DUODENAL ULCER

A REVIEW OF RECENT LITERATURE

AND

A COMPARISON OF THE RESULTS OF MEDICAL AND SURGICAL TREATMENT IN A SERIES OF 480 CASES.

BY

E. LESLIE FARQUHARSON,

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P R E F A C E.

In the more recent publications dealing with any branch of the wide subject, comprised under the heading of "Peptic Ulcer", the authors have in many cases prefaced their remarks with an apology for adding to the already over-burdened literature. If, in offering a thesis on "Duodenal Ulcer", the writer feels that he is exempt from the necessity of making such an apology, it is not because he can claim to have added anything to our knowledge of the subject, but rather from the very opposite reason. In this thesis is to be found little that is new, and perhaps even less that is original. But in a subject so controversial as this, where there is already in the literature a super-abundance of original investigations and original conclusions, it perhaps serves a more useful purpose to collect and comment upon the opinions of others, and by so doing, to attempt a general survey of the more controversial aspects of this disease, in the light of recent research.

In general, this thesis has been confined to the discussion of Duodenal Ulcer alone. In the sections on Aetiology and Pathogenesis, however, it has been found impossible to differenciate between Gastric and Duodenal Ulcer,/

Ulcer, and here the two conditions have been considered together.

It is becoming more generally recognised that the whole question of ulcer pathogenesis, is closely related to the existence of abnormal physiological conditions in the stomach. When a discussion of this "morbid physiology" was attempted, it became at once apparent that there was no uniformity of opinion regarding the normal physiology of gastric digestion, and a further chapter has been included to discuss the more recent views on this subject.

The writer wishes to acknowledge the guidance which he has derived from the most comprehensive work on Gastric and Duodenal Ulcer, published by Hurst and Stewart in 1929: this has been freely consulted and frequently quoted.

With regard to the investigation carried out by the writer into the after histories of duodenal ulcer patients, a brief word of explanation and apology is due. A follow up study of Medical and Surgical results in this condition is by no means a new venture, but as far as can be ascertained, it has not been done before in Edinburgh.

It has been pointed out that adjudication between Medicine and Surgery cannot fairly be made on a direct comparison of the results of treatment in each case, as many of the cases operated on have been specially selected for/

for surgery, and their inclusion in the surgical series confers an unfair advantage. The writer has attempted to make the comparison in a series of cases where this criticism cannot be applied. By excluding from the surgical series cases which may be said to have been specially selected for operation, the investigation has been confined to that type of ulcer which presents the greatest problem in treatment,- the chronic ulcer without stenosis.

This investigation has only been made possible by the kindness of members of the Honorary Staff of the Royal Infirmary of Edinburgh. The writer wishes to acknowledge his indebtedness to Mr W.J.Stuart, Professor D.P.D.Wilkie, and Mr J.M.Graham, for the privilege of being allowed to investigate the after histories of cases of duodenal ulcer operated on under their charge, and to Dr Edwin Matthew, and Dr Alexander Goodall, for similar privileges in regard to cases treated medically. To Dr Goodall, the writer is particularly grateful, for his helpful advice and criticism regarding the manner in which the investigation was carried out.

E. LESLIE FARQUHARSON.

35 Merchiston Crescent,
Edinburgh.

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I N D E X .

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HISTORY.

It is in the writings of Morgagni in 1760, that we find the first recognition of ulceration of the Duo--denum. In his "De sedibus et causis morborum", he re--lates how, in performing a post-mortem on a woman who died twenty four hours after the onset of severe abdominal pain, he discovered several large ulcers of the stomach, and a single smaller ulcer in the duodenum. Ulceration of the stomach alone had been described about two centur--ies previously by Marcellus Donatus, but it was not till the time of Morgagni that there was any mention of a simi--lar condition in the duodenum.

In 1772, George Baker while giving an address to the Royal College of Physicians of London, on Lead Poison--ing, remarked, apparently in parenthesis, that he "was consulted by a gentleman who had taken many medicines, with a view to dissolve the atra bilis, which was supposed to appear as well in what he vomited, as what he voided at stool. After death, this atra bilis was found to be no other than blood from an ulcer at the beginning of the duodenum."

Of late years a document has come to light, which was written by Jacopo Penada of Padua in 1793. In this paper the author gave an excellent clinical and post--mortem description of a perforated duodenal ulcer. The sudden onset of pain was well described, and in recording the /

the condition of the patient he remarked that "....he did not have the slightest inclination to vomit. His pulse was feeble and irregular but there was no trace of fever. The eyes were sunken in and the extremities were cold to the touch. The muscles of the abdomen were tense and he was doubled up." All possible treatment known to Medi--cine at that time including "immediate spiritual succour" was applied, but the patient died about twelve hours after the onset of the pain. At a post-mortem examination, there was found at the commencement of the duodenum "a very singular oblong hole, resembling an incision made with a knife. To the touch it was sensibly hard and some: :what indurated."

In 1793 Matthew Baillie, Physician to George III, in his "Morbid Anatomy of some of the most important parts of the Human Body" gave an excellent account of Gastric Ulcer, describing the smooth edges, punched out appearances and the tendency to form adhesions, the protective functions of which were explained. He does not appear to have recog: :nised ulceration of the duodenum per se, but described a case where "the length of the intestine was filled with a dark bloody fluid, and at the upper end there was a small patch of inflammation, which had passed through suppuration to ulceration." He also mentioned another case which show: ;ed a "scirrhous tumour and a cancerous ulceration" of the duodenum./

duodenum. This description would probably apply to a chronic ulcer with much induration and fibrosis.

In 1816 Benjamin Travers added some further ob--servations as regards post-mortem findings in cases of perforated duodenal ulcer. He observed the frequent pres--ence of bile in the peritoneal cavity, and recognised the value of exuded lymph in closing off small perforations. He also gave a very good description of the clinical picture of perforated ulcer "for the benefit" (as he said) "of those gentlemen whose painful lot it may be to witness cases of such a hopeless nature".

It is to Abercrombie, who at the beginning of last century conducted his pioneer researches on the diseases of the alimentary tract, that modern Medicine owes its greatest debt for putting the knowledge of gastro-intes--tinal disorders upon a sound foundation. Hitherto most workers appear to have contented themselves with describing pathological findings, with little or no attempt to corre--late these with clinical observations. It is thus from the pen of Abercrombie that we have the first clinical pic--ture of duodenal disease. Writing in 1828, he observed that "the leading peculiarity of disease of the duodenum is that food is taken with relish, and that the first stage of digestion is not impeded, but that the pain begins about the time that food is passing out of the stomach, or from two/

two to four hours after a meal". He added that "we should not be deceived, either by the pain having remarkable re--missions and the patient enjoying long intervals of per--fect health, or by the remarkable alleviation of symptoms taking place under a careful regulation of diet".

Abercrombie also drew attention to the danger of haemorrhage in duodenal ulcer, and recalled a case reported by Broussais three years previously, where a patient had died from this cause. At autopsy, the intestinal canal was found to be filled with blood, and the first part of the duodenum showed an ulcer which had formed a communica--tion with the hepatic artery.

It is to Abercrombie also that we owe the first principles of medical treatment in this condition, for he advised abstinence from excessive bodily exertions, a light diet with small meals, and while he did not actually stress high gastric acidity as an important factor in the pathology of ulcer, he recognised the relief obtained by such alkaline remedies as oxide of bismuth and lime water.

This great work of Abercrombie seems to have been to a great extent lost sight of during the remainder of the 19th century. Several statistical investigations of post--mortem findings were published, mostly by Continental writers, among whom may be mentioned Muller in 1860, and Willigk & Krauss in 1872. But with the exception of a monograph/

monograph by Bucquoy in 1887 which confirmed some of Abercrombie's observations, and paved the way for symptom--atic diagnosis of duodenal ulcer, the importance of this condition as a clinical entity was almost entirely missed. Most writers confined themselves to discussion of ulcera--tion of the stomach, which was then fairly well under--stood and widely recognised, and disregarded almost en--tirely the occurrence of a similar condition in the duoden--um. In consequence up to the end of last century, duoden--al ulcer was looked upon as a very rare occurrence, while gastric ulcer was regarded as being relatively common. We find duodenal ulcer very seldom mentioned in the text books of medicine of the 19th Century, and where it was recognised it was usually dismissed immediately as being a condition of rare occurrence. Niemeyer in his "Practice of Medicine" and von Ziemssen in his "Cyclopedia of Medicine" both drew attention to the work of Willigk and Krauss who in 1872, in an analysis of 1000 post-mortems at Prague, found 74 cases of duodenal ulcer. Of these the great majority were in the first part of the duodenum, and the proportion of males to females was 67 to 7. Willigk and Krauss also suggested that duodenal ulcer was quite as common as gastric ulcer. While Niemeyer and von Ziemssen both quoted these findings, they do not appear to have been in agreement with them, and this important work was lost sight of.

The/

The first real advance in our knowledge of the pathology of duodenal ulcer, especially as regards its frequency and anatomical position, resulted from the re--searches of Perry and Shaw, who, in 1893, published the statistics of over 17,000 post-mortems performed at Guy's Hospital up to that date. These investigations showed that ulceration of the duodenum was very much more common than had formerly been supposed, and was often found at autopsy in cases of death from other causes, where no symp--toms of the condition had been present during life. Perry and Shaw also confirmed the observations of Curling, who, some fifty years previously had noted the presence of acute ulceration of the duodenum in cases where death had been due to severe burning injuries, and this was estimated as occurr--ing in 6·2% of all such cases.

From the inauguration of abdominal surgery, in the last quarter of the nineteenth century, there began the great advance in what Moynihan has so aptly called the "Pathology of the Living". The surgery of peptic ulcer began with the adoption of the operation of Gastro-Enteros--tomy, and as this operation must, at the present time, still be regarded as the most generally applicable form of surgical treatment, it is of interest to record the history of its introduction.

On September 27th 1881, Anton Wölfler, later Pro--fessor of Surgery at Graz,while operating in Vienna on a case/

case of pyloric carcinoma, which he had intended to excise by the method of his master Billroth, found that radical operation was prohibited by fixation of the tumour and the presence of secondary deposits. He was about to close the abdomen, when Nicoladoni, his assistant, suggested that the obstruction might be relieved by making an opening between the stomach and small intestine. The suggested anastomosis was carried out, points on the anterior wall of the stomach and on the jejunum about 8 inches below the flexure being selected. The patient made a good recovery from the opera--tion, and enjoyed good health with complete relief of symp--toms for several months thereafter.

The success in this and in many similar cases was an event of great significance, and one of the most import--ant landmarks in the history of abdominal surgery. The operation was received with great enthusiasm, and was soon in wide use over the greater part of Europe. In the Jour--nals of the last decade or so of the century are to be found many descriptions of the operation and its results. It was first performed in England by Reeves of the London Hospital in 1885, in a case of pyloric carcinoma. Done in two stages, the operation had a fatal termination on the tenth day. Within a year, however, Barker reported the first successful case in a female patient suffering from a pyloric carcinoma who obtained complete relief of symptoms for nine months subsequently.

In/

In 1887, Fritzsche of Glarus published the notes of a case where gastro-enterostomy had been performed for "innocent stricture" of the pylorus. This appears to be the first case of operative treatment of duodenal ulcer recorded in the literature. Many others are reported soon after, in two of which, as Page relates, the patients were unfortunate enough to have the stomach anastomosed to a low coil of ileum in mistake for the upper part of the jejunum.

The first gastro-enterostomy in Edinburgh was per--formed by Mr. J. M. Cotterill in 1896 and is reported in the Transactions of the Medico-Chirurgical Society of that year. In 1899, Alexis Thomson, writing in the Edinburgh Medical Journal, discussed the late results of Gastro-Enter--ostomy for innocent stenosis of the pylorus, as shown in a series of 20 cases collected by Hartmann and Soupault, in the Rev. de Chir. Paris, and pointed to the value of the reflux of bile and alkaline jejunal contents, in diminishing the acidity of the gastric juices.

It is noteworthy that the surgeons of that time do not appear to have recognised the relation between "innocent stricture" of the pylorus and chronic duodenal ulcer. I can find no record in the literature of a defin--ite duodenal ulcer being recognised at operation, apart from cases where perforation had occurred.

It was not until the beginning of this century, when Moynihan published the results of his investigations on/

on duodenal ulcer, that any further material advance was made in our knowledge of the subject. Moynihan may very well be said to have started where Abercrombie had left off for he published for the first time a very complete account of the symptoms now known to be so characteristic of duoden--al ulcer.

In 1901, the first of a series of articles by this writer appeared in the Lancet, and offered a very full discussion of the pathology, symptomatology, and treatment of this condition. He emphasised the difference between acute and chronic ulcers, and pointed to the evidence of an infective origin of the former. He reviewed the findings of a large number of Continental workers, and showed that nine out of ten ulcers were found in the first part of the duodenum. He also collected statistics showing that the condition was four times more common in males than in females He commented on fifteen cases of melaena neonatorum, collect--ed by Oppenheimer, which were proved to be due to duodenal ulcer, and recorded a case where a duodenal ulcer was found in a woman of 94.

Discussing the symptomatology of duodenal ulcer, Moynihan referred to pain, haematemesis, and melaena as the three cardinal symptoms of the condition. To his descrip--tion of the character and time of onset of the pain, little can be added in the light of present day knowledge. He was the/

the first to propound the view that the typical pain of duodenal ulcer was caused by the food passing over the diseased area. The characteristic "hunger pain" was also described, and spasm of the pylorus was suggested as being the main factor in its causation. He regarded haematemesis as being a symptom rather more important than would be admitted at the present day, but laid great stress on the importance of melaena, and remarked that the possible presence of this was usually overlooked in the clinical investigations of the time. He discussed fully the complications of duodenal ulcer, and to the comprehensive list given there is little to add today. He was the first worker to dissociate himself from the view, then commonly held, especially by Continental workers, that cancer was a common sequela to duodenal ulcer.

An account was given of six cases of chronic duodenal ulcer, without definite pyloric obstruction, which had been treated by gastro-enterostomy. The immediate results had been uniformly good, and Moynihan advised this operation in chronic cases, where the pain was "persistent and disabling", pointing out the benefit that was obtained from rest to the ulcerated area, and neutralisation of the acid gastric juice.

A most interesting part of this first paper of Moynihan's was an analysis of all the cases of perforated duodenal/

duodenal ulcer, 49 in number, which had been operated on up to that date. The first successful operation had been performed by Dean in 1894, and seven other recoveries were recorded in this series, giving a mortality of 74%. This cannot have been regarded as a promising beginning for surgery, but when we work out that the average time that was allowed to elapse before operation was performed was 20·1 hours, it is surprising that the number of recoveries recorded is so large. Moynihan at this time does not appear to have recognised the value of immediate operation in cases of perforation, and indeed this is not surprising, for we are perhaps apt to forget that an abdominal opera-tion in these days was not the relatively safe procedure of today, and that few surgeons felt justified in advising operation until medical treatment had been judged to have been obviously ineffective. In addition, investigations of the results up to that date gave no indication of the value of early operation, for the average number of hours allowed to elapse between perforation and operation was, in the cases that recovered, only one decimal point less than in the cases which had a fatal issue. Of the cases that recovered, operation was performed 30, 25, 30, 15, 12, 10, 10, and 28 hours after perforation had occurred,- making an average of 20 hours.

In this paper also, Moynihan described the mechan-ism of perforation, and explained how, by reason of the flow/

flow of irritant or infective fluid down the right para--colic gutter, such cases are liable to be mistaken for acute appendicitis.

The great stimulus to abdominal surgery, given by Moynihan's work resulted in far reaching advances in our knowledge of duodenal disease. The publications of the first ten years of the century were almost entirely of a surgical nature. Representing the first fruits of invest--igation on the living subject, the value of the material produced can hardly be over estimated. Associated with Moynihan in this work we must couple the names of C.H. Mayo and Robson. The last named, writing in the Lancet in 1903, summarised an address which he had given to the Oxford Med--ical Society on the subject of gastro-enterostomy. Up to the end of the 19th century this operation had usually been performed upon moribund patients, who as a last resort had been handed over to the surgeon, with the result that the mortality was appalling. In a Hunterian lecture to the Royal College of Surgeons of England three years previously, he had reported on 1879 cases of gastro-enterostomy, which showed a mortality of 36·4%. With the greater reliance placed on surgery and the improvement in operative technique, the position was now very different, and he was able to point to a series of over 1000 cases with a mortality of less than 5%.

Further/

Further publications by these and other surgeons showed an ever decreasing mortality in surgical treatment, and served to put the operation of gastro-enterostomy on a sound foundation in the treatment of duodenal ulcer.

With the establishment of duodenal ulcer as a relatively common condition, the principles of medical treatment came to be laid down on definite lines. The essential similarity between it and gastric ulcer was recog--nised and the term "peptic ulcer" came to be employed as including the two conditions. The es s entials of treat--ment, i.e., rest and alkalies, had been suggested by Aber--crombie about eighty years previously, and further thera--peutic measures had gradually been established. The"rest cure" advocated by Cruveilhier came into wide use, and was warmly advocated by physicians at the beginning of this century. The benefits of a milk diet, and of rectal feed--ing in the acute stage of the disease were well known. The subcutaneous administration of olive oil was regarded as an invaluable remedy in keeping up the calorimetric level. Alkaline medication was by now fully understood, and the drugs recommended are those in use at the present time. The exhibition of silver nitrate was advised as a useful measure in the case of patients who could not afford to undergo the rest treatment. Various systems of diet had been introduced, notably that suggested in 1902 by the Congress for Internal Medicine, Lenhartz, the so-called "Lenhartz" diet.

We/

We recognise that there existed then, as today, the same difference of opinion among physicians, as to the benefit to be obtained from surgical treatment. Dresch--feld, writing in the System of Medicine compiled by Allbutt and Rolleston, one of the standard works of that time, claimed excellent results for medical treatment, and gave perforation as the only indication for surgical interfer--ence. Many physicians, on the other hand, advised that if there was no improvement after a reasonable trial of medical treatment, the patient should be handed over to the surgeon for gastro-enterostomy.

In the writer's opinion, it would be of little interest to carry this historical discussion further, for it was about this time, i.e., shortly after the beginning of the century, that we find Duodenal Ulcer recognised as one of the commonest diseases of the community. In the treatment of the condition, Medicine and Surgery are both on a sound foundation, and the great controversy has begun. The advance in the two Sister Sciences in the treatment of duodenal ulcer has not been very material during the last twenty years, although Radiology and Biochemistry have made matters very much easier for the diagnostician. How far that controversy has been settled, and to what extent we can claim better results than our predecessors, it is the purpose of this Thesis to show.

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I N C I D E N C E.

General Incidence.

Wilkie has pointed out that when we compare the statistical tables of the diseases treated in our large hospitals today, with those of twenty years ago, perhaps the most striking example of increased incidence in a particular disease occurs in the case of duodenal ulcer. In the Royal Infirmary of Edinburgh in 1906, 24 cases of duodenal ulcer were treated, 18 by medical and 6 by surgical means. During the same year 22 cases of perforated duodenal ulcer were operated on. During 1926, on the other hand 336 cases were treated, 73 in the medical and 163 in the surgical wards, and 102 cases of perforation came to operation. When it is noted that the number of perforation has more than quadrup--led, and that it does not include the numerous cases treated in the smaller hospitals in the area now served by the Infirmary, it is obvious that the greater number of cases treated today is not merely due to improvement in diagnosis, but that the disease is markedly on the increase.

It is difficult to give any figure for the general incidence of duodenal ulcer, but the observations of many physicians and surgeons indicate that it may be found in anything up to 10% of all cases admitted to both medical and surgical wards.

Post mortem statistics confirm the great frequency of duodenal ulcer in present day pathology. In an analysis of/

of 3058 autopsies performed up to 1921, Hart, Musa, and Holzweissig, (quoted by Hurst & Stewart) found ulceration, or scarring due to old ulceration, in the duodenum in 5·3% of cases. In a series of 4000 post mortems at Leeds, Stewart and his co-workers found evidence of duodenal ulceration in 6·81% of cases. In a further ·53% of cases a combined gastric and duodenal ulcer was found.

Stewart points out that thus over 7% of all individuals suffer at some time in their lives from duodenal ulcer. To the writer this statement does not seem to be justified, as post mortem findings cannot be said to give a true indication of the pathology of the community as a whole. Very few of the comparitively large number of people who enjoy a healthy life and live to a ripe old age, come to autopsy at hospital, and statistics compiled from this source should be taken as referring in the main to diseased individuals, or at any rate to individuals who have required hospital treatment,- a small proportion of the population. To the writer, it seems that such statis--tics regarding the frequency of a particular disease, should refer to its relative frequency as compared with other diseases, rather than to its general incidence among the community as a whole.

<u>Sex Incidence, and comparitive frequency of Gastric and Duodenal Ulcers</u>.

Within/

Within the last twenty years, our conception of the relative incidence of gastric and duodenal ulcer has undergone a complete reversion. At the beginning of this century, co-existant with the prevalence of chlorosis, and apparently in some way associated with this disease, we find haematemesis noted as a very common symptom, and one causing much unnecessary anxiety and distress among girls and young women. In these days every case of haematemesis was regarded as being due to gastric ulcer, and consequently in the older text books we find gastric ulcer described as a very common disease, and one occurring mainly in "young chlorotic females".

To Hale White belongs the credit of being the first to correct this view. Writing in the Lancet in 1906 he pointed out that gastric ulcer, as diagnosed, appeared to be much more fatal in males than in females. He quest--ioned the truth of this finding, and suggested that many cases of supposed gastric ulcer in the female were wrongly diagnosed, as in several cases of gastric haemorrhage which had been reported, no evidence of ulceration had been found at operation or post-mortem. Hale White gave the name of "Gastrostaxis" to this phenomenon, and although the explana--tions suggested for its causation were far from satisfact--ory, there was ample confirmation of its occurrence.

In spite of these revelations, gastric ulcer still continued/

continued to be regarded as the commoner condition, until, as Osler remarks, "surgical statistics sent the medical figures to the scrap heap".

Although the London Hospital statistics of 1375 operations up to 1925, showed an almost equal proportion of gastric and duodenal ulcers, most surgeons favour duodenal ulcer as being very much more common. In 5733 operations at the Mayo Clinic up to 1920, the proportion of duodenal to gastric ulcers was 4 to 1.

Post-mortem statistics are presented with a great wealth of detail in the work of Hurst and Stewart, who in 1928 published an analysis of 13000 autopsies, where over 600 cases of peptic ulcer were investigated. The sex incidence was very carefully worked out in acute & chronic gastric, and in acute & chronic duodenal ulcer,- four groups in all. There was a slightly greater incidence in the female in the case of chronic gastric ulcer, but in the other three groups the male cases predominated to a marked extent. The results may be shown thus:-

	Males	Females	Ratio.	M : F
Acute G. U.	60%	40%	1·5	: 1
Chronic G. U.	43%	57%	·8	: 1
Acute D. U.	72%	28%	2·6	: 1
Chronic D. U.	78%	22%	3·5	: 1

It would seem justifiable to cast some doubt on the/

the value of post-mortem findings in regard to the fre--quency of acute ulcer. Very few cases of peptic ulcer seek hospital treatment in the acute stage of the condition, except perhaps in the case of acute haemorrhage or perfora--tion, and fewer still will come to autopsy.

Figures published by Wilkie in 1927 caused us to amend very considerably our views of the sex incidence of peptic ulcer. In an analysis of 413 cases of peptic ulcer coming to operation, Wilkie pointed out that the incidence of duodenal ulcer in females is much greater than has been supposed, (26% in his series). It is maintained that the condition is much more difficult of diagnosis in women, and is commonly overlooked. The pain is less severe and less typical, it may be, because the female is more tolerant, or less observant. On the other hand it is possible that the pylorus does not respond to irritation, by spasmodic con--traction to the same extent as in the male, or it may be that the habit of taking food between meals, common to most women, prevents the occurrence of the typical "hunger pain" to which the male, by reason of his longer fasts, is more liable.

It is interesting to compare Wilkie's series with that of Moynihan, published in 1920.

	Moynihan			Wilkie		
	D. U.	G. U.		D. U.	G. U.	G.U.+D.U.
Males	435	82	Males	234	22	33
Females	95	82	Females	76	30	18
Total	531	164	Total	310	52	51

(1)/

(1) Ratio of Duodenal Ulcers to Gastric Ulcers.

Moynihan - 3·2 : 1. Wilkie - 6 : 1.

Do. in the Male.

Moynihan - 5·3 : 1. Wilkie - 10·6 : 1.

Do. in the Female.

Moynihan - 1·2 : 1. Wilkie - 2·8 : 1.

(2) Ratio of Males to Females in Duodenal Ulcer.

Moynihan - 4·5 : 1. Wilkie - 3 : 1.

(3) Ratio of Males to Females in Gastric Ulcer.

Moynihan - 1 : 1. Wilkie - ·7 : 1.

In Wilkie's series combined gastric and duodenal ulceration was present in 14% of cases.

Further figures concerning the sex incidence of gastric and duodenal ulcers were published by Luff about two years ago, and represented the results of a collective investigation carried out by the British Medical Association, into the after histories of patients suffering from such conditions. In the entire series 995 duodenal and 538 gastric cases were investigated.

In the cases of gastric ulcer 66·2% were males, and 33·8%, females, - giving a ratio of 2 : 1. The figures for duodenal ulcer were - males, 83·6%, - females, 16·4%, ratio, 5 : 1.

It is interesting to note that,while the statis--tics of this collective investigation, tend to support the figures/

figures of Moynihan, rather than those of Wilkie, the observations of the latter have been confirmed in almost extraordinary detail by the work of Young of Glasgow. The two great Scottish Schools appear to be in entire agreement, both as regards the disproportion between gastric and duodenal ulcers, and the relative incidence of the latter among females. It appears that the figures in these two respects are higher for Scotland than for other countries.

Since writing the above, some further figures have become available from a paper recently delivered by Goodall to the Medico-Chirurgical Society of Edinburgh. Of 200 cases of peptic ulcer, 157 occurred in the duodenum and 43 in the stomach. Of the duodenal ulcers, 141 were in males, and 16, in females. The corresponding figures for gastric ulcer were 26 and 17 respectively. The ratios work out as follows:-

(1)	Ratio of D. U. to G. U.	3·7 : 1
	Do. in the Male.	5·3 : 1
	Do. in the Female.	·9 : 1
(2)	Ratio of Males to Females in D.U. .	8·8 : 1
(3)	Ratio of Males to Females in G.U. .	1·5 : 1

Age Incidence.

No age is immune from duodenal ulcer. We find two cases reported by Strauss where duodenal ulcer was demonstrated in the foetus, and at the other extreme several cases/

cases have been recorded where the condition was present in patients over ninety years of age.

Among infants and children duodenal ulcer is rare, although cases are periodically recorded. Thus Moynihan relates a case where a five day old child developed symptoms of acute duodenal ulcer with severe haemorrhage, death occurring two days later from perforation. Several cases are recorded where duodenal ulceration was found to be present at autopsy on marasmic infants. The chronic ulcer is even less common, although a few cases have been published, notably two by Theile and Paus (quoted by Hurst & Stewart) where in a girl of 2 and in a boy of 9 definite pyloric stenosis, resulting from a chronic duodenal ulcer, was sat--isfactorily relieved by surgical measures.

Post-mortem statistics indicate a very low incid--ence in childhood. In 370 autopsies at the Great Ormand Street Hospital, Paterson found two cases of peptic ulcer, and in 350 autopsies at Leeds, Hurst found only one case. In a further series of 861 cases, the same writer noted the occurrence of only two cases of duodenal ulcer in children under the age of ten.

Surgical figures are even lower, for in 6664 cases of duodenal ulcer treated at the Mayo Clinic, only one was under the age of fourteen.

Hurst believes that it is not rare on going into the histories of patients suffering from duodenal ulcer, to find/

find that the symptoms have dated from childhood or early adolescent life. The proportion of such cases does not, however, appear to be very high, for in a series of 4000 cases Proctor could only point to 26 instances where such a history was obtained, i.e., ·6%. Moynihan records the case of a medical man aged 30, who had had typical symptoms of duodenal ulcer since the age of ten.

Hurst observes that in 157 new cases at his Clinic, the average duration of symptoms was 15 years in the case of gastric ulcer, and 10 years in the case of duodenal ulcer. In the cases of duodenal ulcer investigated by the writer, the average duration of symptoms prior to medical treatment was 6½ years, and prior to surgical treatment, 9 years.

Very few statistics are available in regard to the average age of patients suffering from duodenal ulcer, at the time of hospitalisation. It should be noted however that the women are usually older than the men. In the writer's investigation the average age for female patients was 42, and for male patients, 37. In a study of 279 cases, Miller and Prendergast of Pensylvania found that 50% of cases of duodenal ulcer were over 40, and that 30% occurred in each of the 3rd and 4th decades. The age incidence for gastric ulcer was higher, 70% of the cases being over 40. Further evidence on this question has been added by the researches of Blackford and Dwyer, who, in 332 cases of ulcer found that 66% of duodenal cases and 33% of gastric cases/

cases were under the age of 45.

Family History.

This is a point upon which investigation is very difficult, especially in hospital practice. Patients of this class can usually give only very meagre particulars regarding the health of their relatives, and what information is available is usually unsatisfactory in respect of detail. Several writers have adduced evidence to show that peptic ulcer has a definite tendency to run in families, and Hurst draws a particularly convincing picture in recording the medical histories of six families, where nearly every member had suffered at one time from peptic ulcer. He further states that he himself has never seen a case where both gastric and duodenal ulcer were proved to have occurred in the same family, and finds in this, support for his belief that the two conditions depend upon totally different diatheses. In the few cases that have been reported, where both types of ulcer have definitely been demonstrated in the same family, Hurst suggests that there has probably been a mixed inheritance of diathesis.

Occupation.

There is today no confirmation of the belief entertained by earlier writers, that peptic ulcer occurs with special frequency among cooks and bootmakers. In the series/

series investigated by the writer, by far the greatest pro-
-portion of cases occurred in coal miners, and I think that this is probably true of all cases of duodenal ulcers treated in the Royal Infirmary of Edinburgh.

Published statistics from other sources differ. Thus Luff in an analysis of the cases investigated by the British Medical Association found the greatest incidence among skilled artisans (28%). Miners (only 4%) were placed ninth on the list.

Statistics of occupational incidence are liable to be misleading, as they are very rarely standardised in regard to the industrial distribution of the population. Thus it is natural that Edinburgh, surrounded as it is by such rich coal bearing areas as the Lothians, Stirling, and Fife, should find a high incidence of duodenal ulcer among miners, as these certainly constitute the largest occupational class of male admissions to the Royal Infirmary. On the other hand, the matter cannot be dismissed thus lightly, for 19% of the male cases of duodenal ulcer in this series were miners, while in a series of 200 male cases of appendicitis, used as a control, the corresponding figure was only 9%. This would indicate that, even allowing for the occupational distribution of the population, duodenal ulcer has a relat-
-ively high incidence among miners. And indeed the trying conditions, under which most pit workers earn their liveli-
-hood, particularly as regards the unhealthy nature of the work,/

work, the lack of sunshine and fresh air, and the absence in most cases of a mid-day meal, would seem to render them specially liable to such a complaint.

Lastly it has often been suggested that duodenal ulcer is very common among members of the medical profession. No statistics are available in respect of this, but the well known aetiological factors of "overwork, mental worry, lack of sleep, and irregular meals" appear to be particularly suggestive.

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Stomach.

Motility.

It has long been recognised that the musculature of the stomach, like that of the heart, possesses the proper--ty of inherent rythmic contraction. That the movements of the stomach are influenced to a marked extent, by the sympa--thetic nervous system is equally well known, but it has been proved by innumerable experiments, that the stimulus to contraction, as in the case of the heart, is essentially of myogenic origin. Thus it has been shown that an excised stomach, which has been severed from its entire nerve supply, will, under suitable conditions, continue to show rythmic peristaltic contractions. The stomach itself derives its motor nerve supply from the para-sympathetic system through the vagus, and stimulation of this nerve will cause an in--crease in both frequency and degree of the contractions. Inhibitory fibres are contained in the sympathetic supply, and accordingly stimulation of the sphlanchnic nerves will cause diminution or cessation of movement. The nervous control of the pylorus is a matter of considerable contro--versy and will be discussed later.

The normal stomach is regarded as being continually in a state of tonic contraction, whether during the active stage of gastric digestion immediately following a meal, or during the period of quiescence in the fasting intervals. In the empty stomach it is generally believed that no peristalsis/

peristalsis occurs, and that it is contracted upon itself in such a way that except for a small area at the upper extremity of the fundus occupied by the residual bubble of gas, it forms a fairly narrow muscular tube, the walls of which are in contact with each other. Towards the end of a fasting period, however, and earlier in individuals with a hyper-sensitive gastric mechanism, there appear the typical "hunger contractions". These are normal peristaltic movements, beginning at the fundus and passing towards the pylorus, but unlike the true peristaltic waves which occur during gastric digestion, they show no tendency to become more forceful in the pyloric part. They also tend to occur in groups, the contractions increasing in degree up to an acme, and then rapidly declining.

When food enters the stomach, its weight is suffic--ient to overcome the tonic resistance of the wall; as the stomach fills the tonic contraction gradually relaxes, allow--ing it to adapt itself in size and shape to the bulk of its contents. As the two orifices of the stomach are relative--ly fixed, and as the lesser curvature is firmly supported by the gastro-hepatic omentum, dilatation takes place mainly in a downward direction, and at the expense of the greater curvature. With the advent of food in the stomach active movement begins immediately. Two definite types of con--traction are recognised. The first and most important of these/

these is true peristalsis, which takes the form of waves of contraction passing from the fundic to the pyloric end. Beginning near the fundus the contractions are there almost imperceptible, but become much more forceful as they reach the pyloric vestibule and approach the pylorus itself. Their greatest effect is seen on the greater curvature, where the constricting ring may be so great as almost com--pletely to exclude the lumen of the stomach. These waves appear with remarkable regularity, as a rule every fifteen to twenty-five seconds, but they may occur with much greater frequency, two or more waves being present in the stomach at the same time.

The peristaltic contractions of the stomach have obviously a dual function to perform; firstly to churn up the contents of the pyloric antrum in such a way that the food is thoroughly macerated and becomes intimately mixed with the gastric juice, and secondly to propel the contents through the pylorus into the duodenum. In this first func--tion they are aided by the second type of muscular contrac--tions noted in the stomach,- the so-called "segmental" con--tractions. These are localised rings of contracture which appear at intervals, mainly in the pyloric vestibule. They have apparently no relationship to the peristaltic waves, but they undoubtedly assist the latter to a lesser degree in the breaking up of the food in the vestibule. So forceful and/

and so complete is the maceration of the food by this pro--cess that the term "pyloric mill" has been suggested by Hurst. The second function of the peristaltic movements, - that of evacuation, is a much more complicated mechanism, and before discussing it, it is necessary to consider the behaviour of the pyloric sphincter, on which it so greatly depends.

It has been shown that the stomach is traversed by a series of peristaltic waves throughout the whole period of gastric digestion. As each of these waves tends to drive the food out of the stomach into the duodenum, it is obvious that were it not for the controlling influence of the pyloric sphincter, the stomach contents would be immedi--ately evacuated. An enormous amount of experimental work has been carried out in an effort to determine the nature of the pyloric control over evacuation, and the factors by which this control is influenced. The numerous explanations suggested prove that no one of them is entirely satisfactory.

In 1907, Cannon first advanced the ingenious theory of the "acid control" of the pylorus. He considered that the great bulk of the food as it entered the stomach was alkaline in reaction, on account of its admixture with sali--va during the process of mastication. As gastric digestion proceeds, the stomach contents become increasingly acid, and it was believed that the chemical stimulus of acid content on/

on the gastric side of the sphincter caused relaxation of this muscle and allowed evacuation. It was further suggest--ed that relaxation was prohibited by the presence of acid in the duodenum, and that consequently no more acid chyme left the stomach until that already present in the duodenum had passed on, or had been neutralised. This theory has been completely disproved by numerous workers who have shown experimentally that the acidity of the gastric contents has little or no effect on the sphincter; thus plain water, deci-normal acid, and deci-normal alkaline solutions are evacuated from the stomach with equal rapidity. (Some ob--servations on this point in a very recent publication by Earl Thomas are discussed later.)

A survey of the literature would indicate that there are two definite schools of thought in regard to the mechanism of pyloric control.

On the one hand it is believed that the pylorus is a true "sphincter". That is to say that, like other sphinc--ters elsewhere in the body, it has a reciprocal nerve supply with the organ whose outlet it guards. Thus when a perist--altic wave of contraction reaches the pylorus, the sphincter relaxes as part of the same reflex act. On the other hand, some very recent researches would suggest that the pylorus does not constitute a true sphincter at all, but that it is more in the nature of a filtering valve, contraction of which occurs synchronously with, and through the same inner--vation as, that of the stomach.

The/

The first theory that the pylorus is a true sphincter has gained some support from a recent publica--tion by Deaver and Burden. These workers refute the view commonly held by anatomists that the pylorus is merely a local aggregation of the circular muscle fibres of the stomach wall. They claim to have shown by dissection that the pylorus is an entirely separate muscle, which has little or no connection with the general musculature of the stomach, and which can be readily peeled off from the underlying sub--mucosa. Deaver and Burden also confirm the observations of several earlier workers, notably Horton of the Mayo Clinic, who described dilator fibres in the pyloric ring. These are formed from the longitudinal muscle fibres of the stomach, 50% of which, on reaching the pylorus, dip deeply down into the ring of circular fibres, in many cases extending as far as the sub-mucosa. Contraction of these fibres would appar--ently cause dilatation of the sphincter. It is pointed out that the pylorus, having both constrictor and dilator fibres, should be regarded as a true sphincter. If this is accepted, a double innervation of the pylorus must also be conceded. As the dilator fibres are a direct continua--tion of the musculature of the stomach, it would seem unden--iable that these must be innervated by para-sympathetic fibres through the vagus, which has been defintely proved to be the motor nerve of the stomach. Also, if we accept the view that the constrictor fibres constitute an entirely separate/

separate muscle, it is in logical sequence to assume that this receives a reciprocal innervation from the splanchnic nerves.

It must be admitted, however, that this theory, attractive though it appears, has many weak points. Exper-imental work lends little to support it. Stimulation of the vagus has always caused contraction of the pylorus as well as of the stomach as a whole, while the opposite effect is obtained, again in both cases from splanchnic stimulation. In addi-tion it has not been possible, by any form of stimulation to bring about relaxation of the sphincter synchronously with contraction of the stomach. Furthermore if we accept the view that the pylorus constitutes a true sphincter, there are many points which require explanation. Why does not this "sphincter" relax at the approach of every peristal-tic wave? There must obviously be certain factors which inhibit relaxation until gastric digestion is satisfactorily accomplished. It has been suggested that relaxation is inhibited by the presence in the pyloric vestibule of any-thing which might injure the delicate mucous membrane of the duodenum, e.g., solid food particles, substances too hot or too cold, etc. But this is only a suggestion, and again it is not supported by experimental work. (vide infra.) It has been abundantly proved radiologically that such type of content is delayed in the stomach, but there is no reason to suppose that in normal cases this is due to contraction, or inhibition of relaxation, of the sphincter.

Much/

Much more attractive is the theory that the pylor--us plays the part merely of a filtering valve, and that normally it contracts as one unit with the rest of the stomach. In a recent publication, Earl Thomas of Philadel--phia records some very helpful experimental work, and offers a suggestion whereby, under this theory, the mechanism of evacuation of the stomach can be satisfactorily explained.

Thomas draws a sharp distinction between mere opening of the pyloric canal, and actual relaxation of the sphincter. He points out that it is not necessary for actual relaxation to occur, in order to permit of the passage of food through the canal. Opening of the canal will occur without actual muscular relaxation, when the intra-gastric pressure occasioned by the peristalsis is sufficient to over--come the resistance offered by the sphincter. By the introduction of balloons into the stomach and pyloric canal of experimental animals, Thomas has been able to compare the tonicity of these two regions under varying conditions. In the empty stomach the sphincter is relaxed and of low tonus. As soon as food enters the stomach a marked tonic contraction of the sphincter occurs, and thereafter during the whole period of gastric digestion, it never relaxes to the low tone level characteristic of the empty stomach. High tonus of the sphincter is maintained throughout the process of evacua--tion, and indeed it is during this stage that the highest tone/

tone level is reached. Rythmic contractions and relaxa--tions, at a high tone level occur, but these have been proved to be synchronous with, rather than reciprocal to, gastric peristalsis.

The experimental results of innumerable workers tend to support this theory. Vagal stimulation will always cause contraction of both stomach and pylorus, and a similar result is obtained from most other forms of excitation. In fact all the evidence seems to show that the stomach and pylorus act together as one functional unit, at any rate as far as muscular contraction is concerned.

To the writer it appears much more satisfactory to think of the pylorus as a filtering valve regulated almost entirely by intra-gastric pressure, than to regard it as a true sphincter which tends to relax at the approach of each peristaltic wave, but is prevented from doing so until digestion is accomplished, by some very complex and imper--fectly understood form of stimulus.

Radiological observations give invaluable assist--ance in the choice of theory. It has been shown by fluoroscopic examination that as soon as food enters the stomach, some of the fluid portion immediately passes through the pylorus into the duodenum. Thereafter small squirts of macerated and liquified food are expelled at irregular inter--vals until evacuation is complete. In the writer's opinion such a type of evacuation is quite incompatible with true relaxation/

relaxation of the pylorus, but is much more characteristic of a control mechanism such as would be afforded by a filtering valve, the resistance of which is intermittently overcome by inside pressure.

To summarise then this conception of the physiology of the pylorus, one would say that it acts as one functional unit with the rest of the stomach. It has the same innerva--tion, and exhibits rythmic contractions, synchronous with those of the stomach. During gastric digestion, when con--traction of the stomach occurs, both as a general increase in tone, and in the form of peristaltic waves, the circular pyloric muscle contracts also. By this contraction the pylorus fulfils a double function: it not only prevents premature escape of gastric contents, but it also provides the resistance to evacuation, which is necessary to enable the gastric musculature to perform its chief function of maceration of the food. Throughout the whole period of gastric digestion, true relaxation of the pylorus never occurs, and evacuation only takes place when the peristaltic contractions have caused a rise in intra-gastric pressure, sufficient to overcome the tonic resistance of the circular muscle. The food thus escapes in small spurts at irregular intervals; the valve like action of the pylorus allows the fluid portion to pass first, while the more solid particles are retained to the last. Confirmation of this theory is obtained/

obtained from animal experiments, and from radiological observations in healthy individuals.

Secretion.

The secreting glands of the stomach are divided into two main groups, the histology of which does not con--cern us here. The glands covering the fundus and main part of the body of the stomach, the so-called "fundic" glands, bear the entire responsibility for the secretion of pepsino--gen and hydrochloric acid. The glands of the pyloric vestibule, the "pyloric" glands, produce only an alkaline mucoid secretion, and are continuous with Brunner's glands of the duodenum. The more exact localisation of these glands will be discussed later under the Peptic Genesis of ulcer.

Of much greater interest to us in our discussion of the pathology of ulcer, is the mechanism of control of gastric secretion, for as will be shown later it is the quantity rather than the quality of the gastric juice that plays the most important part in ulcer pathology.

There are normally two main factors concerned in controlling the secretion of gastric juice.

The "Psychic" stimulus results from the expectation, sight, smell, or taste of food, and is conveyed to the gastric glands by way of the vagus nerve. Thus stimulation of the vagus causes greatly increased secretion, while section of the nerve, or paralysis of its endings by the administration of/

of atropine, has an inhibitory effect. That this psychic stimulus is quite independent of the presence of food in the stomach has been proved by innumerable workers, on animals with oesophageal fistulae, where an abundant flow of juice can be evoked by "sham feeding".

The "Chemical stimulus". A further secretion of gastric juice is brought about by the presence of food in the stomach. Certain foods, i.e., meat extracts, etc., are definite secretagogues, causing by chemical stimulation of the mucous membrane a flow of juice from the secreting glands. Other secretagogues are believed to be derived from the pro--ducts of digestion. Edkins has shown that extracts of pyloric mucous membrane, when injected into the circulation, cause a marked secretion of gastric juice, and it has been suggested that secretagogues derived from the food act upon the pyloric mucous membrane, and form a hormone, which after absorption into the blood stream, stimulates the fundic glands to secretion. To this hormone, the name "gastrin" or "gastro-secretin" has been given. A further flow of gastric juice is said to occur after gastric digestion is completed and the stomach is empty. This is probably due to the action of hormones produced in the area of intestinal digestion.

A third stimulus to secretion results from mechan--ical factors. Solid particles of food coming in contact with/

with the stomach wall, or distension of the organ, especi--ally in the region of the pyloric vestibule, will cause increased secretion. It is however generally agreed that this mechanical factor is of little practical importance and it will not be discussed further.

Opinions are divided in regard to the relative importance of the psychic and chemical stimuli in the pro--duction of gastric juice. Hurst believes that the main flow of juice results from the chemical stimulus, but most physiologists maintain that the psychic stimulus is the essential factor. Only one experiment need be quoted in this connection. "Two dogs were taken and a weighed amount of protein introduced into the stomach of each without their knowledge: one was then "sham fed" on meat, and one and a half hours later the amount of protein digested by this dog was five times greater than that which was digested by the other". (Halliburton). Surely no experiment could be more conclusive.

Duodenum.

Radiological observations have added very greatly to our knowledge of the normal functioning of the duodenum. It has been pointed out by Hurst and others that the first or horizontal part bears a much closer resemblance to the adjacent part of the stomach than to the rest of the duodenum. The/

The anatomical similarity is at once apparent when one com-
-pares the relatively thin mucous membrane with its alkaline secreting glands, found on both sides of the pylorus, with the mucosa of the rest of the duodenum and small intestine. From the physiological viewpoint, radiological observations have shown that this similarity is even more striking. For this first or horizontal part of the duodenum the term "duodenal cap" or perhaps better "duodenal bulb" has been suggested.

The motility of the duodenal bulb is very feeble, and plays little or no part in the propulsion of food onwards to the rest of the small intestine. As soon as food enters the stomach, the more fluid content immediately passes through the pylorus, and, when the individual is in the up-
-right position, collects in the duodenal bulb, which is more or less constantly filled through out the whole period of gastric digestion. The shadow of the duodenal bulb, as shown by the opaque meal is roughly triangular in outline, the base being at the pylorus and the apex at the junction with the descending part of the duodenum. When examined by the fluorescent screen, peristaltic movements of the bulb are sometimes seen, but these are very slight in degree, and evacuation of this segment occurs mainly by a process of overflow, when fresh gastric contents are forced into it. Peristalsis of the second and third parts of the duodenum, on/

on the other hand, is much more rapid and forceful, and resembles that of the rest of the small intestine. Thus when the fluid contents of the bulb overflow into the descending duodenum, they are rapidly carried away, and a satisfactory shadow of this part can rarely be obtained in a radiogram. Reversed peristalsis, as first described by Boldyreff, is also occasionally noted in the duodenal bulb, but it is questionable whether this ever occurs in perfectly normal individuals. It will be discussed later under the section on Pathological Physiology.

It may be said therefore that the duodenal bulb fulfils the function of an additional reservoir for the products of gastric digestion, before they pass to the distal duodenum, where they are submitted to further enzyme action. As Hurst puts it, the bulb is in the nature of an annexe to the stomach, with similar functions, and is subject, like it, to peptic ulceration.

Sensory Functions of Stomach and Duodenum.

The stomach and duodenum, like the greater part of the alimentary tract, are quite insensitive to tactile stimuli, and to heat and cold. It is therefore impossible to evoke painful sensations by any form of trauma to the stomach wall. In 1911, Hurst pointed out that Hydrochloric acid, in strengths considerably greater than that found in even extreme/

extreme cases of hyperchlorhydria, gave no sensation whatever when applied to the mucous membrane of the stomach, and that the only substance which gives rise to a sensory reaction in the alimentary tract is alcohol. Tension of the stomach wall, due to over-distension of the viscus following too large a meal, or to too rapid distension following a hastily swallowed meal, will cause a sense of fullness, which in extreme cases is replaced by actual pain. Abnormal tension on the muscle fibres, and perhaps also the connective tissue fibres of the stomach wall is probably the only adequate stimulus for production of painful sensation. (Hurst.)
The physiology of gastric pain under definitely pathological conditions will be discussed later.

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P A T H O G E N E S I S.

Duodenal Ulcer occurs almost invariably in the first part of the Duodenum, which segment, it has been shown, bears the greatest possible resemblance, both anatomically and functionally, to the pyloric part of the stomach, in which gastric ulcer is most commonly found. Both gastric and duodenal ulcer occur, therefore, in one comparitively small segment of the alimentary canal, the division of which by the pylorus, is apparently of little physiological significance. Ulceration in these two situations conforms to a definite pathological type, both as regards its general characteristics, and its more exact histological picture, and, except under exceptional circum-stances, is found in no other part of the digestive tract.

There are certain symptoms said to be typical of ulcer in each of the two situations, but these differ only in time and degree, and between them there is no dividing line. In each case the principles of treatment are identical, and the response to such treatment, not dissimilar.

In considering the question of pathogenesis, it is neither necessary nor desirable to distinguish between Gastric and Duodenal Ulcer. Individual predisposition to one or other type undoubtedly exists, but in the light of our knowledge at the present time, it seems justifiable to assume that the main causative factors are in both cases the same.

It/

It is probable that more research work has been carried out on the pathogenesis of ulcer, than on any other single disease. Animal experiments conducted during the last quarter of a century have shown that acute ulcers may be produced in literally hundreds of ways. Unfortunately many of the ways recorded are outside the bounds of patho--logical possibility, and the results have only served to confuse the issue. A study of the experimental literature reveals, in many cases, only a misplaced ingenuity on the part of the investigators, rather than any benefit that is likely to accrue to medical science. Thus ulcers have been produced by the most diverse procedures, among which as the most unhelpful, may be mentioned - extirpation of the supra--renals, thyreodectomy, partial hepatectomy, and destruction of the corpora quadragemina.

With regard to the results of what may be described as the more rational experiments conducted on animals, any theories of ulcer causation derived therefrom must be accepted with great caution, as it has now begun to be re--cognised that any surgical procedure which tends to lower the vitality of the animal, may, ipso facto, bring about ulceration of the stomach or duodenum, and that this may therefore occur quite independently of the altered physiol--gy which the operation was designed to produce. Thus Berg and Jobling in a recent publication showed that, whereas/

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whereas ulcer was produced in 100% of cases following certain surgical procedures, the incidence fell to 30% when the animals were subjected to better conditions of feeding and environment.

Unfortunately any really adequate and satisfact--ory theory of ulcer causation must account for a host of factors, and besides explaining the formation of ulcer, must account for the non-appearance of ulcer, when the aetiological factor concerned is proved to be present. Furthermore, even if we succeed in propounding a theory that will satisfactorily account for the production of an ulcer, we still have a more difficult problem to face,- we have to explain why, in some cases, that ulcer does not heal. Acute ulceration of the stomach or duodenum is of fairly common occurrence, but in the majority of cases the ulcer heals and gives rise to no serious trouble. The problem of chronic ulceration is more difficult. A review of the literature reveals that there is no uniformity of opinion as to whether chronic ulcer is due merely to non-healing of an acute ulcer, or whether it should be regarded as being definitely chronic from the outset. If we accept the former view, which appears to be most generally held, we have further to decide whether this chronicity is an accident due to some outside cause, or whether such ulcers, even in their acute stages, are predestined to become chronic.

Although/

Although much valuable work has been done on the subject, there are so many questions to be answered, that no one theory of ulcer causation can possibly satisfy. There are undoubtedly several aetiological factors concerned in the production of peptic ulcer. An attempt will be made to discuss these in detail, and to evaluate their relative importance.

Peptic Genesis.

The association of the Hydrochloric Acid of the Gastric Juice, with the occurrence of ulceration in the Stomach or Duodenum has long been recognised. While it is impossible, in the present state of our knowledge to deter--mine the exact part played by the acid in the production of ulcer, that such a relationship does exist, cannot for one moment be doubted.

That the whole pathogenesis of ulcer is closely bound up with the factor of acid secretion, may be shown by summarising the available evidence under three heads, (1) The association of Hyperchlorhydria with peptic ulcer, (2) The Localisation of peptic ulcer, and (3) The Results of Experimental Work.

(1) The Association of Hyperchlorhydria with Peptic Ulcer.

The association of an abnormally high acidity of the gastric juice with most cases of gastric ulcer, was recognised/

recognised by Guenzburg, as far back as 1856, and Quincke in 1879 was the first to suggest that digestion of the mucous membrane of the stomach resulted from this hyperacidity.

The introduction of the fractional test meal by Rehfuss in 1914, has given invaluable information in determining the association of abnormal acid secretion with nearly all cases of peptic ulcer. That hyperchlorhydria is an exceedingly common, if not an absolutely constant feature in gastric and duodenal ulcer is abundantly proved. The published figures of gastric analysis from many sources differ within fairly wide limits as to the exact percentages of ulcer cases which show high acid values, but all records combine to show that, while hyperchlorhydria is commonly found in all cases of peptic ulcer, it is especially characteristic of duodenal cases. Stewart, in an analysis of 114 cases of duodenal ulcer, found that 10% of cases had a gastric acidity within limits of the average normal; 29% had a "high normal", and 61% had definite hyperchlorhydria. In a series of 220 cases recorded by Kalk, (quoted by Lindau & Wulff,) 25% had gastric acidity within normal limits, and 75% were classed as "super-normal". In gastric ulcer, hyperacidity is not so constantly present. In Stewart's series, the gastric acidity was normal in 32% of cases, and within the limit of a high normal in 26%. A further 32% showed definite hyperchlorhydria.

Sub-normal/

Sub-normal acidity, or even actual achlorhydria is found in a small percentage of peptic ulcer cases, and this has been used as an argument that the presence of free hydrochloric acid cannot be regarded as an essential factor in the pathogenesis. But both Moynihan and Hurst have pointed out that the published reports of achlorhydria in ulcer cases must be accepted with caution: in some cases the diagnosis has been made on clinical grounds alone without radiological or surgical confirmation, and in others the conclusion as to the absence of free acid has been drawn from the result of one fractional test meal alone, or even from a single Ewald breakfast. It is noteworthy that achlorhydria is practically unknown in cases of duodenal ulcer. In the cases investigated by Stewart (114), and by Kalk (220), there was not one single case which showed sub-normal acid secretion, or even one that could be classed as a "low normal".

On the other hand, a definite percentage of gastric ulcer cases have an acid secretion that is below normal limits, and a small number show actual achlorhydria. In Kalk's series of 165 cases, 15% had hypochlorhydria, and 4% showed no free acid at all. Hurst and Stewart, in 53 cases of gastric ulcer, found only three instances of apparent achlorhydria, as indicated by one fractional analysis, but they were able to show that treatment by gastric lavage to remove/

remove mucus, resulted, in two cases, in the reappearance of acid within a few days. In the third case, acidity was established after more prolonged treatment. In view of these findings, Hurst and Stewart maintain that achlorhy--dria in gastric ulcer is always due to a secondary gastritis, and that free acid will usually reappear, after this has been relieved by appropriate treatment. They point out that there is no evidence that ulceration ever occurs in the stomach or duodenum, in the absence of free hydrochloric acid.

The importance of the acid factor in the patholo--gy of peptic ulcer is exemplified by the therapeutic measures employed in the treatment of the condition. The essential principles of treatment are directed towards the prevention of hyperchlorhydria. If we can prevent this hypersecretion, or if we can keep the excess of acid neutral--ised, we can, in most cases, give relief from pain, and allow healing of the ulcer to occur.

(2) Localisation of Peptic Ulcer.

Ulcers of the Stomach and Duodenum resemble each other, not only in the fact that they both occur within the area of activity of the gastric juice, but also in their general pathological and histological characteristics. This very characteristic type of ulceration occurs only within/

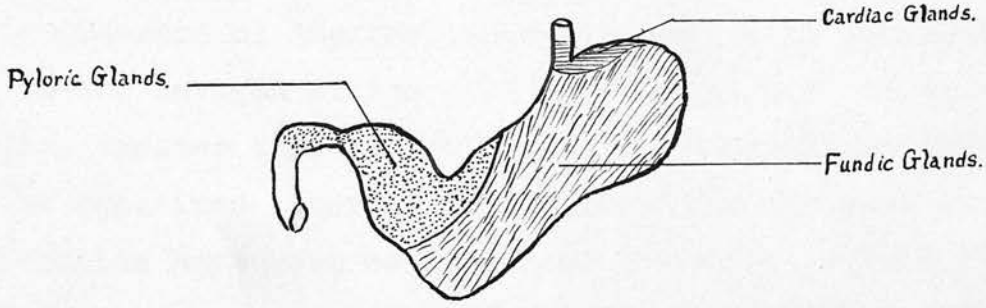
within the limited area of gastric digestion, where the mucous membrane is habitually bathed by acid chyme, and is found nowhere else in the alimentary tract, except in such regions, where, as the result of surgical interference, or developmental anomalies, exposure to the action of the acid juice has resulted.

It is well established that the majority of gastric ulcers occur in the region of the pyloric vestibule, especially towards the lesser curvature. Ulcer is compari--tively uncommon in the body of the stomach, and when it does occur in this part, it is invariably situated on the lesser curvature. In the fundus,ulceration is practically unknown.

In a recent publication, Lindau and Wulff have pointed out that the mucous membrane which contains the acid secreting glands is relatively immune to peptic ulceration, and that such ulceration in the stomach is confined to the regions that play no part in the secretion of acid.

Lindau and Wulff, in company with several other Scandinavian workers have confirmed the observations of Buechner, in regard to the localisation of the biologically heterogenous zones of glands of the stomach, and they main--tain that the position of these glandular zones has a most important bearing on ulcer formation. They point out that the area of the stomach wall, in which ulceration most commonly/

commonly occurs, corresponds almost exactly to the localis--ation of the pyloric glands, which secrete only an alkaline mucus. They are in agreement with the observation of Buechner, that this zone of pyloric glands is not confined to the region of the pyloric vestibule, but extends for an appreciable distance along the lesser curvature of the body of the stomach to a point considerably beyond the incisura angularis. At the upper extremity of the fundus, there is a narrow zone of simple tubular glands, the so-called cardiac glands, which secrete only a small quantity of alkaline mucus. The body of the stomach, and the remaining part of the fundus differ from the rest of the stomach by the presence of fundic glands containing both "chief" and "parietal" cells, which constitute the entire source of the hydrochloric acid and pepsin of the gastric juice.



Schematic diagram of Gland Areas. (Buechner.)

We see then that the portion of the stomach wall which bears the acid secreting glands is relatively immune to peptic ulceration, and indeed it is only a matter of physiological/

physiological justice, that a mucous membrane should not suffer at the hands of its own secretion. But the mucosa adjoining this acid secreting area enjoys no such immunity. This applies particularly to the whole region of the pyloric vestibule with an extension along the lesser curvature on to the body of the stomach, together with the first part of the duodenum. It is in these areas which correspond exactly to the localisation of ulcer, that the greatest activity of the gastric juice occurs, and the mucous mem-brane, having no acid secreting glands of its own, is not immune to injury from such secretion.

The mucous membrane of the lower end of the oesophagus is under similar disadvantages, in regard to its proximity to an area of acid secretion. That it enjoys such an immunity to peptic ulceration, is no doubt due to the presence of the cardiac sphincter, which protects it from the ravages of the acid gastric juice. It is well known however that ulceration of the typical peptic type does sometimes occur in this region, and 51 cases of this condition have been collected by Chevalier Jackson. In many of these cases, islands of heterotopic gastric mucosa were demonstrated; in others incompetence of the cardiac sphinc-ter was established, or the patients had suffered for pro-longed periods from regurgitant vomiting.

That ulceration is so rare in the region of the cardiac/

cardiac glands, is accounted for, by Hurst, by the fact that this area of the stomach is protected from the acid secretion by the bubble of gas, during the greater part of the 24 hours when the individual is in the upright position. An equally satisfactory explanation would be that little in the way of gastric digestion takes place at the extreme upper end of the stomach, and what acid is produced in that area, will immediately run down to more dependent parts.

There seems to be every justification for the claim put forward by Lindau and Wulff that ulcer never occurs in the mucous membrane which secretes the acid, but that it is only found in the adjoining mucosa which is acted upon by such secretion.

Confirmation of this view is available from human sources. A consideration of jejunal ulcer following gastro-enterostomy indicates that the only theory that satisfactorily accounts for this condition is the peptic one. Faults in the surgical technique, haematoma, and unabsorbable sutures have individually and collectively borne the blame, but these will not explain the formation of ulcer below the suture line, or the fact that such ulceration never occurs after gastro-enterostomy performed for malignant disease where the acidity is low.

A most interesting part of the paper by Lindau and Wulff, is a discussion of the occurrence of typical "Peptic" ulceration in certain cases of Mekel's diverticulum, where/

where the intestinal mucous membrane is interspersed by heterotopic mucosa of gastric type. The functional activity of these islands of gastric mucosa has been investigated in cases where the persistance of the divert--iculum has led to an open umbilical fistula. Secretion of both pepsin and hydrochloric acid has been detected by several workers, and it has been shown that such secretion is affected by the same stimuli, as are concerned in the production of normal gastric juice. 37 cases are reported by Lindau and Wulff, where typical peptic ulcers were present in a Mekel's diverticulum. In these cases the ulcer never occurred on an island of mucosa of gastric type, i.e., in the acid secreting area, but was always found on the normal intestinal mucous membrane adjoining such an area. In other cases where the entire diverticulum was lined with "gastric" mucosa, the ulcers were located in the ileum, close to the neck of the diverticulum.

The surgical causation of jejunal ulcer, and the occurrence of peptic ulcer in a Mekel's diverticulum, may be compared to experiments on the human subject, and must be regarded as being of the greatest value in confirming the theory of ulcer localisation held by Buechner, and by Lindau and Wulff.

(3) Results of Experimental Work.

In reviewing the results of experimental work, it is/

is very necessary that we should distinguish between the acute and the chronic ulcer, as produced in laboratory animals. With the pathogenesis of simple acute ulceration, we are little concerned. It has been shown that there is no limit to the number of ways in which this may be produced, and no conclusive evidence is available from these sources. That some of the methods described can have no possible bearing on human pathology, renders a discussion of the subject even less profitable. In the case of chronic ulceration the position is quite different. By "chronic" we mean ulcers, which from the beginning exhibit signs of chronicity, or which, as the result of non-healing, come to earn this designation.

The only experimental method, consistently producing ulceration of a definitely chronic type, is that concerned with producing a disturbance in the hydrochloric acid balance. Such experiments consist in exposing the mucous membrane of the alimentary tract to acid secretion of abnormally high concentration, either directly, or by the exclusion of such neutralising or protective agents, as are normally present.

Thus Silbermann, (quoted by Lindau & Wulff), has shown that "sham feeding" in animals with oesophageal fistulae, causes secretion of large quantities of gastric juice as the result of the psychic stimulus. In the absence/

absence of food content, the stomach is quite unprotected against the acid secretion, and peptic ulceration results in a large proportion of cases. The direct introduction of hydrochloric acid into the stomach will cause ulceration in a certain number of cases, but it is disputed whether this ever occurs from acid concentrations that are within the limits of normal pathology. Chronic ulceration is also brought about by bringing the acid gastric juice into con--tact with parts of the intestine which are not accustomed to such action. Thus Matthews, (quoted by Lindau & Wulff) isolated a Pavlov pouch from the stomach, and implanted this into the ileum, with the production of ulceration in the ileal mucosa in every case.

Similarly it has been found that chronic peptic ulcer is commonly produced by experiments, which, by the exclusion of neutralising agents, bring the acid factor into greater prominence.

It is generally believed that lesser degrees of hyperacidity in the normal individual are compensated for, by regurgitation through the pylorus of the alkaline duodenal secretions. Exclusion or diversion of these secretions from the stomach or duodenum, will result, in a large proportion of cases, in the production of peptic ulceration. The original experiment of "surgical drainage" of the duodenum, performed by Mann & Williamson in 1923 is well known. By transplanting/

transplanting the bile duct to the lower ileum, they were able to produce chronic ulceration of the stomach or duoden--um in 70% of cases. This work has been confirmed by a number of investigators. More complicated surgical pro--cedures have been employed by Weiss & Guriarran, (quoted by Deaver & Burden) to divert the bile and pancreatic juice, and similar results have been obtained. In view of the observation by Boldyreff that the pancreatic juice is more alkaline than the bile, it was maintained by a few workers that the former had the greater value in neutralising the excess of acid. But ulcers are rarely reported after ligation of the pancreatic duct, (Minkowski), whereas exclu--sion of bile alone will cause ulceration in a large propor--tion of experimental animals. The actual method of exclusion appears to be of little importance, although this is strongly disputed by the exponents of each method. Thus ligation of the common duct, (Ivy & Fauley), prolonged drainage of the duct, (Berg & Jobling), and cholecyst--nephrostomy plus ligation of the common duct, (Kapsinow, (quoted by Deaver & Burden),) have all given rise to ulcer--ation with a consistency that is sufficiently conclusive.

In view of these experiments, there can be little doubt as to the importance of the biliary secretion in protecting the mucous membrane of the stomach and duodenum against the action of the gastric juice. Although the alkalinity/

alkalinity of the bile, per se, is less than that of the pancreatic juice, on account of the much greater volume of its secretion, it must be regarded as by far the most important neutralising agent. A dissenting voice comes from the West. Berg and Jobling maintain that the protection afforded by the mucin of the bile is of greater importance than the neutralising properties. The value of mucin as a protective agent will be discussed later, but in the present state of our knowledge, and in the absence of confirmation, we cannot regard it as playing more than a minor role in the production of ulcer.

Corroborative evidence, as to the essential importance of acid in the pathogenesis of ulcer, is avail--able when we study the relation of the acid factor to the production of ulcer by other experimental methods. Of the experiments that do not depend directly upon the acid factor, the one which most consistently gives rise to peptic ulcer--ation, is the injection of "gastro-toxic serum", (Bolton). It has been shown most conclusively that ulceration will not occur by this method, if the free acid in the gastric juice is neutralised by the administration of alkalies; also that if an ulcer is produced by this or any other method, it can be prevented from healing, by keeping up the acidity of the stomach contents. Neutralisation of the free acid will in most cases allow healing to occur.

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The association between the hydrochloric acid of the gastric juice, and the occurrence of peptic ulceration, has been discussed, and an attempt has been made to indicate the grounds for the belief that a disturbance of the acid balance is an absolutely essential factor in the pathogenesis.

Having decided that the action of hydrochloric acid is necessary for the production of ulcer, we have still to determine why ulceration should occur as the result of such action. If we believe that the gastric juice, by reason of its hyperacidity, is itself capable of digesting areas of healthy mucous membrane, it is difficult to explain why such auto-digestion should not occur in the 26% of healthy individuals, who have a definite hyperchlorhydria. (Bennett & Ryle.)

It is therefore generally believed that the action of the acid gastric juice is only a secondary (though essential) factor in the production of ulcer, and that digestion of the mucous membrane takes place only in these cases where it has been injured or devitalised by some external cause. As to the precise nature of this primary injury there is little unanimity of opinion. It may be that bacterial infection is the responsible agent. On the other hand, certain mechanical factors may result in direct injury, or vascular disturbances may lead to anaemia and loss of resistance.

These factors have been studied in such great detail/

detail, and present such interesting possibilities that each is worthy of individual consideration.

The Infective Factor.

The occurrence of acute ulcer of the stomach or duodenum has been frequently observed as a complication of almost any acute infective process in the body. It is found, not only in generalised septic infections, such as septicaemia, pyaemia, endocarditis, pneumonia, etc., but also in toxaemic states, resulting from localised septic processes and from severe burning injuries.

In our discussion of chronic ulceration, we are little concerned with the production of ulcer, in cases of such general constitutional disturbance, but, as the toxae--mia of acute infections can undoubtedly give rise to acute ulceration, it is not unlikely that the toxaemia of chronic infections may have a similar responsibility in the patho--genesis of chronic ulcers.

The evidence in favour of an infective origin of peptic ulcer may be discussed under three heads, - (1) The association of possible foci of infection in cases of ulcer, (2) The results of bacteriological investigations and experiments, and (3) Certain histological considerations.

(1)/

(1) The Association of Foci of Infection.

The existence of chronic infection in some part of the body is of such common occurrence in all classes of the community, that the detection of a septic focus, in cases of peptic ulcer, is by no means conclusive.

In certain sites, however, chronic inflammation is so commonly found in association with peptic ulcer, that the factor of coincidence can safely be ruled out.

It has long been recognised that sub-acute or chronic appendicitis is found with comparative frequency in duodenal, and (to a lesser extent) in gastric ulcer. The frequency of this association has been variously stated, and the published figures vary within wide limits. The reason for this is not far to seek. There is no uniformity of opinion as to what constitutes a "chronic appendix". Most surgeons inspect the appendix, in the course of an operation for peptic ulcer; some remove it as a matter of routine; others, only if it shows naked-eye appearances of disease. Even if the excised appendix is examined micro--scopically, we are at the mercy of the personal opinion of the histologist. Thus Moynihan claims that definite appendicular infection is present in 66% of cases of duodenal ulcer, while Walton puts the figure as low as 4%. Other published figures are intermediate between these two. In a recent paper, comprising over 4000 gastro-enterological stud--ies, Larrimore gives statistics for the incidence of appendicular/

appendicular disease as follows:- 18% of cases of peptic ulcer had had a previous appecdicectomy performed, and a further 40% showed clinical signs of appendicitis. In the remaining 42% there was no evidence of such an association. Of the cases operated on, 65% had a pathological appendix. As Larrimore points out, the high percentage of previous appendectomies may indicate that ulcer occurred as a sequel to the appendix infection, or it may merely suggest that the diagnosis was erroneous, or at least incomplete. In Luff's analysis of the cases investigated by the British Medical Association, the appendix was removed in 29·6% of operations for duodenal ulcer. In Goodall's series of 200 cases of peptic ulcer, only eight had been previously operated on for appendicitis.

Experimental evidence suggesting that the appendix is a likely source of infection, is available from the work of Braithwaite. By injecting dyes into the ileocaecal glands, this worker was able to trace a chain of lymphatics from these to the glands of the stomach and duodenum. In a few cases he was actually able to demonstrate particles of dye in the gastric and duodenal mucosa.

Dental infection and oral sepsis are of such common occurrence among the community as a whole, that their importance in peptic ulcer is difficult to determine. Spencer-Payne found that dental sepsis was present in 47% of/

of "normal" individuals, (i.e., patients consulting a dental surgeon, not on account of any general disease). Various figures are recorded for the incidence of dental infection in peptic ulcer,- 75% by Hurst, and 62% by Moynihan. Goodall's analysis of 200 cases showed that in 92 cases the teeth were classified as bad, in 44 as good, and 64 patients had complete dentures. Goodall remarks that doubtless many of the latter were a belated improvement.

Tonsillar and naso-phanyngeal infection is also frequently present in cases of ulcer. This point was investigated by Gill-Carey in a series of 48 cases, and an incidence of 29% was recorded.

Recent observations by Wilkie have shown that cholecystitis is a frequent accompaniment of gastric and duodenal ulcer, and that the importance of sepsis from this source must not be disregarded.

Other less common sites of chronic infection, such as the prostate, and the Fallopian tubes may also bear their share of the responsibility.

(2) Bacteriological Investigations and Experiments.

It is not proposed to discuss in detail the enormous amount of work that has been done on the experi--mental bacteriology of peptic ulcer.

As early as 1857, Lebert produced acute ulceration of/

of the stomach in animals, as part of a general pyaemia, and since that time numerous workers have reported similar results from the injection of the most diverse organisms, ranging from a haemolytic streptococcus to a meningococcus.

In 1905, Dudgeon and Sargent isolated a streptococcus from the base and edges of ulcers, and suggested that this was the specific infecting agent. In 1916, Rosenow was similarly successful, and, in addition claimed that the streptococcus isolated had a special selective affinity for the mucous membrane of the stomach and duodenum, as experimental inoculation of laboratory animals, gave rise to typical peptic ulceration in a large proportion of cases. This important work received no confirmation at the time, and was not generally accepted. More recently, however, interest was reawakened, by further claims put forward by Rosenow, who stated that streptococci isolated from the infective teeth or tonsils of ulcer patients, frequently produced ulcers in animals, whereas streptococci from the same sources, in patients suffering from other streptococcal diseases, had in the majority of cases no effect. This worker had also been successful in causing ulceration in animals by the injection of dead bacteria, or of filtrates of active cultures, thus showing that bacterial toxins are equally effective.

These findings have since been confirmed by numerous/

numerous investigators, among whom may be mentioned, Haden & Bohan, and Wilkie. The last named has isolated a non--haemolytic streptococcus from the bases of peptic ulcers, and has shown that this organism is frequently harboured by ulcer patients, not only in the teeth and tonsils, but also in the appendix, and gall bladder. When injected into animals, it displays the characteristic selective activity.

In a recent publication, Saunders claims to have isolated a streptococcus viridans from the tissues of 19 resected peptic ulcers. In each case this organism was proved to be identical and specific, by differential cultural tests, and by agglutination, etc., but no relationship with other strains of streptococci, from possible foci of infection such as teeth, appendix, or gall bladder, could be established. The serum of patients suffering from peptic ulceration show--ed specific agglutins for this organism, in 100% of cases, whereas the serum of patients with other streptococcal infections was negative in this respect.

Histological Considerations.

The general microscopical appearances of gastric and duodenal ulcers do not concern us here, but it is permitted to refer to certain features in the histological picture that are suggestive of infection as a primary factor in the causation.

It/

It has been established by Bolton and others that the sub-mucosa of the ulcer bearing area, is particularly rich in lymphoid follicles, these being twice as large and as numerous in the pyloric vestibule, as in the fundus and body of the stomach. Wilkie regards these follicles as providing a nidus for the original infection, inviting a tempting comparison with a similar anatomical arrangement in the appendix.

In the various descriptions of the so-called pre-ulcerative state, there are many features which suggest bacterial infection. The engorgement of the vessels of the mucous membrane and sub-mucosa, accompanied not infrequently by focal haemorrhages, the leucocytic and round-celled infiltration, and the increase in size of the neighbouring lymphoid follicles, all correspond to the classical histolo--gical picture of inflammation.

When ulceration has occurred, the signs of sub--acute or chronic inflammation are even more pronounced, but the evidence here is less conclusive, as secondary infection undoubtedly occurs through the broken surfaces, and is probably largely responsible for the more gross changes.

From the foregoing observations it would appear to be undeniable that infection plays a very important part in the pathogenesis of ulcer. The association of foci of chronic/

chronic inflammation in ulcer patients is much too common to be disregarded. The bacteriological investigations are perhaps even more suggestive, and indicate that there is a specific organism, almost certainly a streptococcus, responsible for the disease. At the same time, infection cannot be regarded as the essential factor in the pathogene--sis. In many cases it is impossible to demonstrate the presence of a primary focus of infection, and bacteriologi--cal examination of the ulcer is inconclusive.

Mechanical Factors.

From certain anatomical considerations, the pyloric part of the stomach, and the first part of the duodenum would appear to be particularly liable to injury.

It is a well established maxim that a fixed point is a weak point. Both the lesser curvature of the stomach and the duodenal bulb suffer from relative fixity of position: the former by its attachment to the gastro-hepatic omentum, is not only fixed, but bears the weight of the dependent stomach; the latter is even more immobile, as it is in part bound down by the peritoneum to the posterior abdominal wall.

In both regions too, the mucous membrane is definitely thinner than elsewhere in the alimentary tract; it is less freely moveable over the muscular wall, and the protecting rugae are sparse or absent.

In/

In the pyloric vestibule, the mucous membrane must be very liable to traumatism, for it is here, that the maceration of the food, caused by the muscular contractions, is most forceful. In a similar way, the first part of the duodenum bears the brunt of the impact of the gastric contents, as they are forcibly expelled through the pylorus.

The nature of the food particles in the stomach must also play an important part. One of the chief functions of the stomach, is to protect the intestine, by not allowing anything to pass through the pylorus, unless it has lost as far as possible its irritating properties. (Hurst.). But sometimes it suffers itself in the process; meals that are hastily swallowed or imperfectly masticated will certainly make the task of the stomach more arduous, and it is undeniable that injury to the mucous membrane must be a common sequel.

A few isolated cases have been recorded in the literature, where typical peptic ulceration has apparently resulted from direct injury, caused by a blow on the abdomen.

The Value of Mucus as a Protective Agent.

In the past two years, two or three papers have been published, which suggest that the mucus secreted by the gastric glands, as well as that derived from the bile and/

and pancreatic juice, is a factor of importance in protect--ing the mucous membrane against ulceration.

Berg and Jobling point out that the healthy duodenum is always covered with a layer of mucus, which is derived from four sources,- the bile, the pancreatic juice, the intestinal glands, and the glands of Brunner, and they believe that the mucous content of these duodenal secretions is of more importance than their alkalinity, in protecting the mucosa against the acid gastric juice.

In a recent paper, Kim and Ivy refer to the experiments of Fogelson, who found that he could prepare from the gastric mucosa, a neutral mucin, which had a high combining power for free hydrochloric acid. It is pointed out that such a preparation has the requirements of an ideal ant-acid, in that it does not markedly excite gastric secretion, and has a definitely protective action on the gastric mucous membrane. Kim and Ivy record some interest--ing experiments with this substance. A biliary fistula was produced in 27 dogs, which were kept under the best conditions of environment. 17 were fed on 15 gm. of mucin twice daily; the remaining 10 received no mucin and were used as a control. Peptic ulcer occurred in 6 of the latter within ten days, while no ulcer developed in any of the dogs which received mucin, who all ate heartily and maintained their weight,- a very unusual occurrence in animals with biliary fistulae.

While/

While the result of these experiments suggests the possible value of mucilaginous solutions in the treat--ment of peptic ulcer, it yields little information on the question of pathogenesis. The protective value of mucus is well known, and it is quite to be expected that the administration of this will prevent ulcers of experi--mental origin. But in the absence of any evidence that the secretion of mucus is in any way deficient in ulcer cases, we cannot meantime regard it as a factor of primary importance in the pathogenesis.

Blood Supply and Vascular Disturbances.

Virchow, in 1852, was the first to suggest that faulty blood supply was a factor of importance in the causation of ulcer. His theory, which was further developed by Hauser in 1926, was that the initial injury was an infarction of the mucous membrane resulting from ebolism of the arteries of supply, or even from venous thrombosis.

Von Bergmann, in 1913, described a state of "constitutional dysharmony" of the gastric blood vessels in cases of peptic ulceration. The arteries were said to be more tortuous than normal, and to show abnormal dilata--tions and varices, as well as definite constrictions. Some rather similar findings were published by Muller in 1920, who in turn suggested the designation of "vaso-neurotic/

neurotic diathesis", for the condition. In general, however, these observations have not been confirmed, and there is little evidence that ulcer is commonly associated with any definite abnormality of blood supply.

The theory of infarction, popular a few years ago, has now been discarded by most workers as untenable. The fact that experimental fat embolism will in many cases give rise to ulceration, is in no way conclusive. The sources of sterile emboli are few, and venous thrombosis is very rare, except as a terminal event.

An obliterative endarteritis of the sub-mucosal blood vessels is a common histological finding in the neighbourhood of an ulcer. If this results from haemato--genous infection, it may possibly be a factor in the causation of ulcer. More probably, however, it results from secondary infection through the ulcerated surface.

It has been suggested that neurogenic spasm of the blood vessels, by causing localised ischaemia, may lead to divitalisation of the mucosa. This suggestion is entirely unsupported, and has nothing whatsoever to commend it.

Although it is not possible to conclude that peptic ulceration, is associated with any variations from normal, in the blood supply to the part, it has been sufficiently well established from the work of Reeves and others that in general the pyloric part of the stomach, and/

and the first part of the duodenum have a relatively poor blood supply, as compared with the rest of the digestive tract.

In the case of the duodenum Wilkie has shown that the horizontal part is much less abundantly supplied with blood, than the remainder. He believes that this part does not derive its blood supply from the main trunk of the superior pancreatico-duodenal artery, but through a small branch, which arises from the first part of the gastro--duodenal artery. This branch, which Wilkie has called the supra-duodenal artery, is of small calibre, and presents no anastomosis with neighbouring vessels. In confirmation of this, Mayo has drawn attention to the anaemic spot which appears on the anterior wall of the first part of the duodenum, when this is stretched by traction on the pylorus, - the so-called "Mayo's white spot".

With regard to the blood supply of the stomach, Einhorn has pointed out, in a recent publication, that the fundus derives its supply from two different channels, - the left gastric artery, from the coeliac, and the left gastro-epiploic artery, from the splenic, while the pyloric part is dependent upon branches of the hepatic artery alone. Moreover, the arteries of the sub-mucosa of the pyloric region are end arteries; they are normally tortuous, sparse--ly distributed, and anastomose imperfectly. It is also suggested/

suggested that in this area the forcible contractions of the interlacing muscle bundles, must cause interference with the circulation, and resultant liability to thrombosis. The arteries of the fundal wall are not tortuous, and they anastomose more freely. Furthermore they are less influenced by forcible muscular contractions.

The results of animal experiments yield satisfact--ory confirmation of the poor blood supply to the pyloric region. Thus ulceration is produced by ligation of the right gastric artery, while ligation of the left gastric artery is without effect.

While these observations indicate that the blood supply to the pyloric vestibule and duodenal bulb is relatively poor as compared with other parts of the digestive tract, there is no evidence to suggest that this factor is any more pronounced in cases of peptic ulceration. Such conclusions, then, are of little value in determining the causation of ulcer, though they no doubt offer a satisfactory explanation of its localisation. In this problem of localisation, however, a much more acceptable explanation is available from a study of the localisation of the glandular zones of the stomach. This has already been discussed in detail, and need not be reconsidered.

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It has been stated that the view generally accepted/

accepted is that the hydrochloric acid of the gastric juice, is only a secondary factor in the causation of ulcer, and depends for its destructive action upon some previous injury or devitalisation of the mucous membrane.

It should be noted, however, that some workers maintain that the hyperacid gastric juice is alone quite capable of producing ulcer, and must in certain cases bear the entire responsibility. They point to the results of experimental work, as showing that disturbance of the acid balance will bring about ulceration in a perfectly healthy mucous membrane. It is strongly denied that only dead or devitalised tissues are digested by the gastric juice: the leg of a living frog undergoes partial digestion, when implanted into the stomach of an animal, and it is said to be common for a living frog to be regurgitated from the stomach of a pike, in a semi-digested condition.

Certain workers, Aschoff, Buechner, Moszkowicz, et alia, (qouted by Lindau & Wulff), have reported on, the regular appearance, in ulcer cases, of a gastritis-like change in the mucous membrane of the pyloric portion of the stomach, to which little attention has been paid by British and American investigators. The microscopal picture is described as showing a state of "fibrinoid necrosis", confined to the area of the stomach where the pyloric glands are situated. The histological details of this process do not concern us here, but it is interesting to note/

note that in the case of several patients, complaining of ulcer-like symptoms, who came to autopsy, and in whom no ulcer was found, Buechner was able to demonstrate similar changes in the gastric mucosa. Accordingly this state of fibrinoid necrosis is believed to be a definite stage pre--ceding the formation of erosions, rather than secondary conditions of irritation in the tissues surrounding an ulcer. The importance of these observations is apparent when we note that Lindau and Wulff claim to have reproduced these exact histological changes by the administration of hydrochloric acid.

These observations are of the utmost importance in indicating that, in some cases at least, hyperchlorhydria is primarily responsible for the occurrence of ulcer. In explanation of the fact that many people suffer from extreme degrees of hyperacidity, and yet never develop ulcer, it is possible that certain abnormal physiological factors, which bring about undue exposure of the mucous membrane to the acid gastric juice, are of greater importance than the actual degree of acidity. These are discussed below in the last section of this chapter.

Constitutional Factors.

It has been recognised, of late years, that there are in many individuals certain constitutional factors, which/

which predispose to chronic ulceration of the stomach or duodenum. The question was first investigated by Muller in 1922, and by Draper, Dunn and Seegel in 1925. These workers first propounded the view that there is a general ulcer diathesis, brought about by certain constitutional abnormalities in the motor and secretory functions of the stomach.

In 1927, Balint, (quoted by Hurst & Stewart), in a series of biochemical investigations, showed that there is an abnormally high acid concentration in both the blood and the tissues, of patients suffering from peptic ulcer. In 89 patients, where the H-ion concentration of the blood was investigated, 93% had a reaction more acid than the average normal for healthy individuals. In addition, after the intra-venous administration of $NaHCO_3$, 39% of ulcer cases showed no increase in the pH of the urine, as compared with only 5% of control healthy cases. It has also been noted that ulcer patients usually have an hyper-acid urine, and that much larger doses of alkali are required to change this reaction, than in the case of healthy individuals.

It must be stated that these findings have not found general confirmation. No further results of such biochemical investigations have been published, and in cases where the alkali reserve in gastric and duodenal ulcer has been studied, this has always been found to be within normal limits.

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In 1920, Hurst first put forward the view that there is a special constitutional diathesis, which deter--mines the localisation of the ulcer to the stomach or duodenum.

Under the term, "hypersthenic gastric diathesis", Hurst refers to an inborn variation from the average normal, which manifests itself in a high short stomach, with active peristalsis and rapid evacuation, and in a hyperchlorhydria with digestive hypersecretion. He points out that this condition is compatible with perfect digestion, and is found in many healthy individuals, but he believes that it is a predisposing factor essential to the development of duodenal ulcer. More common in men than in women, it is frequently present in several members of the same family.

Hurst refers to the investigations of his colleague, Stewart, who showed that in cases of duodenal ulcer, in addition to the hyperchlorhydria already described, abnormally rapid evacuation of the stomach is almost invari--ably present. In some cases, emptying may be prevented by reflex spasm of the pylorus, but after this has been relieved, the characteristic rapid evacuation is at once apparent. It has been shown that in the normal individual, the stomach is rarely empty in the 24 hours, except for brief periods in the early morning and before lunch. In the absence of hunger, gastric secretion is practically in abeyance at these times, and what juice is secreted is in general of low acidity./

acidity. The hypersthenic stomach, on the other hand, is not only empty for several hours each day, but also its contained "fasting" juice is more abundant and more acid than in the normal case.

When we realise the part played by food content in the stomach, in diluting and neutralising the gastric juice, we cannot fail to see the likelihood of ulceration occurring, when the mucous membrane has not only to face a hyper--secretion of acid, but is also denied the protection normally afforded by food content.

In the normal individual, there is little or no peristalsis when the stomach is empty, and consequently un--diluted gastric juice rarely reaches the duodenum. In subjects of the hypersthenic gastric diathesis, on the other hand, the combination of hypersecretion and hypermotility, causes the duodenum to be subjected to the action of undilu--ted gastric juice for several hours out of each twenty-four. As has already been shown, it is the first part of the duodenum, which suffers most, in as much as it will always be full as long as gastric juice is passing through the pylorus. The second and third parts are little exposed to the acid secretion, by reason of their rapid peristaltic movements and their alkaline secretions.

It has already been stressed that many individuals have a hypersthenic gastric diathesis, and yet enjoy perfect health, but it is undeniable that such constitutional factors/

factors must convey a special liability to duodenal ulcera-
-tion, and indeed Hurst believes that duodenal ulcer cannot develop in the absence of this diathesis.

It is interesting here to compare for one moment, the diathesis, described by Hurst, as predisposing to the formation of gastric ulcer,- the "hyposthenic gastric diathesis". Hyperacidity is commonly present, but not with the same consistency as in the case of duodenal ulcer. The stomach is usually longer than the average and is abnormally low: the association with visceroptosis is doubtful. The length of the stomach results in what Hurst calls "orthostatic hour-glass constriction", a condition in which there is, in the middle of the stomach, a definite obstruction to the passage of food, when the erect posture is maintained. This results in the mucous membrane of this region being subjected to an abnormal amount of friction, especially in the lesser curvature, where the vast majority of ulcers are developed.

It is further maintained that the gastric and duodenal diathesis are concerned not merely with the motor and secretory functions of the stomach, but also with the general type of the individual as a whole. The patient suffering from duodenal ulcer is rarely the type one expects an invalid to be. He recovers readily from acute diseases and injuries, and is usually of an active and alert disposi-
-tion. His appetite is good, and he usually enjoys his food.
He/

He is said in general to be of the hypersthenic type, of erect build, and wide costal angle. The patient suffering from gastric ulcer is rarely so robust, and conforms more to the asthenic type, with long abdomen and narrow costal angle.

Hurst supports this most interesting hypothesis, by clinical and radiological observations, but it must be admitted that his views do not seem to have found general acceptance. Deaver and Burden admit that patients suffering from duodenal ulcer usually have short high stomachs, but they deny that this is a factor of any importance in the pathogenesis. The association of a low stomach with cases of gastric ulcer has been amply confirmed, but the true importance of the "orthostatic constriction" in the production of ulcer, is a matter for speculation. Hurst's description of a duodenal diathesis, on the other hand, is well supported by evidence, and in the writer's opinion, appears to be most acceptable.

When we endeavour to ascertain the cause of this diathesis, we find ourselves completely in the dark. To say that it is the product of a deranged nervous control is undisputable, but at the same time unhelpful. Although an unusual degree of activity of the vagus, is no doubt partly responsible, neither a slow pulse, nor other signs of vagotonia are present. Intricate investigations of the nerve/

nerve supply to the stomach have yielded no conclusive results. Altogether the problem of the control of the movements of the alimentary tract is in such a state of confusion, that, with the evidence available, no theory can be fully established. If we consider more general principles of nervous disturbance, the position is little more satisfactory. In a recent publication, Russ described the ulcer-bearing individual as being highly strung and emotional, with a hyper-sensitive nervous system, but such a description cannot for one moment be accepted as a generalisation.

There seems to be little doubt that the diathesis, is not necessarily inborn in the individual, but can be acquired in later life. Peptic ulcer is rare among rural communities, and "along the cool sequestered vale(s) of life". We must regard it as a product of civilisation, brought on by the over-work, mental worry, lack of sleep, and irregular meals which are the heritage of the town-dweller today.

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MORBID PHYSIOLOGY.

The functional behaviour of the stomach in cases where duodenal ulcer is present, shows certain characteristic deviations from the normal. It is a debatable question whether this "morbid physiology" should be regarded as a factor in the causation of ulcer, or whether it should be described as being due to the disturbing influences of an ulcer already present.

A review of the literature indicates that the concensus of opinion is definitely in favour of the former view. Such functional abnormalities as are about to be described, are not confined to cases where actual duodenal ulceration is present. They are found in cases of simple hyperchlorhydria, and in patients who have the hypersthenic gastric diathesis, but in whom no ulcer can be demonstrated. These disturbances have also been present in cases where, although no actual ulcer had occurred, mucosal changes of the pre-ulcerative type, were demonstrated at autopsy. (Deaver & Burden).

The evidence available indicates that this abnor-
-mal physiology has not only a very definite place in the pathogenesis of ulcer, but also that it is the essential factor in the prevention of healing, and in the causation of symptoms. In other words, the symptoms are the expressions of a disturbed physiology, of which ulcer is a sequel.

In/

In this chapter, also, the mechanism and causation of gastric pain are discussed, and a short review is given of the most recent views on this difficult problem.

Secretion.

It was originally suggested by Pavlov, that the juice as it flows from the gastric glands has a constant acidity, within fairly narrow limits; this has been confirmed by various workers, and the average acidity is determined at ·5%. In the fasting juice of normal individuals, a some--what lower acidity is found, but higher figures are never recorded. Thus it follows that hyperchlorhydria is brought about, not by a greater acid concentration, but either by hypersecretion, or by incomplete neutralisation,- or by a combination of these two factors.

The mechanism of hypersecretion as a constant feature is not known; it appears as a part of the hypersthenic gastric diathesis, the nature of which has already been dis--cussed. As an occasional feature, hypersecretion is commonly found in normal healthy individuals, as the result of nervous or other influences, but in these, certain pro--tective or neutralising mechanisms are quickly at work, and prevent the occurrence of actual hyperacidity. Slight degrees of hypersecretion are probably compensated for by an out-pouring of mucus. When more profuse secretion occurs, the/

the stomach has a valuable protective mechanism in the regurgitation of alkaline duodenal contents through the pylorus. This duodenal regurgitation was first observed by Boldyreff in 1914, who maintained that it occurs normally, whenever the stomach is empty, and provides for neutralisa--tion of the fasting juice. While this view has some support, most workers believe that the healthy stomach is quite capable of controlling its own secretion, when this is normal in amount, and that regurgitation only occurs, when for some reason or another, the gastric acidity reaches an unduly high level.

Whichever view is accepted, it is apparent that in normal individuals, duodenal regurgitation plays a definite part in the prevention or control of hyperacidity. In subjects of the hypersthenic gastric diathesis, whether they have actual ulceration or not, in whom hyperacidity is definitely established as a constant feature, duodenal regurgitation is of the greatest value, in keeping this under control. If regurgitation is prevented, this con--trol is removed and the acidity is markedly increased.

According to Hurst, it is extremely doubtful whether the presence of an ulcer in the stomach or duodenum has any effect, reflex or otherwise, upon gastric secretion. Hyperchlorhydria exists before the ulcer develops, and is not influenced by its presence. Any changes in the gastric acidity,/

acidity, that may be noted after the occurrence of ulcera-
-tion, are probably due to the absence of duodenal regurgi-
-tation, resulting from functional or organic occlusion of the pylorus, or to interference with the normal evacuation of the stomach, from the same cause.

Motor Functions.

It has already been shown that one of the most characteristic features of the hypersthenic gastric diathesis is a short high stomach, with forceful peristalsis and rapid evacuation. In the majority of cases where duodenal ulcer-
-ation occurs, the picture remains unchanged in the early stages. Very soon, however, delayed evacuation makes its appearance, and is due to interference with the normal functioning of the pylorus.

Hurst, in company with several other workers, believes that this failure of the pylorus to open is due to "achalasia", or inhibition of normal relaxation, and that this is a reflex mechanism engineered by the ulcerated duo-
-denum, in a futile attempt to escape irritation from the acid chyme in the stomach. But if we accept Thomas's view, (detailed in an earlier chapter,) that true relaxation never occurs during gastric digestion, the theory of achalasia is untenable. In any case, it is difficult to think of obstruction as being due to inhibition of an act of relaxation;

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we have no parallel elsewhere in the body where inhibition occurs as a protective act. Spasmodic contraction of a circular muscle, on the other hand, is well recognised as a protective mechanism, and in the writer's opinion there is no need to look elsewhere for the cause of functional pyloris obstruction.

Flouroscopic examination has shown that pylorospasm is a very common complication of duodenal ulcer. The exact causation of this is not well understood. It is particular--ly common when the ulcer is situated near the pylorus, and would appear to be simply a protective reflex when the ulcer is irritated by the gastric juice, as neutralisation of the free acid will almost invariably relieve the spasmodic con--traction. In addition, pylorospasm is of fairly frequent occurrence, in cases of simple hyperchlorhydria, where the acid factor would again seem to be responsible for irritation. Some confirmation is available from experimental work. Carlson and Litt found that the introduction of strong hydrochloric acid into the duodenum, or irritation of the mucous membrane by other means, will usually cause spasmodic contraction of the pylorus. While there appears to be ample confirmation of these results, it is interesting to note that a direct contradiction has been offered by Earl Thomas, in an investigation carried out some months ago. This worker admits that pyloric spasm is caused by duodenal irritation, but maintains that this is only true in the case of/

of anaesthetised or narcotised animals. He claims that the opposite effect, i.e., actual relaxation of the pylorus, occurs in the case of the conscious animal. Such a suggest--ion strikes at the very roots of our conception of the pathologic physiology of the stomach, and very ample confir--mation will require to be available before such a revolution--ary view can be accepted.

In some few cases, pylorospasm occurs in the absence of definite hyperchlorhydria. It is often ascribed to reflex irritation from a focus of infection in the gall bladder or appendix, but the evidence in respect of this is inconclusive, and the mechanism of causation in such cases must remain a matter of some doubt.

Once pylorospasm is established, there results a disturbance of the normal functioning of the stomach, which not only predisposes to ulceration, but prevents healing, if ulcer has already occurred. Two factors are at once present. The occlusion of the pyloric canal results, first--ly, in increased acidity of the gastric contents, from failure of duodenal regurgitation, and secondly, in the accumulation of these hyperacid contents in the stomach, as a result of the delayed evacuation. When the resistance of the sphincter is eventually overcome, there occurs a sudden ejection into the duodenum, of gastric contents of much more highly acid character, than it is equipped to neutralise.

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We can visualise, therefore, the formation of a particularly harmful type of vicious circle. Simple hyper--acidity gives rise to pylorospasm; the pylorospasm results in increased acidity, and from this ulceration develops: the irritation from the ulcer aggravates the pylorospasm, the acidity is again increased, and so on.

A further result of the pylorospasm is that the peristaltic contractions of the stomach become more forceful, in an attempt to overcome the resistance offered by the sphincter. If the obstruction is not relieved, the gastric musculature gradually becomes exhausted, and loss of tone of the stomach or actual dilatation results. Where the ulcer is situated near the pylorus, the degree of obstruction occasioned by the pylorospasm is increased in the early stages by inflammatory oedema round the ulcer. In the late stages, cicatricial stenosis of a healed or semi-healed ulcer may dominate the picture.

Sensation.

Causation of Ulcer Pain.

In most cases of duodenal ulcer, pain occurs in relation to the taking of food, after so constant an interval, that it is obvious that something must happen at this particular time, which is responsible for the stimulus required for the production of pain.

Since/

Since the time of Abercrombie it has been known that the characteristic pain of duodenal ulcer occurs later than that of gastric ulcer, or from one and a half to three hours after a meal. It was believed that this pain was due simply to irritation of the ulcerated area, by the passage over it of the acid gastric contents. This has been completely disproved. It has been shown most con--clusively that the acidity of the gastric contents is not by itself the cause of pain, as the mucous membrane, whether healthy or ulcerated is quite insensitive to such form of stimulation. With the exception of alcohol, which induces a sense of warmth, no chemical substance applied to the mucous membrane, and no form of mechanical or thermal stimulation, will give rise to conscious sensation of any kind. That mere hyperacidity alone is not responsible for the production of pain, is further demonstrated by the fact that during the periods of remission, when pain is absent, there is no diminution of the gastric acidity.

On the other hand, it cannot for one moment be doubted that hyperchlorhydria, while not in itself the direct cause of pain, is a very essential factor in its production. The immediate relief of ulcer pain, that follows neutralisation of the free acid, is sufficient grounds for this assertion. It has been shown too by Palmer, that the administration of hydrochloric acid to ulcer patients will give rise to attacks of pain, similar to those of spontaneous origin.

Considerable/

Considerable difficulty has been experienced in explaining why the onset of the pain should be so long delayed, if, as can hardly be doubted, the pain is due primarily to the presence of an ulcer in the duodenum. This led to the suggestion that the pylorospasm associated with the ulcer, delays evacuation of the stomach, and that the pain commences only when the gastric contents first reach the duodenum.

It has been pointed out by Hurst, however, that evacuation is not delayed in the early stages. The stomach begins to empty itself, immediately after food enters it, and the ulcer is subjected to the passage, over it, of gastric contents from the very first.

According to Hurst the occurrence of pain in duodenal ulcer, coincides with the period of the greatest acidity of the gastric contents. The food as it enters the stomach is alkaline in reaction, and it is only after secret--ion has been going on for some time, and part of the food has been evacuated, that the acidity gains the upper hand. Fractional test meals have demonstrated that, in cases of duodenal ulcer, the amount of free acid is usually at its greatest, about two hours after the meal.

It has been shown also by fluoroscopic examination that the pain usually begins, when the stomach has partly but not completely evacuated its contents,- the stage at which one would expect the acidity to be greatest.

Having/

Having noted the association of hyperacidity in the production of pain, and having offered an explanation of its delayed onset, we have still to determine the mechanism whereby painful stimuli arise.

As has already been noted, the stomach and duodenum are quite insensitive to ordinary forms of stimulation, and the only stimulus which gives rise to any form of sensation, is an abnormal degree of tension of the muscle fibres of the wall. It must be obvious therefore that the only theory that can satisfactorily account for ulcer pain, must be one that depends upon this factor.

In duodenal ulcer, the stomach, at least in the early stages, is of the hypersthenic type, and by rapid peristalsis, tends to empty in an abnormally short time. If rapid emptying is allowed to take place, pain is rarely present. Such a condition of affairs occurs during the periods of remission of symptoms.

It has been shown, by means of the opaque meal that the onset of pain in duodenal ulcer coincides with a sudden arrest or slowing down of this rapid evacuation. As there is no diminution in the force of the peristaltic movements, this delayed evacuation must be regarded as being due to spasmodic contraction of the pylorus. We know that pylorospasm is caused by the acid factor, and its occurrence here coincides with the period of maximum acidity.

If we accept the view that in duodenal ulcer, pylorospasm/

pylorospasm is a necessary factor in the production of painful symptoms, we have in the opinion of Hurst a satis--factory explanation of the origin of such sensation. The tension on muscle fibres is the same, whether they are con--tracted or relaxed. It is therefore possible to visualise that a definite increase in tension will occur, not only in the region of the pylorus, as a result of the spasmodic contraction, but more particularly in the musculature of the pyloric vestibule. The functional obstruction offered by the closed sphincter causes the peristaltic waves to become unusually forceful. The greatest effect of this is seen in the distal end of the stomach, and the lumen of the pyloric vestibule is almost completely cut off from that of the body, by the deep waves of contraction. The vestibule contracts strongly in an endeavour to overcome the resistance at the pylorus. The resultant increase in pressure, within this part of the stomach, leads to an abnormal degree of tension in the muscle wall, and so gives rise to pain.

By the acceptance of this view, we regard pyloro--spasm as an essential factor in the causation of ulcer pain. The pylorospasm is undoubtedly caused by the hyperacidity. Why it should be only an occasional rather than a constant result, we do not know. But neutralisation of the free acid will almost invariably relieve the pylorospasm, and with it, the painful sensations. The relief that is obtained by/

by lying down is explained by Hurst, on the grounds of the mechanical emptying of the duodenal bulb into the descending part of the duodenum; the irritative action of acid chyme upon the ulcerated area is removed, and the stimulus to pylorospasm is withdrawn.

With reference to the "hunger pain", which occurs when the stomach is empty, and is relieved by taking food, a similar explanation is applicable. In cases of duodenal ulcer, the fasting juice is abnormally abundant. Pyloro--spasm occurs as the result of this hyperacidity: the stomach is unable to evacuate the accumulation of acid juice, and abnormal tension occurs as already described. Immediate relief is obtained by neutralisation of the free acid by alkalis, or by dilution of the juice from food swallowed.

The pain of duodenal ulcer is referred to the anterior abdominal wall, and is localised to the epigastrium, some little distance below the ensiform cartilage,- in the mid line or slightly to the right. This localisation to the right side is described by Hurst, as being due to the fact that the afferent nerves from the pyloric vestibule, where the painful stimuli arise, run mainly to the right side of the spinal cord, as a result of which cutaneous sensation is referred to the right.

Mechanism of Deep Tenderness.

In the light of the celebrated researches of Mackenzie/

Mackenzie and Head, on the question of referred pain, the tenderness on palpation, in cases of peptic ulceration, was believed simply to be due to the "viscero-sensory reflex". In other words, it was thought that such tenderness originated only in the part of the anterior abdominal wall, which derived its sensory innervation from that segment of the spinal cord, which was irritated by afferent impulses from the ulcerated area.

The advent of radiology has shown that this theory is untenable. It was shown by Hurst that the localisation of deep tenderness, not only corresponds very closely with the site of the ulcer, but also that it alters with changes of posture. Such tenderness cannot be due merely to a referred irritability of the abdominal wall, but must originate at or near the actual situation of the ulcer.

Hurst believes that the tenderness associated with peptic ulcer, is of two distinct types,- (1) reflex tenderness, and (2) true visceral tenderness. In dealing with the reflex tenderness, Hurst still accepts the well known theories of Mackenzie, in that he regards this as a referred pain to the abdominal wall. This type of tenderness is not constant, is worse during the attacks of pain, and when this is severe, is accompanied by reflex rigidity. Under the heading of visceral tenderness, he describes a localised deep tenderness, which corresponds accurately with the position of the ulcer as visualised by X rays, and shifts/

shifts with the ulcer in different positions. He con-
-cludes that the only explanation of these phenomena must be that the ulcerated viscus is itself sensitive to pressure, but believes that this only occurs when the inflammatory process round the ulcer involves the serous coat, (visceral peritoneum), or the sub-serous connective tissue. This type of tenderness, then, is not aggravated during the attacks of pain, and is fairly constant, except during the remission periods when the inflammation subsides.

Morley and Twining, in a recent publication, have recorded some very interesting observations in regard to deep tenderness in peptic ulceration, and have put forward an entirely new suggestion as to its causation.

In a series of cases of both gastric and duodenal ulcer, in which deep tenderness could be elicited, the location of the tenderness was marked with a small metal ring, and a radiogram was taken after an opaque meal. This was repeated in various postures, and it was found that the shadow of the ring was almost always coincident with that of the ulcer crater (in the case of gastric ulcer) or of the duodenal cap. Morley and Twining therefore confirm Hurst's observation that the localisation of tender-
-ness corresponds very closely to the position of the ulcer, and moves with it, but they put an entirely different interpretation upon such findings. While Hurst believes that the stomach or duodenal wall at the site of ulcer is endowed/

endowed with true visceral tenderness, Morley and Twining uphold the complete insensibility of these organs, whether ulcerated or not. They record a case where a patient suffering from a large pre-pyloric ulcer, was operated on, under local anaesthesia (infiltration of the abdominal wall). The stomach wall adjacent to the ulcer was grasped with toothed forceps, without any pain whatsoever being elicited. Similarly, it was impossible to cause painful sensation by handling the ulcer, or by direct pressure thereon. The only pain complained of throughout the operation, resulted from traction on the meso-colon, and the tearing of an opening in it for the purposes of gastro--enterostomy.

This proves decisively that the stomach wall, immediately overlying, and adjacent to an ulcer, is quite insensitive to direct pressure, or other mechanical stimul--tion. As tenderness had been elicited on pressure over the same area through the parietes, Morley and Twining maintain that the only possible conclusion is that this must originate in some part of the anterior abdominal wall. They believe that contact between the parietal peritoneum, and the inflamed visceral peritoneum overlying the ulcer, provides the necessary stimulus to pain production.

Morley and Twining find additional support for this theory, in their observation that the deep tenderness in pre-pyloric and duodenal ulcers, disappears in the right lateral/

lateral position, when the ulcerated area becomes separated from the parietal peritoneum by the liver. Similarly, it has been noticed that tenderness often disappears on lying down, and can only be elicited in the upright position, when the organs lie nearer to the abdominal wall.

While we must agree that these workers appear to have entirely disproved the existence of true visceral tenderness, we cannot regard their alternative suggestion as being any more acceptable. It is difficult to understand how painful sensations could originate in the parietal peritoneum, after such momentary contact, even if we could formulate some idea as to the nature of the stimulus. In addition, the deep tenderness associated with ulcers on the posterior wall of stomach or duodenum, remains quite un--accounted for.

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A COMPARISON OF THE RESULTS OF MEDICAL AND SURGICAL TREATMENT.

In presenting a comparison between the results of medical and surgical treatment in duodenal ulcer, it is in no way the purpose of this thesis to press the claims of either Medicine or Surgery. It is rather an attempt to evaluate the relative positions of the two sister sciences, and to discuss the benefits, which in the average case of ulcer may be obtained from each.

During the last twenty years, the treatment of peptic ulcer has too often been the subject of a somewhat acrimonious discussion between physicians and surgeons, as to whether ulcer should be regarded as a medical or a surgical disease. Happily this fundamental question is now settled. Few people today will question that peptic ulcer is primarily and essentially a medical disease, and that surgery holds but a secondary place in its treatment. Even the most enthusiastic surgeon cannot regard his art as having precedence over that of the physician, in the primary stage of the condition. On the other hand, the most rigid adherent of the ultra-conservative school will not deny the great benefits offered by surgery, in the case of the old--standing duodenal ulcer, where organic stenosis has super--vened.

At these two extremes, then, Medicine and Surgery hold/

hold undoubted sway. The early acute ulcer is essentially the province of the physician, and with energetic medical treatment, can be cured in the vast majority of cases. At the other end of the scale, the late complication of cicatricial stenosis renders medical treatment unavailing. Gastro-enterostomy has undisputedly excellent results in this condition, and there is little need to look further for the ideal method of treatment.

Unfortunately, however, the great majority of cases of duodenal ulcer, do not permit of such a simple selection. It is comparatively rare for either the medical or the surgical specialist to see an ulcer patient in the early stages of the condition. Unless acute emergencies, such as severe haemorrhage or perforation, suddenly establish the diagnosis, the condition is usually overlooked, or treated in the early stages as simple dyspepsia. Energetic medical treatment is very seldom employed before the diagnosis is definitely established. The modern necessity of radiologi--cal and biochemical facilities, as aids to diagnosis, means that the ulcer patient very rarely receives adequate medical treatment, until he is referred to the hospital or to the specialist. Various statistics have been published regard--ing the duration of symptoms prior to hospitalisation. A review of these would indicate that, at a moderate estimate, at least 70 per cent of patients have symptoms for three years or more, before the diagnosis is established, and adequate/

adequate medical treatment commenced. It will be seen, therefore, that although it is well recognised that peptic ulcer, in its early stages, can be cured by medical treat--ment alone in almost every case, the opportunity rarely occurs where such an ideal can be attained.

If we turn to the other extreme, where the decision as to treatment again offers no difficulty, we find that cicatricial pyloric stenosis, that most definite indication for surgery, is present in only a small percentage of the large number of cases, with which we are called upon to deal.

Between these two extremes, therefore, that of the early acute ulcer, and that of the chronic ulcer with stenosis, is to be found the average ulcer patient as he is referred to the specialist. He has usually had digestive symptoms off and on for years. He has had medical treat--ment of a kind, from which he has not derived more than temporary benefit. The diagnosis is confirmed by X rays and by gastric analysis; there is no pyloric stenosis. - What have we to offer him from Medicine and from Surgery?

In this country, at the present time, there is unquestionably a strong trend of opinion, in favour of prolonged medical treatment of peptic ulcer, no matter in what stage of chronicity the ulcer may be.

It/

It has been proved most conclusively by Hurst and other physicians, that even the most chronic ulcers can be completely healed by medical treatment alone, and it is believed by many that if every patient with ulcer were to receive adequate medical treatment, the number requiring operation would be very small indeed. To quote Hurst, "The last twenty years has been the surgical era in the treatment of gastric and duodenal ulcer; if the lessons it has taught have been properly learnt, it should be followed by a second medical period, which should show such improve--ment in diagnosis and non-operative treatment, that the surgery of the stomach will be almost confined to the performance of gastrectomy for carcinoma".

While there is no lack of evidence to show that medical treatment alone <u>can</u> cure the most chronic of duodenal ulcers, it is justifiable to ask in how many cases it actually does so. The literature is rich in estimates of 60 to 80 per cent of cures by medical means, but there are compara--tively few articles from which accurate conclusions, ascer--tained from follow up study in after years, can be obtained.

Such statistics as are available indicate that the longer the duration of the ulcer symptoms, and the greater the number of attacks before the patient comes under medical treatment, the more refractory will the ulcer prove to such treatment. Thus Neilson, (quoted by Rendle Short,) estimated/

estimated that in cases where symptoms have been present for less than one year, 60 per cent will be cured by medical treatment. Where ulcer has been present for five to ten years, only 11 per cent will be cured.

The determination of cure in duodenal ulcer is a problem of the greatest importance. It is pointed out that in almost every case medical treatment will bring about complete relief of symptoms. In many cases, however, the ulcer persists in a quiescent state, although on account of shrinkage in size, it is no longer demonstrable in a radiogram. Accordingly, relapse is not infrequent, in cases which have apparently been completely cured.

Einhorn and Crohn, writing in 1926, investigated the after-histories of 100 medical cases, and found that whereas 67 per cent had been stated to be "cured" one year after treatment, the figure fell to 29 per cent, when the cases were examined five to fifteen years later. Very similar findings were obtained by David Smith, who analysed the medical results in 214 cases of peptic ulcer. At the time of leaving hospital, 67 per cent of the males and 76 per cent of the females were pronounced cured, while 22 per cent and 14 per cent were improved. At the end of a five to fifteen year period, however, the figures for patients cured had fallen to 29 per cent for the males, and 40 per cent for the females. 31 per cent of the male cases, and 25 per/

per cent of the female, were regarded as unsatisfactory.

Barford has investigated the after-histories of 130 private patients suffering from duodenal ulcer, who were treated at the New Lodge Clinic. In 41 per cent of cases the result was satisfactory, and in 28 per cent, "fairly good". There was a recurrence in 24 per cent of patients, and in half of these operation was ultimately performed. Hutchison comments,- "Considering that these results were obtained in private patients treated under the best conditions, they must be regarded as disappointing".

It is pointed out by Hurst and others that these so-called "failures" cannot fairly be regarded as an argument against medical treatment, but should be taken rather as a proof that medical treatment as usually employed, is totally inadequate. But we cannot judge medical treat-ment by its potentiality to effect a cure in the cases where it is possible adequately to employ it; we can only judge from its results, immediate and remote, in the average case.

To what extent can we hope for an improvement in the future? Earlier diagnosis will no doubt lead to a larger number of ulcers being cured in their early stages, but it can hardly be doubted that the problem of the chronic ulcer will still be with us. In spite of many assertions to/

to the contrary, the healing of a chronic ulcer can never be regarded as a rapid process, and if medical treatment is to be declared adequate, the strict dietary regimen necess--ary in the initial stages, must be followed by a careful supervision of the patient's diet and habits, for some con--siderable time after his symptoms have been relieved. In so many cases in all walks of life, this represents an ideal impossible of realisation. In the words of Moynihan, "the medical treatment of duodenal ulcer is not so much a medical problem as a problem in social economics. Rest in bed, freedom from worry, abstinence from work,- complete repose in fact, are essential if treatment is to have the best chance of success. A counsel of almost unattainable perfection!"

With the realisation that in many cases, the ulcer patient, whether from economic or other reasons, cannot be promised a cure from medical treatment, we have to consider what we have to offer him from Surgery.

Gastro-enterostomy must be regarded both as the original operation for duodenal ulcer, and the one which the majority of surgeons still favour at the present time. During the last two decades, which Hurst has described as the surgical era in the treatment of duodenal ulcer, the operation of gastro-enterostomy has been performed by hundreds/

hundreds of surgeons upon thousands of patients with an optimism that has outweighed discretion. The majority of cases of duodenal ulcer were referred to the surgeon without having had anything approaching adequate medical treatment, and in some cases, even, the anastomosis was carried out, where no ulcer was demonstrable, in the belief that it would relieve ulcer-like symptoms.

In spite of the abundance of material from which conclusions as to the results of gastro-enterostomy can be drawn, we find little agreement between physicians and sur--geons, as to the benefit that is likely to be obtained from this operation. Ogilvie has suggested that although the literature is full of statistics showing satisfactory results in about 80 per cent of cases, the other 20 per cent vary "from unsatisfactory to dreadful", and Hurst has drawn a gloomy picture of the victims of surgery whose lives have been made wretched by the development of jejunal ulcer, and gastro-jejuno-colic fistula!

As Wilkie has pointed out, however, the arguments of the ultra-conservative school against operative treat--ment, are based on their experiences with the "surgical derelicts" - the very few with regurgitant vomiting, and the rather larger number with secondary jejunal ulcer, who admittedly constitute a small minority of the cases operated on. "Medical derelicts" are no less common; - these are the/

the cases which, after years of unavailing medical treat-
-ment, are referred to the surgeon only as a last resource.

Gastro-enterostomy has almost invariably been attended with excellent results in cases of duodenal ulcer accompanied by cicatricial stenosis of the pylorus. In the group of cases without stenosis where an irritible ulcer with marked hyperacidity and hypermotility is present, the results are not so favourable, and the danger of a jejunal ulcer is a very real one. The consequence has been that the injudicial selection of cases for gastro-enterost-
omy, has prejudiced the just reputation of this operation as one of the most beneficial of surgical procedures.

As Rayner remarks, this swing of the pendulum is long overdue, and must be welcome to many surgeons, in that it makes for a higher standard of medical treatment and after-care, than has previously been attained, and a more just discrimination in the selection of cases for surgery.

Much has been written in condemnation of the futility of drawing any conclusions from a statistical race between Medicine and Surgery for priority in the treatment of duodenal ulcer. But it is only by comparing the after-
-results of sufficiently large groups of cases, that one can determine just what one is justified in promising the ulcer patient, and also which offers the best prospect for relief or cure, medicine or surgery.

Statistics/

Statistics relating to the after-results of gastro-enterostomy are legion, and need not be referred to in detail. All combine to show between 60 and 90 per cent of satisfactory results. Several physicians have maintain-ed that the statistics of individual surgeons are somewhat misleading, as they present in most cases the work of acknowledged experts. A large proportion of the gastric surgery in this country is carried out by general surgeons, who lay no claim to the skill of a Moynihan or a Mayo, and it is suggested that the published statistics do not represent the results obtained by the surgical community as a whole.

In this respect, the collective investigation carried out by the British Medical Association some two years ago, has a special value, because it shows the results of the operation of gastro-enterostomy, as performed by no less than 86 surgeons.

In this investigation, the after-histories were studied in the case of 995 patients who had had gastro--enterostomy performed for duodenal ulcer, between 1920 and 1924 inclusive. The results were classified as follows:-

"Very good"	450 cases	67·2 per cent.
"Good"	149 cases	22·3 per cent.
"Fair"	34 cases	5·1 per cent.
"Poor"	36 cases	5·4 per cent.

Of/

Of the many other statistical reports that are available, perhaps the most interesting is that published by Balfour of the Mayo Clinic. It concerns the after histories of 100 medical men, who were operated on in the Clinic for duodenal ulcer. In 92 of the cases, gastro--enterostomy was performed; excision was carried out in 6, and gastro-duodenostomy in 2. The investigation was made after a 5-15 year interval, the average time being 8½ years. In 90 per cent the result was complete relief of symptoms, and in the majority of cases the reports were almost extravagant in their praise of the effects of the operation.

When we examine the evidence against gastro--enterostomy, we find little more than the liability to post-operative jejunal ulcer. While this is undoubtedly a much dreaded complication, and one which has caused much suffering and distress, we have still to be convinced that it occurs with such frequency as to constitute a grave objection. The incidence of jejunal ulcer following gastro--enterostomy is variously stated by different workers, but there is little doubt that with the more careful selection of cases for surgery, and with the recognition of the essential importance of post-operative medical treatment, this complication is becoming more and more infrequent. The alarmist statistics of certain American surgeons are discounted by Luff's analysis of the collective investigation carried out by the British Medical Association. In this large series of gastro-enterostomies, jejunal ulcer was reported in only 2·8 per cent of cases.

For those surgeons who view with disfavour the operation of gastro-enterostomy, in the case of the chronic duodenal ulcer without stenosis, several alternative procedures are available. Pyloroplasty and gastro--duodenostomy have many advocates, and the more radical procedures of pylorectomy or sub-total gastrectomy, although in the main condemned by surgeons in this country, enjoy some popularity on the Continent and in the United States.

It is difficult to see what advantages pyloro--plasty and gastro-duodenostomy have over gastro-enterostomy. The older operation provides the two essential factors of rest to the ulcerated area, and neutralisation of the acid gastric juice. Pyloroplasty allows neutralisation, and prohibits spasm, but makes no provision for rest for the ulcer. Gastro-duodenostomy presents the same advantages as gastro-enterostomy, and in addition the liability to anastomotic ulcer is greatly reduced. As already indicated, however, jejunal ulcer is of comparatively rare occurrence after gastro-enterostomy, and the avoidance of this compli--cation cannot alone decide in favour of gastro-duodenostomy, unless the results of that operation can be shown at least to equal those of gastro-enterostomy.

From the evidence available, it would appear to be sufficiently well established that gastro-enterostomy is attended by a successful result in the majority of cases of duodenal/

duodenal ulcer. Balfour's statistics of the result of this operation on medical men are particularly illuminating, as they indicate the results which can be obtained by surgical measures, when the cases are carefully selected, and the operation is followed by careful post operative treatment. These doctors undoubtedly constituted ideal subjects for surgery, in that they were aware of the dangers of their operation, and recognised the importance of post--operative medical treatment.

Physicians would seem to have every justification for their claim that, if all cases of peptic ulcer were to receive adequate medical treatment, there would be little need for surgery. But there still remains the insuperable problem of how this adequate treatment may be brought within reach of the average ulcer patient. Until this ideal becomes a reality, Surgery will continue to hold a very definite place in the treatment of duodenal ulcer. With the increasingly careful selection of cases for surgery, and with the recognition of the essential importance of post-operative medical treatment, there is every reason to believe that the successful results will increase in number, and the failures grow less.

Nature of Investigation

Numerous writers have seen reason to doubt the value/

value of a direct comparison between the results of medical and surgical treatment of duodenal ulcer, in determining the choice of procedure in the individual case. It is pointed out that statistics of the after results of surgical treat--ment as a whole, are apt to be misleading in that, in a definite proportion of cases they are concerned with the chronic ulcer with cicatricial stenosis, where the results of gastro-enterostomy are undisputedly excellent.

Medical treatment is, as a rule, employed primarily in cases which are quite unselected, and it is suggested that the results in such cases cannot fairly be compared with those of surgical treatment, where the cases have, in many instances, been selected as being essentially suitable for operation.

In this investigation, an attempt has been made to compare the results of medical and surgical treatment, in a series of cases where such a criticism cannot be applied. As pyloric stenosis must be regarded as the indication par excellance, for operation, and therefore the most important factor in the selection of cases for surgery, no case where this complication was present is included in the series of cases investigated. The after histories have only been studied therefore, in that type of ulcer where the decision as to treatment presents the greatest problem,- the chronic ulcer without stenosis.

By/

By the kind permission of members of the Honorary Staff of the Royal Infirmary of Edinburgh, I have been enabled to investigate the after-histories of 480 cases of Duodenal Ulcer. These cases are taken from the records of the Infirmary, and concern patients treated between January 1924 and June 1931 inclusive.

For the investigation of the results of medical treatment, 200 cases were taken where the patient had been treated in a medical ward. In the great majority of these, the diagnosis was confirmed by radiological or biochemical findings. In each of the cases, the patient was discharged from hospital, as "cured" or "improved". No case where the patient was at the time referred to a surgeon, is included in the series.

For the study of the surgical results, the after--histories were investigated in 200 patients who had had gastro-enterostomy performed for duodenal ulcer. Patients in whom definite pyloric stenosis had been observed at operation, were excluded from the series. No figures are given for operative mortality, as the enquiry concerns after results alone.

An additional series of 80 cases where the operation of gastro-duodenostomy had been carried out, was also studied for the purposes of further comparison.

The investigation took the form of a questionnaire, which was sent out to each patient. Copies of the medical and surgical questionnaire are appended below.

M *No*..... *Date*.....

1. How many times have you had MEDICAL TREATMENT IN HOSPITAL, for stomach trouble? ... ...

2. Indicate the results of the treatment, as regards your *present* condition :— Mark with a **X**

(*a*) Completely cured. Can eat anything. No pain. Able for full work	
(*b*) Greatly improved. *Occasional* slight pain or discomfort Able for full work ...	
(*c*) Improved, but have *frequent* attacks of indigestion, and have *always* to be careful with diet. Able for light work	
(*d*) *Constantly* troubled with indigestion, and can eat very little. Unable for work ...	

3. For how long were you off work *after discharge*? ... ... } .....weeks. .....months.

4. Since returning to work, have you been off *again* on account of indigestion? ... .

5. If you have had any OPERATION for stomach trouble, give—

   (*a*) No of Ward ... ...

   (*b*) Date of Operation ... .

MEDICAL QUESTIONNAIRE.

S *No*..... *Date*.....

1. For how long *before operation* were you troubled with indigestion? ... ... } ... .weeks. .....months. ....years.

2. Were you kept off work by your trouble *before operation*? ... ...

3. Did you have MEDICAL TREATMENT IN HOSPITAL, *before operation*? ... .

   If more than once, state how many times .....

4. What has been the result of your operation? Mark with a **X**

(*a*) Completely cured. Can eat anything. No pain. Able for full work	
(*b*) Greatly improved. *Occasional* slight pain or discomfort Able for full work ...	
(*c*) Improved, but have *frequent* attacks of indigestion, and have *always* to be careful with diet. Able for light work	
(*d*) *Constantly* troubled with indigestion, and can eat very little. Unable for work ...	

5. For how long did you carry on with light diet and medicines *after the operation*? } .....weeks. .....months.

6. For how long were you off work *after the operation*? ... ... } .....weeks. .....months.

7. Since returning to work, have you been off *again* on account of indigestion? ... .

8. Have you had any medical treatment IN HOSPITAL, *since* your operation? .....

SURGICAL QUESTIONNAIRE.

PRINTED MATTER.

DR E. L. FARQUHARSON,

C/O WARD 18,

ROYAL INFIRMARY,

EDINBURGH.

WARD 18,
ROYAL INFIRMARY,
EDINBURGH.

An investigation is being made into the results of treatment of certain cases of stomach trouble, treated in the Royal Infirmary, during the last few years.

It would be appreciated if you would kindly fill in the particulars asked for in the enclosed stamped addressed post card, and return it to me as soon as possible.

E. L. FARQUHARSON,
M.B., Ch.B.

Result of Investigation.

300 MEDICAL CASES.

Replies received from	152
Untraced	27
Did not answer	15
Died	6
Total	300

Of the 152 patients who answered the questionnaire, 75 per cent had been in hospital once, and 15 per cent, twice. Of these 152 patients, 34 had undergone an operation subsequent to discharge from the medical wards. The remain--ing 118 cases are classified later.

200 CASES WHERE GASTRO-ENTEROSTOMY HAD BEEN PERFORMED.

Replies received from	143
Untraced	35
Did not answer	17
Died	5

In the case of the 143 patients who replied to the questionnaire, the first three questions were answered as follows.

(1) Duration of symptoms prior to operation.

The average duration of symptoms prior to operation was/

was 9 years. 4·2 per cent of patients had a history of less than 1 year's duration. 14·7 per cent less than 2 years, and 22·6 less than 3 years. 46 per cent had had symptoms for 5-10 years, and 27 per cent, over 10 years.

(2) Loss of work before operation.

110 patients, or 72 per cent. stated that they had been kept off work, on account of digestive symptoms prior to operation.

(3) Previous Medical Treatment in Hospital.

39 per cent. of patients had had medical treat--ment in hospital, prior to operation, and 5 per cent had been treated on two or more occasions.

The results of Medical and Surgical treatment are compared below.

		MEDICAL.	SURGICAL.
A.	Completely cured. Can eat anything. No pain. Able for full work.	15·3 %	48.3 %
B.	Greatly improved. Occasional slight pain or discomfort. Able for full work.	43·2 %	25·2 %
C.	Improved, but have frequent attacks of indigestion, and have always to be careful with diet. Able for light work.	32·2 %	21.6 %
D.	Constantly troubled with indigestion, and can eat very little. Unable for work.	9·3 %	4·9 %

Return/

Return to work after treatment.

In the medical series, the average time between discharge from hospital, and resumption of work was $3\frac{3}{4}$ weeks. (Periods over 3 months were regarded as being due to some outside cause, and were not considered.)

In the surgical series, the average time was $2\frac{3}{4}$ months. (Periods over 6 months were not considered.)

Subsequent Unfitness for work.

Since returning to work, 17 per cent of the medical cases, and 12 per cent of the surgical cases, have been off again on account of digestive symptoms.

Post-Operative Medical Treatment.

The investigation into the duration of post-operative medical treatment has yielded some interesting information.

In the 69 cases in class "A", the average duration of such treatment was $5\frac{3}{4}$ months. 37 returned to normal diet within 3 months, and 51 within 6 months. 5 patients continued treatment for 2 years.

In class "B", (36 cases) the average duration of treatment was $6\frac{1}{2}$ months. 13 patients returned to normal diet within 3 months, 20 within 6 months, and 31 within the year.

In/

In class "C", (31 cases) 7 patients gave up treatment within 3 months, 18 within 6 months, and 25 within the year.

Of the 7 cases in class "D", 5 gave up treatment within 6 months.

Two points stand out in contrast from the above investigation. Firstly, in 5 of the patients in Class "A", post-operative medical treatment was employed for 2 years before a cure was claimed. Secondly, in the case of the poor results, (class "C") and the failures, (class "D"), 60 - 80 per cent of the patients abandoned all medical treatment within 6 months of operation, and 80 - 90 per cent, within the year.

80 CASES WHERE GASTRO-DUODENOSTOMY HAD BEEN PERFORMED

Replies received from	65
Untraced	6
Did not answer	9
Total	80

The after results are classified as follows:-

A. Completely cured. Can eat anything. No pain. Able for full work. . . . . 27·7 %

B. Greatly improved. Occasional slight pain or discomfort. Able for full work.. 44·6 %

C. Improved, but have frequent attacks of indigestion, and have always to be careful with diet. Able for light work. . . . . 21·5 %

D. Constantly troubled with indigestion and can eat very little. Unable for work. . . 6·3 %

Conclusions.

The benefits to be obtained from gastro-enterostomy in duodenal ulcer, are by no means confined to the cases where pyloric obstruction is present. In the case of the chronic ulcer without stenosis, which has formed the subject of the investigation, the results of this operation compare very favourably with those obtained under conservative treatment alone. 48 per cent of the surgical cases were completely cured, and 25 per cent were greatly improved. The figures for the medical cases are 15 per cent cured, and 43 per cent greatly improved.

The value of these results may be criticised in that some of the cases are too recent for a complete cure to be claimed. The same doubt exists, however, in regard to both the medical and the surgical cases, and does not affect the pertinency of the comparison. Furthermore, while some of the more recent cases, who now regard themselves as cured, may possibly suffer relapse later, there are doubtless others, now classified as "improved", who will claim a complete cure at a later date.

No definite conclusions may be drawn from a comparison of the number of failures of medical and surgical treatment in this series. The "derelicts" appear to be about equally divided. The clause "unable for work" in/

in Class D, doubtless drew to this class several patients, whose unfitness was due to some outside cause. In 5 cases, information to this effect was supplied by the patient.

In the small series of cases investigated, where gastro-duodenostomy had been performed, the results of this operation could not be shown to equal those of gastro--enterostomy.

In 65 per cent of the cases investigated, post--operative treatment, in the form of restricted diet and alkaline medication, was abandoned within six months of the operation. While very little guidance is available as to what may be regarded as the necessary duration of such treatment, six months cannot be looked upon as an error on the side of safety. It seems reasonable to suggest that, if treatment had been continued over a more prolonged period, the number of unsatisfactory results recorded would have been considerably less.

In general, the results of treatment of the chronic duodenal ulcer, must be regarded as disappointing. It is difficult to foresee to what extent improvement may be expected, from further advances or elaborations in medical or surgical treatment. In the writer's opinion, our hopes for the future must rest almost entirely upon the prospect of a closer co-operation between Physician and Surgeon, than has hitherto been attained.

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