A GASTROSCOPIC STUDY OF RADIOLOGICALLY NEGATIVE DYSPEPSIA*

BY

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In 1937, when reviewing the diagnoses made in digestive disorders in my last 10,000 out-patients (Bulmer, 1938), I was concerned to find the unsatisfactory state of what might be called the "gastro-duodenal" group: those cases which had symptoms suggesting disturbed functions of stomach or duodenum. In about one-third of these patients the diagnosis I had made was tentative and the significance of the symptoms was unexplained, even after a careful consideration of the history, physical state, x-ray examination of stomach and duodenum, and occasionally a fractional test meal or cholecystogram. The figures are given in Table I, and they need little comment. Chronic gastritis was diagnosed without gastroscopy; therefore its presence remains conjectural. That so large a group was called "dyspepsia of uncertain origin" has been a matter for later self-congratulation, as gastroscopy showed that the usual diagnosis of "gastric neurosis" would have been inaccurate in more than half.

TABLE I.—The Diagnoses in 1,575 "Gastro-duodenal" Cases

<i>Group A, Definite: 966 (61%)</i>					
Gastric and duodenal ulcer	..	..	..	..	859
Gastric cancer	..	..	..	..	89
Acute gastritis	..	..	..	..	18
<i>Group B, Indefinite: 589 (38%)</i>					
Dyspepsia of uncertain origin	..	..	..	..	288
Chronic gastritis	..	..	..	..	111
Aerophagy	..	..	..	..	103
Upper abdominal colic	..	..	..	..	33
Gastroptosis	..	..	..	..	24
Gastric neurosis	..	..	..	..	20
Vomiting of uncertain origin	..	..	..	..	10
<i>Group C, Rare: 20 (1%).</i>					

In January, 1938, the Department of Surgery of the University of Birmingham placed an 85-degree Wolf-Schindler flexible gastroscope at my disposal, and I determined to make a systematic study of such cases as would fall into Group B in Table I. The majority of the patients were drawn from my out-patient department, and I attempted to get a consecutive series, although this was not always possible. Latterly the work has been much facilitated by the use of a 50-degree Wolf-Schindler gastroscope which has been bought by the hospital; the greater magnification obtained with this instrument has enabled a more adequate inspection of the gastric mucous membrane to be made.

Table II gives an analysis of my personal series, and in extenuation of the failures the inclusion of Table III may be permissible,

TABLE II.—An Analysis of the 250 Patients Gastroscooped to April 20, 1939

Radiologically negative or inconclusive dyspepsia	..	147
Duodenal ulcer	..	14
Gastric ulcer	..	38
Gastric cancer	..	7
Miscellaneous—anaemia, dermatitis, gall-bladder disease, post-operative gastric conditions, neurosis, etc.	..	29
Failure to make an adequate examination (excluding 9 in radiologically negative dyspepsia group)	..	15

* Based on a paper read on May 27, 1939, at a meeting of the Association of Physicians in Birmingham.

TABLE III.—The Reasons for Failure to make an Adequate Examination in 24 Patients

<i>Gastroscope passed into stomach (16)</i>					
Poor view in stomach	..	..	..	..	7
Stomach indistensible	..	..	..	..	3
Pyloric stenosis	..	..	..	..	2
Patient coughed	..	..	..	..	2
Pain produced in epigastrium	..	..	..	..	1
Light failed	..	..	..	..	1
<i>Gastroscope not passed into stomach (8)</i>					
Patient non-cooperative	..	..	..	..	5
Spasm of oesophagus	..	..	..	..	2
Pain produced in throat	..	..	..	..	1

Radiologically Negative or Inconclusive Dyspepsia

Cases in this group must be familiar to everyone. Some seek advice because of symptoms so definite that diagnosis of peptic ulcer is made but remains unconfirmed by the radiologist; others have symptoms of a much less definite character—discomfort in the upper abdomen related to meals, nausea, vomiting, perhaps disturbances of appetite; others again may be under treatment for unexplained haematemesis or melaena; in yet another large group a physical explanation of the varied symptoms seems doubtful, yet there is sufficient justification for a radiological examination. As has been already admitted, my own efforts in the diagnosis of a group comprising one-third of my hospital gastro-duodenal series have been unsatisfactory. During the past fifteen months opportunities have presented themselves for the gastroscopic study of 147 patients with radiologically indefinite dyspepsia. The results have been most interesting from the diagnostic standpoint, as in more than half the cases organic disease of the stomach has been found which could have been detected in no other way.

Table IV summarizes the gastroscopic results in the patients personally examined, and some explanation is necessary. In sixty-six patients no abnormality was found, and this has been expressed in so many words in order to leave open the possibility of some abnormality being present; an increasing experience of gastroscopy has made me increasingly reluctant, as in other spheres, to accept a negative finding as significant. The contractions of the pylorus still arouse wonder, but it is tinged with apprehension when the lesser curvature of the antrum refuses to unfold itself: in one of my apparently normal cases an unseen ulcer perforated there. Other blind areas exist, and an ulcer known to be present may not be seen by the gastroscopist. I have been most careful in the diagnosis of chronic gastritis, and I have demanded a gross departure from the normal before so diagnosing a case. I am satisfied that there would be no dispute about the presence of gastritis in the series, although there might be differing opinions as to its type.

TABLE IV.—The Gastroscopic Findings in 147 Cases of Radiologically Negative or Inconclusive Dyspepsia

No abnormality found (in one case an ulcer later perforated)	..	66
Chronic gastritis	..	60
Failure to make an adequate examination	..	9
Gastric ulcer	..	8
Simple ulcer later shown to be an ulcer-cancer	..	1
Curious abnormality later shown to be an ulcer	..	1
Cancer suspected (not found at operation)	..	1
Inoperable cancer	..	1

The series has been further subdivided into two groups according to whether the x-ray findings were negative or inconclusive.

RADIOLOGICALLY NEGATIVE DYSPEPSIA

Whilst convenient, this term is not strictly correct, as in most of the patients it implies that an x-ray examination of the stomach and duodenum gave a negative result; in view of the frequently atypical manifestations of gall-bladder disease I doubt whether the term is applicable until a cholecystogram has also proved negative. The results are rather striking: almost half the patients were found to have abnormal stomachs, the abnormality being such that there was every reason to think that it gave the explanation of their symptoms. Gastritis was the condition most commonly found, and the discovery of gastric ulcers in six patients is a proportion confirmed by other gastroscopists. Gastroscopy in no way detracts from the value of radiology, and it is unlikely that a gastric ulcer will escape detection if both methods are used, although one instance of this has occurred.

TABLE V.—*The Gastroscopic Findings in 117 Cases of Radiologically Negative Dyspepsia*

No abnormality found (in one case ulcer later perforated)	..	..	..	..	..	59
Chronic gastritis	..	..	..	..	..	45
Gastric ulcer	..	..	..	..	..	6
Curious abnormality later shown to be an ulcer	..	..	..	..	..	1
Failure to make an adequate examination	..	..	..	..	..	6

RADIOLOGICALLY INCONCLUSIVE DYSPEPSIA

This is a considerably smaller group, and Table VI needs little amplification. Two-thirds of the patients had a gastroscopic abnormality; one case of ulcer-cancer was thought, both by myself and by the surgeon, to be innocent, and its true nature was not recognized until a microscopical examination was made. Gastroscopy has no value in the diagnosis of duodenal ulcer, and the "doubtful duodenal ulcer" cases are included to show the gastric abnormalities which were found in them; a duodenal ulcer may have also been present.

TABLE VI.—*The Gastroscopic Findings in 30 Cases of Radiologically Inconclusive Dyspepsia*

X-ray Findings		Gastroscopic Findings	
Early cancer 7	{	Gastritis	4
		Ulcer	1
		Inoperable cancer	1
		Ulcer—later shown to be cancer	1
? Duodenal ulcer 9	{	Gastritis	5
		Normal	2
		Ulcer	1
Rapid emptying ? leather bottle 1	{	Failed	1
Normal stomach (one-third retention in 4 hours) 1		Normal	1
Suggests gastritis 5	{	Normal	1
		Failed	2
		Cancer (not confirmed)	1
Spasm in front of pylorus 6	{	Gastritis	2
		Normal	2
Very shallow posterior wall depression, suggesting surface ulceration 1	{	Gastritis	4
		Gastritis	1

The Types of Gastritis Encountered

Table VII shows the types of gastritis found. Schindler's classification (Schindler, 1937; Schindler and Ortmayer, 1936) is used, but as I experienced difficulty in some of the cases an indeterminate group has been introduced. The atrophic type is simple to diagnose in its developed form, while the other types are easy to recognize as being examples of gastritis, but difficult to fit into a classifica-

tion. I have been specially impressed by the rarity of Schindler's hypertrophic form, and here I would emphasize that this name is applied by other gastroscopists to a variety which in no way resembles Schindler's account or his illustrations of it. This is a source of some confusion in reading the literature, and it would make for clarity if each writer would explain his classification.

TABLE VII.—*The Types of Gastritis found in 46 Patients (Schindler's Classification)*

Atrophic gastritis	3
Chronic hypertrophic gastritis	8
Chronic superficial gastritis	30
Indeterminate types, not atrophic	5

Some Clinical Considerations

Perhaps the important outcome of this study has been the recognition of chronic gastritis as a common cause of obscure dyspepsia; but the way has been tedious, an expensive instrument is necessary, and a good deal of time has to be spent upon an examination which requires experience in both interpretation and technique. It is difficult to foresee any short cut to the diagnosis of chronic gastritis, as the history, gastric chemistry, and radiological examination are all inconclusive, and an inspection of the gastric mucous membrane is essential. While, for example, the causes of chronic hoarseness are well known, no method save laryngoscopy would be considered in diagnosis; even more so is this the case with a relatively superficial lesion like gastritis. Radiology will in the great majority of cases exclude the ulcerative lesions of ulcer and cancer, but even when this has been done diagnosis must remain conjectural unless a gastroscopy is carried out.

The difficulties of making a non-gastroscopic diagnosis of chronic gastritis are well illustrated by the following notes of two patients whose symptoms had something in common.

Case 1.—A married woman aged 40 was referred to me by Dr. Mildred Russell of Walsall. She had a long history of dyspepsia, worse during the last two years, and complained of distension after meals, of a poor appetite, and of loss of weight perhaps due to her very restricted diet. Examination revealed only an anaemia shown to be microcytic, and radiographs of the stomach and gall-bladder were negative. Gastroscopy showed a severe gastritis corresponding to Schindler's chronic hypertrophic type.

Case 2.—A single woman aged 52 was referred to me by Dr. Willett of Kidderminster on account of dyspepsia which had been present for many years. Her chief symptom was of constant nausea associated with acid eructations, but the appetite was good and pain was present only during an occasional attack of diarrhoea. Examination was negative, radiographs of the stomach and gall-bladder were quite inconclusive, and a fractional test meal showed a low free acidity. I felt fairly confident that chronic gastritis accounted for the symptoms, but gastroscopy failed to reveal any abnormality of the gastric mucous membrane.

Two patients with severe dyspepsia came under observation after the crisis of September, 1938, and they again demonstrate very clearly the pitfalls in the way of a clinical diagnosis of gastritis.

Case 3.—A man aged 50 was referred to me by Dr. Bence of Birmingham with a view to gastroscopy. He had always been highly strung and had had two nervous breakdowns. During the crisis he was chief air warden for his district, and he began to get nervous and anxious owing to the difficulties of the position. He developed hunger pain and, later, lost his appetite and began to lose a little weight. Physical examination was negative, but a radiograph showed hyper-

trophy of the folds of the upper third of the stomach with an irregularity on the lesser curvature—the radiologist suggested a gastritis with perhaps a small ulcer. While the psychological aspects of the case were obvious on talking to the patient, the symptoms and inconclusive x-ray report raised questions of grave import. Gastroscopy showed a severe superficial gastritis with numerous gastritic ulcers, but the changes were chiefly in the distal parts of the stomach, and there was no hypertrophy of the folds, so that the x-ray report suggesting gastritis did not correspond either in position or character to what was seen in the mucous membrane.

Case 4.—A man aged 48 was seen in consultation with Dr. P. W. Tait of Sutton Coldfield on October 4, 1938. He had had a digestive upset in 1937, which began with complete loss of appetite, vomiting after food, and a sense of dull irritation in the epigastrium. The condition cleared up in two weeks, but a radiograph showed a normal gall-bladder, with a duodenal deformity suggesting an ulcer. He had a similar attack, immediately after the crisis, during which I saw him. I had difficulty in accepting his symptoms as being due to a duodenal ulcer, and with Case 3 fresh in my mind I made a diagnosis of gastritis. I was asked to see him again in March, 1939, as he had had three or four slighter attacks of the same type as before, during one of which he had melaena. He was investigated thoroughly in view of these events; a fractional test meal showed a very high free acidity, and a radiograph revealed a marked duodenal deformity, but gastroscopy failed to show any abnormality in the stomach; there were no signs of gastritis. At the operation by Mr. H. H. Sampson a very chronic and adherent duodenal ulcer was found and dealt with appropriately.

Cases 3 and 4 illustrate both the psychogenic basis of some dyspepsias and the fallacies in the way of making a clinical or radiological diagnosis of gastritis. Case 3 is especially interesting and recalls the work of Cullinan (1938) and Wittkower (1938) on the psychogenic factor in ulcerative colitis. It is unfortunately outside the scope of this paper to pursue the clinical aspects further, but the few illustrative cases may vivify the monotonous series of tables.

Summary and Conclusions

In 1,575 "gastro-duodenal" cases, culled from nearly 10,000 new out-patients, an indefinite diagnosis was made in 38 per cent.

Using the Wolf-Schindler gastroscope, 147 patients with radiologically negative or inconclusive dyspepsia have been studied; the series is almost consecutive.

The gastroscope has proved to be of great value in the routine investigation of this type of dyspepsia, and in about one-half of the patients an organic lesion of the stomach has been seen: usually a chronic gastritis of the superficial or hypertrophic types, atrophic gastritis being much less common.

Chronic gastritis can only be diagnosed with certainty by gastroscopy, and four case histories are given to emphasize the difficulties of clinical diagnosis.

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The Association of Port Health Authorities of the British Isles has published a pamphlet on the prevention of infestation of ships by the bed-bug. The illustrations in this are reproduced from the Ministry of Health *Memorandum on the Bed-Bug and How to Deal with It*. Requests for copies should be addressed to the honorary secretary of the Association, City Hall, Cardiff.

PROBLEMS OF CHANCE IN MEDICINE AND RESEARCH*

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In 1936 Mainland published an interesting paper in which attention was drawn to the frequency with which problems of chance in clinical medicine were ignored or falsely estimated. He formulated a method by which the odds could be calculated, even in small series, for or against a certain eventuality. Our reasons for doubting the validity of this method are given under the heading of "Statistical Appendix," where they are open to the criticism of statisticians. It is our intention in this paper to present a more exact method of estimating significance in a form easily accessible to those who are not conversant with statistical methods.

Significance

The term "significance" is widely and loosely used by many writers; to statisticians, however, it means something very definite—namely, "What are the odds against this result being due solely to the workings of chance?" As a first illustration, let us take two series of 100 patients in an epidemic of, say, influenza. It is assumed that these series are equivalent in every known respect and that they are observed during the same period of the epidemic and are subjected to precisely the same treatment. The mortality in one series is 15; what mortality may we expect in the other? If 15 die in the other series the agreement is closer than one can reasonably expect; with mortalities of 13, 14, 16, or 17 no surprise would be felt. But what if 35 die in the second series? There would be little hesitation in looking for an unknown factor—a "cause" for this difference in mortalities. Now somewhere between 17 and 35 in the present example there must be drawn a borderline separating differences which would arise so frequently in sampling that we may ascribe them to chance, and differences which would occur so seldom that some other cause must be sought.

The type of problem we are considering, then, is one where we want to know the answer to the following question: "What are the odds against 20 or more, 21 or more, 22 or more, etc., deaths in the second series?"

When these odds become great—for example, 199 to 1—we assume that chance has had very little to do with the matter, and some other factor must be responsible for the difference. An arbitrary line must therefore be drawn somewhere, and odds in excess of this arbitrary value counted as "significant." This is precisely what is done in statistical tables: the term " $P = 0.05$ " simply means that the probability (P) of such an eventuality happening through the workings of chance is 5 in 100, or, in betting parlance, "19 to 1 against." This is the borderline arbitrarily made between chance differences and significant differences.

In the table which we give two limits of significance are used—0.05 and 0.005. These are equivalent to odds of 19 to 1 and 199 to 1 respectively. The smaller figure in each cell, which represents the lower odds, is the

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