Test-meal findings have not been adequately reported, but we find three of them normal except for slight hypochlorhydria.

No neurological changes have been found by any observer. Finally we regard the dramatic and permanent response to transfusion as the outstanding diagnostic criterion.

Differential diagnosis from pernicious anaemia, infective endocarditis, acholuric jaundice, and acute leukaemia would seem to present most difficulty, but the features emphasized should serve to obviate this.

Treatment

Early transfusion is at present the only known therapy which influences the prognosis. This response is well borne out in the preceding account of our cases. A fatal termination is reported by Payne⁴ after transfusion in a severe case, despite satisfactory compatibility tests.

Recently a case has come under our care in extremely grave condition, where it was impossible to transfuse owing to incompatibility with a large series of tested donors. This patient died two days after admission, and complex post-mortem findings are being investigated.

Witts and O'Donoghue stressed the need for further knowledge of response to liver therapy. Cases I, II, and IV demonstrate conclusively that there is no response to intensive treatment by this haematinic factor.

Conclusions

Four cases of haemolytic anaemia of Lederer have been described.

It is probable that this condition is more frequent than is generally recognized, and that full investigations should be undertaken of all anaemias prior to treatment. Reticulocyte counts are of value in differential diagnosis. Liver therapy can only be of value in treatment of anaemia where the haematinic factor is absent—that is, in pernicious and the allied anaemias.

The therapeutic value of transfusion has been stressed.

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- ² Parsons, L. G., and Hawksley, J. C.: *Arch. Dis. in Child.*, 1933, viii, 184.
- ³ O'Donoghue, R. J. L., and Witts, L. J.: *Guy's Hospital Reports*, 1932, lxxxii, 440.
- ⁴ Payne, R. V.: *Ibid.*, 1934, lxxxiv, 65.

K. A. Seggel (*Münch. med. Woch.*, June 7th, 1935) gives an account of the blood transfusion service organized in connexion with the University Hospital in Leipzig. At first patients with minor ailments and members of the hospital staff served as donors. Now a regular panel has been organized, and every would-be donor (men between the ages of 21 and 50) has to undergo a searching medical examination which is repeated every three months. To be acceptable, donors must have at least 80 per cent. haemoglobin, 4.5 million erythrocytes, a normal leucocyte count, with no left displacement or eosinophilia. There must be no evidence of any infectious disease, and at every re-examination the donor is required to sign a statement to the effect that he has not acquired venereal disease, malaria, or other communicable disease since the last examination, and that he knows nothing of any such disease in his family. A criminal record or an ancestry not purely Aryan is a disqualification for a would-be donor. Blood is paid for at the rate of 5 Reichsmarks per 100 c.cm., and it has been found fairer to pay on this scale than to give a fixed sum per transfusion of any quantity of blood; for when frequent transfusions of small quantities of blood are given, such a rigid system of payment would be too expensive for the patient. The donor is not expected to part with more than 400 c.cm. at a time; only in an emergency and with his express consent can he be asked to provide more.

THE HISTIDINE TREATMENT OF PEPTIC ULCER OF THE LESSER CURVATURE

WITH A NOTE ON TWELVE CASES *

BY

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How seldom in these days does one pick up a medical journal and fail to find an article, an annotation, or correspondence on the much-vexed question of peptic ulcer! The symposium on the subject published in the recent issue of *St. Bartholomew's Hospital Reports*¹ bears testimony to the interest which all sections of medicine have in this difficult problem.

It is gratifying to know that co-operation is gradually replacing antagonism, and one feels that a real advance in knowledge is now made possible. The physician must not forget his able scientific helpers, and the surgeon must cease to think that by operation he cures peptic ulcer. He removes the ulcer area, or by his able craftsmanship he manages to place it out of the line of traffic, but he leaves the individual still the same, although relieved of symptoms, at least for a time. It is a question whether the great advance in surgical technique has not hindered more than helped our knowledge with regard to the aetiology of peptic ulcer. The physician is no less culpable, for by treatment he only allays symptoms and fosters healing, but fundamentally the patient is still prone to relapse.

In the present state of our knowledge—or probably ignorance—we each might be more helpful to humanity if we confessed our shortcomings and concentrated less on friendly rivalry concerning a statistical evaluation of cure. In the past the physician has “cured” peptic ulcer by directing his attack on the factors which prevent healing. By dieting, alkalis, and the exhibition of drugs to depress secretion and relieve spasm, he has undoubtedly promoted healing. The patient, relieved of his symptoms and the immediate danger of active ulceration, has no guarantee that his symptoms will not return and his dangers again make life itself an uncertainty. The unfortunate sufferer has to lead a restricted life, especially as regards diet. It is for reasons such as these that critical examination of any new theories should be explored and treatment based on logical experiment investigated.

Origin of Histidine Treatment

Treatment based on a new conception of the aetiology of peptic ulcer has been instituted recently by Aron,² working in Strasbourg. In his thesis a working hypothesis is based on Mann and Williamson's³ operation for producing peptic ulcers experimentally in dogs. If the natural secretions of the duodenum are diverted into the terminal ileum experimental ulcers develop in the stomach and there are other severe nutritional disturbances, with death of the animals in a few weeks' time. It is argued that these ulcers are caused by the lack of regurgitation of the duodenal contents, but Aron considers it is the lack of certain amino-acids. If tryptophan and histidine are administered by injection ulcers do not develop. Histidine alone has the same effect, but tryptophan has not. Aron found, however, that the latter increases the rate of cicatrization of experimental wounds of the gastric mucosa. He was satisfied with his animal experiments, and clinical investigation on patients was instituted. He records that on normal diet, and with the patients receiving ambula-

* In this study the histidine used was larostidin brand histidine, kindly supplied to me by the Hoffmann-La Roche Chemical Works, Ltd.

tory treatment, there was a disappearance of symptoms and an increase in weight. The treatment has been explored with success by Bogendorfer,⁴ Weiss,⁵ Deloyers,⁶ and Hessel.⁷

Recently Bulmer⁸ in this country has published his results up to date. He states definitely that his report is preliminary, and although his results are on the whole favourable he is drawing no conclusions until some years have passed. In this report I wish to endorse his caution. In a critical examination of any form of treatment it is necessary to review a large number of cases, and this can only be done if different observers will record their results, giving specific information which may be used in a grand summation at a later date.

The histidine treatment of peptic ulcer is new, and it is logical. It is therefore worthy of trial. For these reasons it was decided to try its effect in a small series of cases which fulfilled certain criteria—namely, (1) a history suggestive of gastric ulcer, (2) the exclusion of cases obviously surgical, and (3) unequivocal radiological evidence of ulcer of the lesser curvature.

Case Histories

CASE I

Male, aged 46 years, engineer's labourer, was admitted to hospital on November 30th, 1934, complaining of pain in the stomach after meals, which had troubled him for the past ten years. In 1924 he first became aware of having "indigestion." The discomfort was slight, and he found relief by taking alkali. He paid little attention to his disability until in May, 1933, he became aware of severe pain, burning in character, which came on two and a half hours after every meal. This pain was accompanied by flatulence and water-brash. He had medical treatment, with very little relief. In October, 1934, after the condition coming and going every few weeks, he had a severe relapse. Pain, flatulence, and water-brash were worse than formerly, and he began to have vomiting. There was no blood in the vomitus, but he found that his pain was relieved when he vomited acid-tasting material. At times the taking of food helped to relieve pain. He was constipated, and the faeces were very dark during September and October, 1934. He stated that he had lost a few pounds in weight. Sometimes pain wakened him at night, and he felt sick and brought up sour mouthfuls.

On examination he was ill-looking. He was edentulous and had a furred tongue. There was marked tenderness in the epigastrium and left hypochondrium. Special examination showed hyperchlorhydria, occult blood in the faeces, and a large ulcer of the lesser curvature. He was a ward case and was treated as described. In twenty-nine days, and after twenty injections of larostidin he felt perfectly well. He had increased his weight by 4 lb., there was no occult blood in the faeces, and the stomach was normal after critical screening and examination of films. He was discharged from hospital on January 5th, 1935.

He relapsed on March 13th, complaining of pain, which was felt through to the back. Ordinary treatment was advised, but he became worse, and on March 30th he had a further four injections of larostidin because a small ulcer was seen on the lesser curvature at the old site. After the fourth injection he felt quite well, and remained so. Examination by x rays on April 7th showed the stomach normal, and it has remained so up to date (June 1st). When he relapsed it was found that he had lost 2 lb. in weight, but after his larostidin he gained 4 lb.

CASE II

Male, aged 62 years, crucible builder, was admitted to hospital on December 10th, 1934, complaining of discomfort in his stomach of five years' duration. In 1929 he had a feeling of distension, which he likened to a ball in his stomach. This came on immediately after a meal, and lasted one or two hours. He had no actual pain. Later he began to complain of flatulence, heartburn, and water-brash. His discomforts seemed to bear little relation to the character of the food

taken. He found his greatest comfort in eructations. He did not complain of constipation, and he had no melaena. This indefinite condition continued with short remissions till June, 1934, when he began to have pain at irregular intervals after food. The pain spread from the epigastrium across the upper abdomen. He obtained no relief from food or alkaline mixtures. Gradually the pain became worse, and he was rarely free from it. He felt sick, but had no vomiting. He lost considerable weight, which he estimated at about 2 st.

On examination he was pale and had some palpable glands in his neck, axillae, and inguinal regions. He had a slow, auricular fibrillation, which gave rise to no symptoms. He was edentulous but had artificial teeth. His tongue was clean and his fauces healthy. Palpation revealed tenderness below and to the left of the umbilicus. Special examination showed slight hyperchlorhydria, occult blood in the faeces, and an ulcer of the lesser curvature. He was a ward case, and was treated as described. After seven injections of larostidin he was well except for troublesome flatulence, which came on while he was at his meals. A full course of twenty-five injections was given, but his flatulence did not improve. He was given two tablets of larostidin daily, and his flatulence disappeared in one week. In thirty-two days he was feeling perfectly well. He had put on 7 lb. in weight. There was no occult blood in the faeces, and the stomach was normal after critical screening and examination of films. He was discharged from hospital on February 2nd, 1935.

CASE III

Male, aged 24 years, farm servant, was admitted to hospital on November 25th, 1934, complaining of weakness and of vomiting blood of one day's duration. Seven months before (in April of the same year) he had had pain in the stomach, which came on one to two hours after food. It usually lasted about an hour, and was relieved when he ate more food or took an alkaline mixture. He had no vomiting at that time. This pain continued for three weeks and then became easier, but returned with greater severity in October, 1934. This time he felt sick and vomited, but his pain was not relieved. Three days before admission to hospital he collapsed at his work, and on the day of admission he had a severe haematemesis and fainted. Throughout his illness he was constipated, and for a short time prior to admission he had noticed his faeces dark in colour. He had lost so much weight that he thought he was "in a decline."

On examination he was pale and perspiring. His tongue was moist and clean. The teeth were good and the fauces healthy. Palpation of the abdomen was generally resisted, and this was especially so over the upper region of both recti. There was marked tenderness an inch and a half above the umbilicus in the mid-line. Special examination was not carried out at once owing to the haematemesis. He had marked melaena. He was treated in the usual way for severe bleeding, and on December 25th special examination was carried out. He had a profound secondary anaemia. Gastric acidity was normal. Occult blood was present in the faeces, and an extensive ulcer was present on the lesser curvature. He was now allowed up, and as a ward case was treated as described. Treatment was not commenced until January 12th, 1935, because it was thought that the haematemesis might be a contraindication. As x rays showed no improvement the patient was given a full diet, ferri et ammon. cit. 30 grains t.i.d., and larostidin daily. On January 24th, after twelve injections, the ulcer was hardly seen on the lesser curvature, and occult blood was no longer found in the faeces. Six more injections were given, and on February 1st there was no evidence of ulcer. He was in the ward seventy-three days, but only twenty-four days under larostidin treatment, during which time he had eighteen injections. He tolerated his iron perfectly, and was discharged on February 5th feeling very fit. He had a full blood count, and after careful screening and examination of films there was no evidence of ulcer. He increased his weight 1 st. 12 lb.

CASE IV

Male, aged 54 years, blacksmith, was admitted to hospital on October 21st, 1934, complaining of pain in the stomach going through to the back and accompanied by severe flatulence of twenty years' duration. He had been consti-

pated during the greater part of his life, and in 1914 he experienced a sharp pain in the stomach, which came on after food. He paid little attention to this, and in a month or so it disappeared. In 1919 it recurred, but he did not consult a doctor until 1920. He was given an alkaline powder, and this relieved him. He was not so severely pained during the next eight or nine months, but he was never really happy about his digestion. The pain came on one to two and a half hours after food, and was not relieved by it. He had severe flatulence, but eructations did not ease him. In June, 1934, the pain became very commanding and flatulence "doubled him up." Vomiting commenced, and at times gave him relief. He had lost weight. He was seen as an out-patient on September 17th, and an ulcer was found on x-ray examination. For personal reasons he could not come under observation until five weeks later.

On examination he was ill-looking. He had artificial teeth. The tongue was clean and the fauces normal. The recti were both rigid in their upper thirds. Tenderness was elicited an inch and a quarter above and half an inch to the right of the umbilicus. Special examination showed hyperacidity, occult blood in the faeces, and an ulcer of the lesser curvature. He was a ward case, and was treated as described. In thirty days, and after twenty-nine injections of larostidin, he was feeling perfectly well. He had increased his weight 1 st. 1 lb.; there was no occult blood in the faeces, and after careful screening and examination of films no evidence of ulcer was seen. He was discharged from hospital on November 20th.

CASE V

Female, aged 58 years, housewife, was admitted to hospital on November 5th, 1934, complaining of gnawing pain under the ribs on the left side of eight months' duration. At the beginning of March, 1934, she had begun to lose her appetite, and became aware of a dull, gnawing pain under the left costal margin. It was not very severe and was not constant. The pain had no relation to the taking of food. She had no sickness. Neither food nor alkalis relieved the pain. She was constipated, and very troubled with flatulence and heartburn. She stated that she was losing weight.

On examination she was rather pale, and had a foul breath. Her tongue was dry. Her upper teeth were artificial and her lower teeth much decayed. She resisted palpation in the epigastrium, and there was a localized tender spot just to the left of mid-epigastrium. Special examination showed normal acidity, occult blood in the faeces, and an ulcer of the lesser curvature. She was a ward case, and was treated as described. In twenty-nine days, and after sixteen injections of larostidin, she was feeling perfectly fit. She had increased her weight by 7 lb. There was no occult blood in the faeces, and the stomach was normal after careful screening and examination of films. She was discharged from hospital on December 4th.

CASE VI

Female, aged 59 years, housewife, admitted to hospital on December 15th, 1934, complaining of pain in the stomach with "belching of wind" of two years' duration. In December, 1932, she became aware of indigestion. Pain and flatulence would come on at various times after food, but it had no definite time relationship to meals. Sometimes she vomited, and on other occasions induced vomiting, for she found this relieved her. She obtained relief by means of bicarbonate of soda. The vomitus was sour, but never contained blood. She was constipated. She doctored herself for almost a year, and in September, 1933, attended the surgical out-patient department. She was treated there, but with no improvement. She had some bronchitis, and on x-ray examination an ulcer of the lesser curvature was observed. She was recommended to the medical out-patient department for treatment for her bronchitis and was to return for surgical treatment by operation. At the medical out-patient department, when her bronchitis improved, she was given a scheme of diet and an alkaline mixture. This gave her no relief. She continued to suffer, and in July, 1934, developed asthma, for which she was treated. During the autumn of 1934 she became worse, and surgery was considered, but it was thought that she should have ward treatment for her chest and then be transferred to a surgeon.

On examination on December 15th she was an unhealthy-looking woman, with physical signs of bronchitis, and gave a history of asthma, which proved to be justified. Her teeth were carious. Her tongue was dirty, and there was marked tenderness in mid-epigastrium. She had no appetite. Special examination showed normal acidity, occult blood in the faeces, and a very large ulcer of the lesser curvature. In thirty-four days, and after twenty-five injections of larostidin, she was perfectly fit. She had increased 4 lb. in weight. There was no occult blood in the faeces, and the stomach was normal after critical screening and examination of films. Her bronchitis had cleared up, and she had ceased to have attacks of asthma. She was discharged from hospital on January 8th, 1935.

CASE VII

Female, aged 47 years, spooler, was admitted to hospital on January 24th, 1935, complaining of pain in the stomach of fifteen years' duration. About the beginning of 1920 she began to have pain after food. At first she could only say that it came on between meals when she was at her work, and then it went away. Sometimes the pain would go away for a few weeks. After about a year she began to have severe spasms two to three hours after food, and she obtained relief by eating or drinking. An alkaline powder gave her some relief. She was treated by rest, diet, and alkaline mixtures but with little effect. She lost her appetite and was troubled with water-brash. She had no heartburn, flatulence, or vomiting. Sometimes she was awakened at night with water-brash, but not with pain. She was constipated, and lost about 1 st. in weight. Before admission she was beginning to feel very weak and unfit.

On examination she was ill-looking, and had a tendency to acne rosacea. She had artificial teeth. Her tongue was clean and the fauces healthy. Palpation revealed tenderness two inches above the umbilicus in the middle line. Special examination showed a normal acidity, occult blood in the faeces, and an ulcer of the lesser curvature. She was a ward case, and was treated as described. In thirty-nine days, and after twenty-five injections of larostidin, she was perfectly well, and taking her food with good appetite. She had gained 1 lb. in weight. There was no occult blood in the faeces; the stomach was normal after critical screening and examination of films. She was discharged from hospital on March 4th, 1935.

CASE VIII

Male, aged 40 years, compositor. He was not admitted to hospital, but was treated while he continued his work. He was first seen in 1930, complaining of pain and flatulence of six years' duration. In 1924 he began to have a feeling of distension, and was tender in the stomach one hour after food. He was much troubled with eructations, and was sometimes awakened at night with pain in the mid-epigastric region. He obtained some relief from alkalis. He had undergone many forms of treatment, and had been told he had an ulcer of his stomach. There was a marked family predisposition to peptic ulcer. From 1924 until 1930 he was rarely free from symptoms.

When seen in 1930 he was pale, emaciated, and miserable-looking. He had penetrating pain coming on one to two hours after food, and always had a loaded feeling in the pit of his stomach. Food did not relieve his pain. He was constipated and felt sick, but did not vomit. Special examination revealed hyperacidity, occult blood in the faeces, and prepyloric ulcer on the lesser curvature. He was given adequate medical treatment, commencing with four weeks' rest in a nursing home and diet, and medication for one year. During this time he was under constant observation, and, apart from the disappearance of occult blood, there was little improvement. From then until December 3rd, 1934, he remained a gastric invalid, and now wished for something surgical.

Routine examination revealed much the same as in 1930, and occult blood was again present. He was persuaded to undergo medical treatment by larostidin, and twenty injections were given. He improved rapidly, and stated he was better than he had ever been. A persistent flatulence yielded to the administration of two larostidin tablets daily. On January 21st, 1935, he had gained 7 lb. in weight, and there

was no occult blood in the stools. The stomach was normal on critical screening and examination of films.

CASE IX

Male, aged 47 years, clerk. He was not admitted to hospital. He was first seen on December 21st, 1934, complaining of pain all over the upper abdomen of twelve years' duration. In 1922 he began to have a sense of distension immediately after meals. At first this was relieved by eructations. Soon this discomfort became actual pain, and it came on half an hour after meals. He did not think that the character of the food made much difference. He rarely felt sick and did not vomit. He was very constipated. He had been treated by rest, diet, and holidays, and had consumed much powder and swallowed many mixtures with only relief at the time. His doctor reported that an ulcer was present on the lesser curvature in 1933.

On examination he was thin, and palpation of the abdomen revealed rigidity of the upper part of the left rectus muscle. He had a definite tender spot two inches above the umbilicus and one inch to the left. Special examination showed hyperacidity, occult blood in the faeces, and an ulcer of the lesser curvature. Twenty-five injections of larostidin were given, and there was steady improvement. On January 23rd, 1935, he had increased 8 lb. in weight, and was feeling perfectly fit. There was no occult blood in the faeces, and the stomach was normal after critical screening and examination of films.

CASE X

Male, aged 25 years, book-keeper. He was not admitted to hospital, but was treated while he continued his work. He was first seen on November 30th, 1934, when he was complaining of pain in the stomach coming on one and a half hours after food. This began in 1930, and during these four years he was only free from gastric discomfort for short periods. He found that a heavy meal upset him most, and he usually had greatest discomfort after his dinner, which he took about 6.30 p.m. He also noticed that he was badly constipated and required much medicine to move his bowels. He was not sick and did not vomit. A gastric ulcer had been found on radiological examination early in 1934, and adequate medical treatment had failed to give him much relief.

On examination he had a clean tongue, good teeth, and healthy fauces. Palpation of the abdomen was described as painful, and he had a tender area in mid-epigastrium. Special examination revealed normal acidity, occult blood in the faeces, and a prepyloric ulcer of the lesser curvature of the stomach. Twenty-five injections of larostidin were given, and he responded well. He gained 6 lb. in weight, and on January 3rd, 1935, there was no occult blood in the faeces and the stomach was normal after critical screening and examination of films.

CASE XI

Male, aged 60 years, traveller. This patient was treated as an ambulatory case at home, though not at his work. The history is rather indefinite, but for years he had complained of his stomach, and he attributed this to his irregular habits, necessitated by his occupation. He had frequently been told that it was gastritis. He partook of much alkaline powder, which relieved his discomfort, and he was able to continue his work. If he did not take powder regularly he had heartburn and was constipated. He had neither sickness nor vomiting. In September, 1934, he had influenza, and was just recovering when he had a severe haematemesis and melaena. The emergency was treated, and in October, 1934, he was x-rayed, a large ulcer being found on the lesser curvature. Treatment for the ulcer was then carried out, but he remained very anaemic and his gastric discomfort was unrelieved.

On examination on January 6th, 1935, he was anaemic and ill-looking and had lost weight. Palpation revealed tenderness in the epigastrium two inches above the umbilicus, and half an inch to the right. Special examination revealed normal acidity, occult blood in the faeces, and an ulcer of the lesser curvature of the stomach. Twenty-five injections of larostidin were given, and at the same time ferri et ammon. cit. 30 grains t.i.d. On February 11th the patient's blood count was normal, and he was feeling fitter than he had done

for many years. He had increased 5 lb. in weight. There was no occult blood in the faeces, and the stomach was normal on critical screening and examination of films.

CASE XII

Male, aged 38 years, canvasser. He was not admitted to hospital, but was treated while he continued his work. He was first seen on August 1st, 1934, complaining of pain in the pit of the stomach of ten years' duration. In 1924 he had acute pain in his stomach after eating tainted meat. He consulted a doctor, who said it was gastritis. The pain was constant. He had no vomiting. It passed off in two or three days. He had diarrhoea. Apart from vague indigestion he was not much troubled until June, 1931, when he had a bad attack after eating ice-cream and fruit. The pain awakened him at night, and it was diagnosed by his doctor as "colic." He was exhausted after the attack. The same vague uneasiness followed, and in November, 1931, he had another attack with sickness and vomiting, which gave him relief. He began to lose weight, and he had now definite pain one to two hours after meals. Treatment by rest, diet, and alkaline mixtures had little effect. He gradually felt he was unable to take any kind of food without pain and a sense of fullness. Alkalis had no effect in relieving his distress.

On examination when first seen he was thin and miserable-looking. His tongue was coated. He had artificial teeth and his fauces were healthy. Palpation of the abdomen revealed tenderness in the mid-epigastrium. Succussion was present three hours after a meal. Special examination showed normal acidity, occult blood in the faeces, and an ulcer of the lesser curvature. Treatment with belladonna, bromide, and chloral hydrate was tried, with no material benefit. On November 19th larostidin treatment was commenced. Twenty-five injections were given, and improvement was noticed after the first few injections. On January 4th, 1935, he had gained 8 lb. in weight and there was no occult blood in the faeces. He felt very fit, and stated he had not felt so well for years. The stomach was normal on critical screening and examination of films.

Summary of Cases

These twelve patients' case-histories fulfil the criteria stated. Nine are men and three are women. Their ages range from 24 to 62 years. Fractional analysis after a gruel test meal showed curves of gastric acidity within normal range in seven, while five showed moderate hyperacidity. The duration of gastric symptoms varied from seven months to twenty years. The onset of pain was from immediately after food up to two hours later, and was described as burning, stabbing, gnawing, acute stab through to the back, etc. In seven cases there was complaint of flatulence, and in these heartburn and water-brash gave rise to marked discomfort. The taking of an alkaline powder gave relief in six cases, and in five vomiting occurred, but in only three was relief obtained. Ten complained of constipation, and in two there had been severe haematemesis. Occult blood was present in ten and melaena in two. All patients stated they had lost weight, and tenderness was elicited on palpation in every case. The tender spots varied from mid-epigastrium to left or right hypochondrium. Radiological examination was carried out in all cases, and definite ulceration of the lesser curvature was seen.

Method of Treatment

These twelve cases were treated as follows: (1) The patients were allowed to be up and about. (2) Ordinary diet was permitted without restriction. (3) Daily injections of 5 c.cm. larostidin—that is, 4 per cent. histidine—were given. (4) No other form of treatment was used. Of the twelve cases, seven were treated in the wards, in order to study them more carefully, and five were treated as ambulatory cases in private. The hospital patients were allowed to be up, and assisted in various

ward duties. Four private patients continued their ordinary occupations, and one was up and about but not at his work.

The first symptom to disappear was discomfort. This refers to the vague feelings of fullness, soreness, "as if a ball was present," nausea, tastes in the mouth, and the many other colourful expressions which are retailed by the sufferer from gastric ill-health. Any vomiting was almost immediately controlled, and before long pain ceased to be a disturbing factor. Loss of appetite was not a common complaint, but when present there was a speedy return of a desire for food. A striking

FIG. 1.

FIG. 2.

feature was the rapidity with which the general nutrition of the patients improved. They soon looked healthier and had a better colour, and their weight increased each week. In no case was there a failure to gain substantially in weight. The function of the gastro-intestinal tract improved. In cases where there had been gastric retention due to pylorospasm the emptying time improved. The better function was also seen in the relief from constipation. Definite flatulence was the most obstinate subjective symptom. In two cases where it persisted throughout the whole course of injections it was completely relieved by the daily administration of two larostidin tablets each containing 0.2 grain histidine. Tenderness on palpation was present in all cases until several injections had been given, but the most refractory yielded after the twentieth dose.

It is not claimed by Aron that radiological cure is achieved in all cases, but in this small series striking radiological results were obtained. It is impossible to show the appearances before and after treatment in all

cases, but as an index of the results obtained Figs. 1 and 2 are illustrative, but are in no way exceptional.

Conclusions

In reporting these results I do not wish to acclaim histidine as a certain cure for peptic ulcer, even of a simple lesser curvature type; but the rapid clinical improvement, together with the radiological evidence, goes far to show that the treatment is beneficial in relieving gastric distress and hastening the healing of an obvious ulcer. Its healing value is illustrated in the record of the following case.

Male, aged 50 years, joiner. Complained that he had been troubled with pain after food since 1919. Suffice it to say that his condition was suggestive of prepyloric ulcer, and he was x-rayed in 1920 and the diagnosis was confirmed. From

FIG. 3.

1919 to 1928 he was treated adequately on medical lines, and obtained little if any relief. At this latter date he perforated, and an emergency operation was performed with suture of the perforation. His symptoms returned within a few weeks, and he led a miserable life until 1934, when in the month of November he began to have signs of pyloric obstruction and was admitted to hospital. A fractional test meal and x-ray examination confirmed the diagnosis that he had obstruction and that there was considerable gastric dilatation. In addition, there was found a large ulcer on the lesser curvature (see Fig. 3). Surgical treatment was advised and the surgeon who operated in 1928 was consulted. He considered that the intra-abdominal condition encountered then was such that he was against further operation unless the obstruction became complete. The patient was sent home and under his own doctor. Twenty-five injections of histidine were given. During this treatment there was increasing improvement, and on completion an x-ray examination showed no sign of ulcer on the lesser curvature. There remained the deformity from the old operation, and partial obstruction (see Fig. 4). He stated that he felt better than he had done for years.

The above case is still a surgical one, but it is recorded here to illustrate the marked healing power of histidine, even in a case complicated by pyloric stenosis. So far the lapse of time since these cases were treated is too short to make dogmatic statements. One case has already relapsed, but it is interesting to note that only four injections have been necessary to effect again a clinical cure, and there is no radiological evidence of ulcer in less than three weeks' time.

A question that obviously arises is: If there is an absence of histidine, or a failure of its utilization, is cure at all likely to be permanent? It seems that some means of maintaining the supply of histidine must be considered, and that relapse will only be prevented by a continued administration either orally or by injection.

Treatment by histidine has some beneficial action, however that is brought about, and further trial and study are indicated.

FIG. 4.

Summary

1. A plea is advanced for greater co-operation in the quest for truth relating to peptic ulcer.
2. Treatment based on a new aetiological theory is indicated.
3. Criteria of diagnosis and case histories are detailed.
4. The method of treatment is stated and a synopsis of the results obtained is given.
5. The healing power of histidine is discussed, and an illustrative case is recorded.

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A NOTE ON CLOSED METHODS OF ANAESTHESIA IN THE SURGERY OF THE CHEST

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Thoracic surgery demands from anaesthesia something more than the mere production of unconsciousness. The patient must arrive at the table in a quiet frame of mind; this must be accomplished, however, without recourse to excessive premedication, with its post-operative disadvantages. Next a quiet induction must be assured, and an anaesthesia of sufficient depth without anoxaemia in those whose pulmonary ventilation is usually below normal. Thus only can the surgeon be shown a quiet operating field and a patient who is not unduly distressed.

These ideals are approachable by various methods, more recently through the newer anaesthetic agents, cyclopropane and divinyl ether. Their administration by the closed method is essential, and while it would appear that they open up new fields and a nearer approach to the ideal, their use is still in the experimental stage. Nitrous oxide and ethylene, on the other hand, have proved their worth, and it is the use of these gases by the closed method which is the object of this note.

Action of Nitrous Oxide and Ethylene

1. Nitrous oxide and ethylene are respired unchanged, and produce their characteristic effect by simple oxygen displacement from the blood. Ethylene has a slight lipid solubility, and gives, therefore, a 15 per cent. deeper anaesthesia.

2. Nitrous oxide 85 per cent., oxygen 15 per cent.; ethylene 80 per cent., oxygen 20 per cent.; are recognized as average gas quantities required in the production of anaesthesia, but with continuous or intermittent flow machines the gas percentages found in the bag are nitrous oxide about 75 to 80 per cent., carbon dioxide and oxygen in varying proportions making up the rest. With ethylene the oxygen percentage is slightly higher. Thus the addition of the expired carbon dioxide brings the levels of successful anaesthesia with no oxygen lack and anaesthesia with anoxaemia very close in those with normal pulmonary ventilation. In "thoracic" patients these levels often overlap. By the addition of premedication, local and regional anaesthesia and chloroform, a compromise can be reached. This, however, is at the expense of a slower recovery, and a heavier burden is thrown on the patient's metabolism in their elimination. The immediate neutralization of the carbon dioxide in the closed machine allows of a higher oxygen percentage being used, and if the depth of anaesthesia is insufficient, the smallest trace of chloroform or ether added to the gas and oxygen with positive pressure at once overcomes the difficulty.

3. With ethylene a greater percentage of oxygen can be used, but to offset this advantage its odoriferous and endothermic properties must be reckoned with, and also the fact that nausea of varying severity is common after its employment. The use of the closed method obviates the first drawback, and although a sufficient number of cases have not been considered as yet, it would appear that the closed method certainly reduces the third disadvantage. The explosion risk is, however, always present.