omission of these 17 cases from the appropriate categories makes no difference to the general trend of the results.

Serum reactions were noted in only 3 of the 114 patients in the series treated with antitoxin; these occurred after some hours or days in the form of a rash or pyrexia, and apparently gave no cause for anxiety.

General Remarks

The reduction of the fatality rate in the group receiving both surgical treatment and antitoxin can be reasonably held to establish the value of antitoxin in the treatment of gas gangrene. It is to be hoped that with a more effective use of antitoxin the fatality rate of 45% for treated cases will fall considerably. Speed in the administration of antitoxin is clearly essential for good results, but it is no less important that the amount of antitoxin given should be adequate for the individual case, since the neutralization of toxin by antitoxin is a quantitative reaction. It has been recently recommended (*M.R.C. War Memorandum No. 2*, revised second edition, 1943) that the initial therapeutic dose of polyvalent antitoxin should be not less than 50,000 units; the figures in Table VII indicate that, though often enough such a dose may be more than ample, it is not excessive as a routine.

The clinician still has the onus of judging quickly whether the dose given has been sufficient to neutralize all the toxin—that is to say, whether a previously rapidly progressive toxæmia has been arrested—or whether the dose of antitoxin has been insufficient and the progress of toxæmia is still acute. Delay in the neutralization of the toxin present cannot be compensated by giving an excess of antitoxin at a late stage; on the other hand, since the individual capacity to recover from the effects of toxæmia is incalculable, there is no justification for withholding an adequate dose of antitoxin from a patient received late for treatment, however small the chance of recovery may be. In the treatment of gas gangrene the probability should be borne in mind that the amount of toxin present in the body is increasing so long as the infection is spreading in the affected tissue. A patient received late for treatment, or one in whom surgical and chemotherapeutic measures have not been completely effective in eradicating the infection, may therefore need heroic or repeated doses of antitoxin, not because an excess has at any time a beneficial effect, but because an amount equivalent to the toxin present is the dose justifying a hope of recovery. This is entirely different from deprecating the continued administration of large doses of antitoxin to a patient in whom the infection has been controlled and the effects of the toxæmia are already vanishing.

Patients in whom the site of gas gangrene involved the thigh, buttock, or abdomen showed a poorer response to doses of antitoxin of the order recommended than those in whom the site was more favourable to the elimination of the infection both by the surgeon and by Nature. These findings support the recommendation that surgical treatment should be supplemented by chemotherapeutic measures as well as by antitoxin therapy, and point to the need for local chemotherapeutic agents more effective against clostridia than the sulphonamide drugs alone.

Summary

The value of antitoxin in the treatment of established gas gangrene has been examined in a series of 139 cases in which the patients were suffering from toxæmia to a marked degree. The fatality rate was significantly lower among the patients who received antitoxin, and this difference between treated and untreated cases persisted in those who received major surgical treatment, including a group in whom the site of primary infection was rapidly extirpated by amputation. The combined use of surgery and antitoxin was therefore more effective than that of surgery alone.

The effect of antitoxin was more pronounced in those who received the initial therapeutic dose soon after diagnosis, but this difference was probably due not only to the speed of administration but also to the fact that a greater proportion of the patients in this group received a large total dosage (50,000 units or more) of antitoxin.

The fatality rate of the patients who received no major surgical treatment was nearly 100%, and in the cases reported here the rate in this group was not reduced by antitoxin therapy. Patients in whom the site of the gas gangrene involved the thigh, buttock, or abdomen showed a poorer response to doses of antitoxin of the

order recommended than those in whom the site was more favourable to the elimination of the infection.

These results emphasize the necessity for the early and combined use of surgery, effective chemotherapy, and antitoxin in the treatment of gas gangrene.

This evaluation of antitoxin in the treatment of gas gangrene has been made possible by the work of the medical officers who reported their cases, often in difficult conditions. Thanks are due to the Medical Directors-General of the three fighting Services and the E.M.S. for making the case records available for analysis. I am greatly indebted to Prof. M. Greenwood and Dr. E. Lewis-Faning for their constructive criticism and for the verification of the significance of the data; to Mr. C. H. S. Frankau for his advice on the clinical aspects; to Dr. F. H. K. Green for his help in preparing this report; and to Lieut.-Col. H. J. Bensted for much useful information. It is a pleasure also to thank Major-Gen. L. T. Poole and the members of the Anaerobic Wound Infection Subcommittee for their criticism and many illuminating discussions.

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DYSPEPSIA: AN INVESTIGATION

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The enrolment into the Forces of most of the young manhood of the country has presented us with an opportunity for statistical investigation of some of the commoner ailments. The immediate demands of warfare are so far uppermost that the clerical assistance necessary for statistical research cannot be spared. Thus little can be done towards elucidating the medical problems which in civilian life were so urgent and which we shall have to face again in the years of peace. One of the most important of these problems from a sociological and industrial standpoint is dyspepsia. In the years preceding the war the project of a research centre for gastric disorders was very much before the mind—a centre whose sole object was research into the causation of these disorders. The clinical, radiological, biochemical, and sociological data were to be collected and collated, and submitted to statistical analysis.

An opportunity of doing something along such lines presented itself at a military hospital. A scheme was devised and put into practice which had a twofold object: (1) to make some contribution to the immediate problem of dyspepsia among the troops the hospital served; (2) to furnish data for statistical research. A "gastric board" was formed consisting of the officers in charge of the medical and surgical divisions, the medical specialist, the radiologist, the pathologist, the psychiatrist, and a general-duty officer.

All dyspeptics were admitted into a 30-bed ward for investigation. None was treated there—an important point, and a partial answer to the criticism levelled against the segregation of dyspeptics. The general-duty officer examined each patient on admission, and took the history according to an agreed schedule. The whole worth of the scheme depends upon the way this part of the work is done, and it requires for its performance a medical officer of ability who is really interested in the problem. In the present instance we were fortunate in having the services of Capt. (Miss) Phoebe Charlton, who, except during brief periods of leave, was responsible for all the histories taken. Within five days of admission each patient was x-rayed (Major Baird; later Major Wearing), and test-meal and occult-blood examinations were done (Major Roper; later Major Stewart). The board met weekly, and saw and discussed each case, and decided upon disposal. If indicated gastroscopy was performed. Cases in

which there was no evidence of organic disease or in which there seemed to be a psychological background were sent for interview with the psychiatrist (Major Barber; later Lieut., now Major, Stungo). It was the duty of the medical specialist (Major Slot; later Major Cherniack) to examine each patient from the general standpoint, and to prevent the board from falling into the error of attributing all symptoms to the stomach or duodenum.

After 12 months, during which 436 patients were seen, the data were collected and submitted for analysis. Through the agency of Lord Dawson of Penn, Mr. W. J. Martin, of the Division of Epidemiology and Vital Statistics of the London School of Hygiene and Tropical Medicine, paid a brief visit to the hospital and took away the case sheets for analysis. The policy of having the analysis made by a disinterested and unbiased worker was deliberate. It resulted, however, in certain unforeseen disadvantages—for example, the "lumping" together of gastric and duodenal ulcers, and difficulty in interpreting the data on gastric analysis (which for this reason has been omitted from Mr. Martin's report). It is now realized that a closer liaison between clinician and statistician would have been an advantage.

For reasons of space it is not proposed to publish the actual figures furnished by the statistician, excepting one table as a specimen; we shall confine ourselves to quoting the headings and a statement of what the figures tended to show. Unfortunately, it was impossible to obtain data from a similar age group of non-dyspeptics to act as a control.

Analysis of Cases

There were 436 cases in all. These were divided into two groups—139 ulcer and 217 non-ulcer cases. The remaining 80 cases were not included in the statistical analysis: in 65 no diagnosis had been made, as evacuation interrupted investigation, and in 15 the symptoms were thought to be due to a lesion other than one affecting the stomach or duodenum.

The Ulcer Group.—We accepted the following criteria in making the diagnosis of ulcer: (1) the presence of an ulcer crater in the radiograph; (2) a typical clinical history, with high acidity and positive occult blood (even if the radiological diagnosis was doubtful or negative); (3) a previous history of perforation; (4) visual evidence at gastroscopy—this, of course, only in the case of gastric ulcer.

The Non-ulcer Group.—In this group were placed all cases complaining of dyspeptic symptoms in which there was no radiological evidence of an ulcer and in which the clinical evidence of ulcer was insufficient. Most of the cases were gastroscopied. The 217 cases are made up as follows:

No physical disease detected (functional dyspepsia)	..	..	180
Gastritis (diagnosed at gastroscopy)	..	..	23
*Duodenitis or duodenal enteritis	..	..	9
Gastro-enterostomy	..	..	3
Pyloric spasm	..	..	1
Hypersecretion and hyperchlorhydria	..	..	1

*Radiological diagnosis.

It is probable that some of the cases in the non-ulcer group actually had a duodenal ulcer. For instance, in one case an operation for perforated duodenal ulcer was performed at another hospital within a week of discharge. It is thought unlikely that many cases of ulceration were overlooked, however, though it must be admitted that the influence of pending medical boards was felt considerably, for few of them are prepared to accept a diagnosis of duodenal ulcer unless there is definite radiological evidence of it. There is no doubt that the frailties of radiological diagnosis of duodenal ulcer are not sufficiently recognized.

Findings

1. **Civilian Occupations.**—No difference in the two groups (ulcer and non-ulcer) was found relating to occupation except in the case of miners, in whom the percentage in the ulcer group was 2.9 (4 out of 139) and in the non-ulcer group 7.4 (16 out of 210). There is thus a suggestion that miners may be subject to a type of dyspepsia in which localized ulceration does not occur.

2. **Marital State.**—The incidence of both ulcer and non-ulcer dyspepsia appears to be equal in single and childless married

men. Ulcer dyspepsia is, however, relatively more common than non-ulcer dyspepsia in men with two or more children. This is probably due to the fact that the mature married man is less likely to seek treatment unless he has definite cause.

3. **Rank.**—Private soldiers in the non-ulcer group numbered nearly twice those in the ulcer group (172 : 98), whereas there were rather more N.C.O.s (lance-corporals, corporals, and sergeants) with an ulcer than those without (38 : 34). There are two explanations for this: (a) the selection of the best types for promotion; (b) responsibility diminishes the tendency to report sick without adequate cause.

4. **War Service.**—One-third of the cases in each group were Regulars or Reservists and two-thirds were war enlistments. In about one-third of the cases in both groups (ulcer and non-ulcer) the symptoms began during civilian life. There is thus no evidence that Army service has any influence upon the development of non-ulcer dyspepsia as opposed to ulcer dyspepsia. This is a point of interest, for it suggests that functional dyspepsia is as common, relative to organic dyspepsia, in civilian as it is in Army life. It is possible, indeed probable, that more use is made of it in Army life in order to evade the performance of duties.

5. **Family History of Dyspepsia.**—As expected, this is common, and occurs almost equally in both groups (ulcer in 57% and non-ulcer in 54.3%).

6. **Duration of Symptoms.**—There was no difference between the two groups in the duration of symptoms, which averaged six years. Both the age at onset of symptoms and, it follows, the age when seen were earlier in the non-ulcer group.

7. **Habits.**—There were few heavy drinkers and few teetotallers—most drank beer in moderation. Likewise with smoking. The largest group was in fact composed of those who drank and smoked moderately—61.6% of the ulcer patients and 61.2% of the non-ulcer patients. This does not suggest that smoking and drinking are not a factor in the cause of dyspepsia—a comparison of non-dyspeptic cases would be of especial value here—but that whatever part these habits may play is equal in both ulcer and non-ulcer dyspepsia. In both groups two-thirds of the patients stated that their meals were regular.

8. **Symptoms.**—(a) *Pain in relation to food:*—The average interval between food and pain was much higher in the ulcer than in the non-ulcer group, and the presence of a considerable period of freedom after food is significant of ulceration. (b) *Nocturnal pain:*—This was significantly more common in the ulcer group, and emphasis is laid upon this. If the patient is awakened by pain an hour or two after falling asleep and the pain is alleviated by taking something by mouth the probability of an ulcer is high. (c) *Miscellaneous:*—There was no significant difference between the two groups in the following: appetite—good in 57% of ulcer and 55% of non-ulcer patients; nausea—present in 82% of ulcer and 85% of non-ulcer patients; vomiting—present in 71% of ulcer and 76% of non-ulcer patients; flatulence—present in 79% of ulcer and 82% of non-ulcer patients. It is a matter for some surprise that vomiting is so common a symptom of an uncomplicated ulcer. In most cases, however, it was only an occasional incident.

9. **Relation of Symptoms to Food and Alkalis.**—The findings here are significant, and the statistician's figures and remarks are given in full.

Reaction to Food and Alkalis

	Ulcer		Non-ulcer		Difference Ulcer/Non-ulcer
	No.	%	No.	%	
Food:					
Relieved by food	92	71.9	70	42.7	29.2 ± 5.9; significant
Not relieved	36	28.1	94	57.3	
Total	128		164		
Alkalis:					
Relieved by alkalis	99	77.3	101	61.6	15.7 ± 5.5; significant
Not relieved	29	22.7	63	38.4	
Total	128		164		

Difference between percentage relieved by alkalis and percentage relieved by food:

Patients with ulcers, 5.4 ± 5.4; not significant.
Patients without ulcers, 18.9 ± 5.5; significant

Distributions

	Ulcer			Non-ulcer		
	Alkalis		Total	Alkalis		Total
	Relieved	Not Relieved		Relieved	Not Relieved	
Food:						
Relieved ..	78	14	92	55	15	70
Not relieved ..	21	15	36	46	48	94
Total ..	99	29	128	101	63	164
	$\chi^2 = 8.8756$ $P = 0.01$			$\chi^2 = 13.6682$ $P = 0.01$		

Remarks by Statistician: The percentage of patients with ulcers who were relieved by food and alkalis was statistically significantly larger than in the group without ulcers. The percentage relieved by alkalis was not significantly larger than the percentage relieved by food in the group with ulcers. In the group without ulcers the percentage relieved by alkalis was significantly greater than the percentage relieved by food. The χ^2 's show that there is a relation between food and alkalis; the numbers who reacted in a similar way to both food and alkalis were larger than would be the case if the reaction of food and alkalis were independent.

The findings are clear-cut:—In most ulcer cases the pain is relieved by both alkalis and food. In the non-ulcer cases food usually fails to relieve but alkalis usually do. These findings are of the greatest diagnostic importance.

10. *X-ray Diagnosis.*—It should be noted that the 9 "negative" cases of ulcer were those in which either the clinical evidence was sufficient for a diagnosis or, in cases of gastric ulcer radiologically negative, diagnosis was by gastroscopy. The two terms "duodenitis" and "duodenal enteritis" crept in because of a change of radiologist. They are, we believe, synonymous, though we put little faith in either diagnosis.

	Ulcer	Non-ulcer
Negative ..	9	169
Inconclusive ..	4	12
Ulcer ..	119	—
Gastritis ..	—	9
Hypertrophic gastritis ..	—	1
Gastro-enterostomy ..	1	2
Duodenitis ..	1	7
Duodenal enteritis ..	—	2
Deformity of stomach (external causes) ..	—	4
Cholecystitis ..	—	1
? Adenoma ..	1	—
Congestion ..	1	—
? Prepyloric ulcer ..	—	1
	136	208

11. *Gastroscopy and Radiography.*—The gastroscope should be regarded as complementary to radiological examination. Its chief value is in those cases in which the symptoms appear genuine but in which the radiograph is negative, and in cases in which the radiograph suggests a lesion of the stomach but is not conclusive. Twenty-three gastroscopies were done in the ulcer group and 86 in the non-ulcer group. Gastroscopy diagnosed a gastric ulcer on 3 occasions when the radiological diagnosis was in doubt. It diagnosed gastritis on 23 occasions. In these the radiograph was positive in 7 cases, doubtful in 6, and negative in 10. In 3 cases of gastro-enterostomy the radiograph showed a duodenal ulcer in 1 and a normal stoma in 2. Gastroscopy showed evidence of a stomal ulcer in 1 and of peristomal gastritis in 1, passing 1 as normal. The gastroscope is thus an invaluable addition to our means of diagnosis.

12. *Psychiatrist.*—Only selected cases were referred to the psychiatrist—2 of the ulcer-group and 101 of the non-ulcer group. No abnormal psychological state was found in 36 (including one of the ulcer cases). Some evidence of a psychological background was found in the remaining 67, varying from an anxiety state (25 cases) to maladjustment to surroundings (1 case). No conclusions can be drawn from these findings without the psychiatrist's assessment of a similar numerical group with no gastric symptoms, apart from the fact that no one personality type was characteristic.

13. *Previous Operations.*—Of the ulcer cases 23 and of the non-ulcer cases 28 had had an operation upon the abdomen. Of the 23 ulcer operations 7 were for perforation. There was a very significant finding in that of the 51 cases with a history of operation 26 had been for chronic appendicitis. In each case the operation had been done to relieve the symptoms of dyspepsia. We have no means of telling how many "chronic appendices" are successfully removed for this purpose, but the present figures

suggest strongly that the diagnosis of chronic appendicitis is made, and acted upon, too frequently.

14. *Disposal.*—It may be of some interest to include the following details of disposal:

Disposal of 336 Cases

	Ulcer	Non-ulcer
Returned to unit ..	1	116
Returned to unit after period of treatment or convalescent home ..	—	5
Evacuated (convalescent home or hospital) for treatment or observation ..	2	18
Transferred to another unit or change of duties ..	—	18
Prolonged period of convalescent treatment ..	1	—
To be kept under observation and x-rayed in six months' time ..	1	—
Category B (minor disability) ..	—	2
Category C (home service only) ..	4	29
Category E (discharged from the Army) ..	119	20
	128	208

Summary of Findings

Of 356 cases completely investigated 139 were regarded as having a peptic ulcer. Of these, 16 were gastric and 121 duodenal. Of the remaining 217 cases, 37 had evidence of a gastric or duodenal lesion other than ulcer; in 180 no organic lesion was found, and the condition was labelled "functional dyspepsia."

The more significant results of the statistical returns were:

(a) Ulcer was relatively more common than non-ulcer dyspepsia among N.C.O.s than among privates.

(b) There was a family history of dyspepsia in a little over half the patients in both groups.

(c) Duration of freedom from pain after food was longer in the ulcer than in the non-ulcer group.

(d) The pain is relieved by food in nearly three-quarters of the ulcer dyspepsia cases, but in less than half of the non-ulcer dyspepsias.

(e) True nocturnal pain, alleviated by taking something by mouth, is a more pronounced feature of ulcer dyspepsia than of non-ulcer dyspepsia.

(f) Gastroscopy is an invaluable aid in diagnosis.

(g) Of 103 patients referred to the psychiatrist (only 2 had ulcers) evidence of a psychological background was found in 65%.

(h) 26 of the patients had been operated upon previously for chronic appendicitis without relief from their dyspeptic symptoms.

Commentary

How did the scheme serve the two objects for which it was intended?

As a help to the immediate problem of dyspepsia in the Army, it was a success. The special features were: (a) The formation of a team to represent various aspects of knowledge. (b) Admission of patients for investigation only. They were kept on normal diet unless this was contraindicated; very few cases were treated. Investigation was carried out expeditiously and on an organized plan. (c) Rapid decision as to disposal. The president of the medical board in making the final decision in cases recommended as Category E was helped materially by the fusion of all the expert opinion available.

As a method of research the project is sound, but in the way it was carried out there are defects, which this experience should enable us to correct in future. The two chief lessons are: (a) a medical statistician should be employed; (b) a constant control should be kept of healthy men in similar age groups.

Our thanks are due to Col. M. J. Williamson, M.C., late R.A.M.C., for permission to publish, to Lord Dawson for his interest and help, and to Mr. W. J. Martin for his masterly analysis of the data.

W. H. Gordon, F. B. Parker, jun., and S. Weiss (*Arch. intern. Med.*, 1942, 70, 396) record their observations on three cases of gummatous aortitis in patients aged from 35 to 42. In the first case the gummatous process completely occluded the right coronary artery and partially occluded the left one. In the second, gummatous lesions were present also at the base of the aortic valve; and in the third an extensive gummatous process affected not only the aorta but the pulmonary artery. Symptoms of gummatous aortitis such as dyspnoea, orthopnoea, precordial distress, cardiac asthma, pulmonary oedema, and haemoptysis are present only where there is narrowing or occlusion of the coronary arteries.