1954-63 inclusive.

I do realise that this will involve quite a number of people in some rather tedious searching, but I believe the information which will be collected is of importance. Your assistance in this project is essential for its success and will be most sincerely appreciated.

If you would like any further information, please let me know. I hope to be able to start analysing the results of this study early in June.

Thank you for your help.

Yours sincerely,

(J. G. R. Howie)

The form below was enclosed for each patient about whom information was requested and the sheet entitled "Notes for Guidance" was also enclosed.

NAME .. ..AGE.. .. DATE OF DEATH .. ..Ref. No. ..

1. What was the state of the appendix at operation? .. ..

2. Was the diagnosis confirmed by histological examination?
YES/NO (delete inapplicable)

3. Was any other intra-abdominal lesion seen? .. .. ..

4. Under what circumstances was the operation done? .. ..

5. How long had symptoms been present at operation? .. ..

6. Was there a past history of similar abdominal pain? YES/NO
(delete inapplicable)

7. If yes to (6) please give details .. ..

8. How long after operation did the patient survive?.. .. ..

9. Was drainage used at operation? .. ..

10. Was a post-mortem examination carried out? .. ..

11. Any other details of interest? .. ..

(Please see accompanying notes where difficulty arises)

NOTES FOR GUIDANCE

Q.1: The classifications I have been using are: (a) normal, (b) mildly inflamed - this implies uncertainty of diagnosis on the basis of naked eye examination (c) acutely inflamed (d) gangrenous and (e) ruptured. If the patient did not have an operation, please answer "No operation."

Q.3: This refers to ovarian cysts, mesenteric adenitis, perforated peptic ulcers and the like.

Q.4: This refers to (a) as an emergency, (b) as a planned operation for recurrent mild pain (c) as an incidental at laparotomy for symptoms not apparently related to the appendix or (d) as a "cold" procedure some time after an appendix abscess.

Q.5: In terms of days, in cases of emergency operations only.

Q.7: Please say if the patient had ever been (a) seen by a general practitioner (b) referred to hospital as an outpatient (c) referred to hospital as an emergency or (d) admitted to hospital for observation.

It would also help if approximate dates were given where possible.

- -

Approximate number of appendicectomies carried out each year.

HOSPITAL:

YEAR	No. of operations.
1954	.. ..
1955	.. ..
1956	.. ..
1957	.. ..
1958	.. ..
1959	.. ..
1960	.. ..
1961	.. ..
1962	.. ..
1963	.. ..

All but eight of the hospitals supplied the information asked for.

4. As a preliminary to the study of the relationship between cancer and appendicectomy (page 164-73) the letter shown below was sent out to all hospitals who had made the original notification of cancer in any patient expected to be included in the follow-up study.

University of Glasgow,
Bacteriology Department,
Western Infirmary,
Glasgow, W.1.
February, 1965.

Dear Sir,

An article published recently in Cancer by McVay (Cancer, 1964, 17, 929-37) showed that patients dying from cancer of colon and other sites contained a significant excess of persons who had had previous appendicectomies, when compared with persons dying from vascular disease.

If true, this is a finding of great importance. It is however necessary to confirm these findings in a larger study than McVay has done, and if possible to obtain information from live patients as against using post-mortem data as done by McVay.

With the co-operation of Professor White and Dr. A. K. Bowman, we have obtained the names of the patients most recently registered in the Regional Board's Cancer Register as cases of cancer of breast, cervix uteri, colon and rectum. Where possible patients who have died have been excluded.

It is proposed to send the enclosed circular with

a reply-paid envelope to the 600 most recently registered patients with each of the above tumours.

We should like to stress two points in particular. (1) By using so recently notified patients we hope to avoid as far as is possible sending letters to deceased persons. (2) The circular contains nothing which might suggest to the patient the true nature of his ailment.

We hope that in view of the important implications of this possible relationship between cancer and appendicectomy we may have your permission to send the proposed circular to those patients from hospitals within your Group. We shall be glad to provide further information if necessary.

Yours faithfully,

(J. G. R. Howie, M.B., Ch.B. (Glasg.))

(W. R. Timperley, M.A., B.M. (Oxon.))

Medical Superintendents or Deputy,
Hospitals in the Western Regional Board.

No criticisms of the proposed study were made and the circular letter shown below was sent to 1656 patients as described in the text.

Western Infirmary,

Glasgow, W.1.

February, 1965.

Dear Sir or Madam,

We are trying to find out the number of people attending hospital who have had previous operations to have their appendix out, their tonsils out or their gall-bladder out.

To do this, we have taken a random selection of patients who have recently attended hospitals throughout the West of Scotland.

We would like you to show below which operations you have had, and send the form back to this hospital in the pre-paid envelope supplied.

Thank you for your help.

Yours sincerely,

J. G. R. Howie, M.B., Ch.B.

- -

Please put a tick in the box or boxes which apply to you and show the approximate year when the operation was done.

I have had my appendix out Year________

I have had my tonsils out Year________

I have had my gall-bladder out Year________

I have had none of these operations

What is your age now?________

were used as a control for this study, and they received the letter

Patients selected from a Glasgow general practitioner's list were used as a control for this study, and they received the letter shown below.

Western Infirmary,
Glasgow, W.1.
March, 1969.

Dear Sir or Madam,

We are trying to find out the number of people who have had previous operations to have their appendix out, their tonsils out or their gall-bladder out.

To do this, we have taken a selection of patients from lists of Doctors in the West of Glasgow.

We would like you to show below which operations you have had, and send the form back to this hospital in the pre-paid envelope supplied.

Thank you for your help.

Yours sincerely,

J. G. R. Howie, M.B., Ch.B.

- -

Please put a tick in the box or boxes which apply to you and show the approximate year when the operation was done.

I have had my appendix out year______

I have had my tonsils out year______

I have had my gall-bladder out year______

I have had none of these operations year______

What is your age now?______