the patient, but prolonged boiling is to be avoided." There is evidence that a smaller quantity of liver is sufficient to maintain the improved condition, and that the dose should be reduced when the blood picture approaches the normal.

SUMMARY.

Nineteen patients with pernicious anaemia have been treated with whole liver or a liver extract. Nine of them were in the first attack or in a relapse, and seven of these showed a prompt response to treatment, with a temporary rise in the percentage of reticulated red cells in the circulating blood, and a steady increase in the total red cells and the haemoglobin. The reason for the failure of the treatment in the other two patients is not clear.

Ten patients commenced treatment during the remission stage or received other forms of treatment in addition, so that observations on the immediate effects of the treatment were not possible. The condition of these patients at the end of varying periods of treatment (up to six months) affords confirmatory evidence of the value of this treatment.

Our thanks are due to the physicians of St. Bartholomew's Hospital and others who kindly enabled us to make these observations on their patients.

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THE TREATMENT OF GASTRIC ULCER.*

BY

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It is possible to-day to cure the majority of cases of gastric and duodenal ulcer without having recourse to surgical intervention, and since the surgical treatment of this disease is attended by a definite, if small, immediate mortality, and by an even more definite percentage of subsequent relapses and complications that are often of a nature far more serious than those encountered in patients treated by purely medical methods, the present position is a grave one. The frequency of these cases is greater every year, and the problem of treatment one upon which practitioners as a whole remain in considerable doubt. I do not propose to bring before you any statistics, nor to go deeply into theories of causation or into experimental work bearing upon the etiology of peptic ulceration, but I am going to outline the treatment which ten years' experience has shown me to yield excellent results in a very large proportion of cases.

Removal of Septic Foci.

The first step in the treatment of gastric ulcer is one which must be adopted in every case, whatever the decision may be as to whether the general treatment is to be on medical or surgical lines. I refer to the eradication of septic foci in the mouth and elsewhere.

Oral sepsis is probably the most important cause of gastric and duodenal ulcer, bacterial emboli being carried from the region of the dental roots by the blood stream to the region of the pylorus and lesser curvature. The work of Rosenow, of Haden, of Christophe, and a score of others, may be quoted as supporting this view, which

is very widely held in all countries at the present day. In addition to dental sepsis, or in its absence, chronic sepsis of the tonsils, nasopharynx, and nasal sinuses must be eliminated. Cases have been observed by many clinicians in which the recurrent attacks of pain in patients with chronic ulcer have corresponded with acute exacerbations in chronically infected tonsils. In a few cases chronic appendicitis and chronic disease of the gall bladder appear to be important factors, and I have on more than one occasion received the assistance of my surgical colleagues in removing a factor of this type without any surgical treatment being applied to the ulcer, which has subsequently responded well to purely medical treatment. It often, perhaps usually, happens that the removal of these septic foci is better effected after a few weeks' treatment rather than at once. It would, for example, be foolish to subject a patient recovering from a severe haematemesis to the risk of extensive dental extractions; but in all cases focal sepsis must be eliminated at some stage if a permanent successful result is sought, and I place it in this early and prominent position in order that its importance may not be overlooked.

Choice of Cases Requiring Surgical Treatment.

In spite of my opening words concerning the efficacy of medical treatment, I do not wish it to be imagined that such treatment is to be applied without restriction. On the contrary, I feel that in every case seen for the first time the physician should ask himself whether surgical treatment should be employed immediately. For whereas to-day hundreds of cases are sent to the surgeons without any real attempt at medical treatment ever having been made, others are allowed to linger in the hands of physicians when nothing but surgical treatment can help them.

The following cases call for surgical treatment as soon as it is safe for it to be undertaken:

1. All cases with a high degree of pyloric or duodenal stenosis, or with marked hour-glass deformity of a permanent nature.
2. All cases with deep ulceration involving adherence to or excavation of neighbouring structures, such as the pancreas or liver.

In the first of these groups there is mechanical defect which can only be put right by mechanical means. In the second group there is evidence of ulceration so deep that healing can hardly be expected, and amputation—that is, surgical treatment—is called for.

We now come to four further groups of very different type:

3. Cases which have relapsed after a thorough course of medical treatment.
4. Cases which have recurred in spite of treatment during many years.
5. Cases in which there has been recurrent and dangerous haemorrhage in spite of careful medical treatment.

To fall into one of these groups a case must have had previous and unsuccessful medical treatment, and it requires considerable judgement for a physician to decide whether the previous medical treatment has been such as to justify the abandonment of all but operative intervention at the time when the patient comes under his care. If a patient has been properly treated and still relapses, a new line of treatment must be adopted. If a case has gone on relapsing for many years the ulcer will probably be so callous that healing is problematical, but increasing experience has taught me that it is so rare for these cases to have received what, in my opinion, can be described as thorough treatment that I hesitate more and more to ask for surgical intervention until I have satisfied myself that they are incapable of healing when given drastic treatment on the lines I shall indicate.

6. Cases in which proper medical treatment is impossible, owing to the patient's habits and economic position.

This is an important group, but it is certainly less numerous than I used to believe. We are too ready to assume that the working man cannot devote the time and effort necessary for dieting himself on proper lines, and many such patients, if they can be got to grasp the seriousness of the position, will carry out medical treatment

* An address to the Hampstead Division of the British Medical Association on January 12th, 1928.

fully and thoroughly and give results which a few years ago were impossible. There are, however, certain reckless and greedy individuals who are incapable in any circumstances of following a simple line of dietetic treatment. If by chance they have diabetes they die; if, on the other hand, they suffer from peptic ulceration it is more in their interest to endeavour to get them cured by surgical means than to waste their time and that of their doctor by giving instructions which they will not attempt to obey.

We are now left with the cases suitable for medical treatment—an enormous group constituting probably more than 80 per cent. of all who come under observation. Alvarez, in a recent article, stated that he had never seen a case of gastric or duodenal ulcer which had been properly treated before coming to him. I cannot personally corroborate this. I know that I have seen at least two cases which I considered to have been well treated, and probably I have seen half a dozen during the last ten years, but I doubt whether I have seen more. It is usually so easy to point to factors such as injudicious food, or to an amount of alkali which could not possibly have affected the gastric juice, or to residual septic stumps in the mouth, the removal of which no one had ever suggested, that it is extremely rare to encounter a case in which it cannot immediately be demonstrated that previous treatment has been obviously incomplete and faulty.

GENERAL MEDICAL TREATMENT.

The first question which arises in general medical treatment is whether the patient is to be kept in bed or allowed to be up and about. A patient in bed requires less food, and, by confining these cases to bed for a week or two, treatment can be started on a lower total diet than otherwise. Further, it is difficult to make a patient realize that he is being seriously treated for a very grave disease if he is allowed to go about his business from the start. For these reasons—and the second is probably even more important than the first—I usually urge patients to abandon work for three weeks, of which the first ten days at least are spent in bed, either at home, or in hospital, or in a nursing home, but it must be admitted that many cases selected from amongst the more intelligent classes can be well treated without any interruption of their work.

The two main objects of medical treatment are: (a) to secure the most complete rest for the stomach compatible with sufficient nutrition for the body, and (b) the choice and administration of food and drugs in such a manner that contamination of the ulcer with acid gastric juice is prevented. It is to the late Bertram W. Sippy of Chicago that we owe the full recognition of the logical importance of these factors, and to him must be given the credit for their successful application. The use of alkalis dates back for centuries, and the use of frequent and graduated feeds in gastric ulcer has been going on probably for fifty years; but during the last decade the treatment of these cases has become infinitely more successful than it was before the war, and though considerable variation will be found in the exact regimes employed by various authorities, examination of the more successful reveals the fact that they are on the lines which Sippy so strenuously and successfully advocated. I claim no unique merit for the alkalis and foods which I suggest, nor do I imply that no variation from them can be made. Clearly many such variations can be made, and providing that treatment remains thorough, to the point of extreme caution, the result will probably be the same. I give, therefore, a specimen scheme of treatment which I know from frequent experience to be effective in the majority of cases. This does not refer to cases with any grave complications, but to patients in whom haemorrhage, if present at all, is in the form of slight occult bleeding, and the x-ray evidence of ulceration, however deep, is without signs of adhesions to, or penetration into, other organs. In the following table are set out the diets to be used in such cases during the first three weeks.

Peptic Ulcer Diets.

First Week.

Citrated milk, egg and milk, Benger's food, arrowroot, ovaltine, Glaxo, milky coffee, or strained white vegetable soups. One of these to be given every hour from 7 a.m. till 9 p.m. Amount not to exceed an ounce, or an ounce and a half. Cream to be added to six feeds.

Second Week.

The same foods are to be used, but the amount may be increased to two, and two and a half ounces. Alternate feeds may be omitted twice in the morning and twice in the afternoon. One dry rusk to be given at 8 a.m. and 7 p.m. Two tablespoonfuls of milk pudding as an addition to lunch. A lightly cooked egg at breakfast and supper gradually.

Third Week.

Three tiny meals, with two-hourly feeds between.

Breakfast.—Lightly cooked egg, milky coffee, 3 oz.; one rusk with butter.

Lunch.—Milky soup with a beaten egg in it, 4 oz.; milk pudding with cream, 3 oz.

Supper.—One poached egg, one rusk, ovaltine, or junket with cream.

Three 1 oz. feeds of fluids originally used to be given in addition to these meals, at intervals of two hours.

It will be observed that at first the feeds are entirely fluid, and are given every hour, but that at the end of three weeks they have assumed the nature of three very small meals, with two-hourly fluid feeds in between. The type of diet indicated in the third week must be continued for months to come—that is, the meals must remain very light, and the patient in no circumstances is to go longer than two hours without taking either a small milky feed, or, if this be impossible, munching a dry biscuit. The bulk of the main meals may be cautiously increased, but reliance should be put on cream and olive oil to increase the calorie value, rather than use being made of more bulky articles of diet. Pounded fish or minced chicken, in small amounts, with potato mashed with milk, are to be added once a day from the fourth week onwards, and a little ingenuity makes it easy to add small delicacies to the diet without transgressing the rules of safety. Fish, egg, and cheese soufflés are valuable additions, and the patient must be gradually taught to use his knife and fork and his teeth as substitutes for the mincing machine.

Drug Treatment.

During the time this dietetic treatment is in progress various drugs are employed as a further aid. Of these, the first is atropine, either as such, or in the form of tincture of belladonna. It is my custom to give seven drops of tincture of belladonna in a little water as soon as the patient wakes in the morning. At that moment the drug can reach a considerable part of the surface of the stomach, and a useful effect is achieved as regards diminishing the gastric secretion. Once food has been taken it is no use giving belladonna, except in such large doses that a central effect is obtained, and this will be accompanied by such dryness of the mouth that the treatment will have to be stopped. Apart from this initial dose of belladonna, reliance must be placed on the use of alkalis throughout the treatment, taken half-way between the feeds, whether these are being given hourly or less often. The strongest neutralizing salts are those of magnesia, with bismuth oxy carbonate as the next most valuable; the former has the disadvantage of being laxative, and the latter is very expensive. A useful formula for the early stages is as follows: *Magnesii carbonas ponderosus*, *magnesii carbonas levis*, bismuth oxy carbonate in equal parts, 1 drachm to be taken between feeds. If this proves too relaxing the magnesia should be diminished and the bismuth salt increased, or sodium bicarbonate, calcium lactate, or prepared chalk used as partial substitutes. Various emulsions of magnesium hydroxide, such as the *mist. magnesii* of Parke, Davis and Company, or Martindale's well known emulsion, are useful; but I find that patients generally prefer powder preparations to fluid ones. During the taking of alkalis additional water may be required on account of thirst. This may always be conceded, and thirst does not become serious if the bowels are not relaxed. Care must be taken to avoid alkalosis. Loss of appetite, headache, vomiting, or even general convulsions have been observed in certain cases in which the use of alkalis had been pushed to an extreme degree, especially in patients where renal deficiency or pyloric stenosis was present. Such complications must be looked for with care, and at any suspicion that the absorption of alkalis is producing a general toxæmia, the administration should be stopped, and neutral phosphates of magnesia and calcium

employed in preference to the alkalis. It must be noted here that sodium bicarbonate is probably the most dangerous of the alkalis as regards its capacity for producing alkalosis, and as it is generally considered that, after neutralizing the gastric acid, this salt has a tendency to stimulate late secretion, I have, in common with many other observers, practically given up its use. I may add that with this practice, and with the further precaution of instructing patients in the later weeks to abstain from the use of alkalis on two days in every month, I have never observed a case in which these symptoms caused any anxiety.

Duration and Control of Treatment.

How long is this rigorous treatment to be continued? I cannot give a definite answer in weeks, months, or even years, but if in the first place the patient is told that for proper medical treatment he must give up, before attempting work, a fraction of the time which he would require if a surgical operation was contemplated, the doctor will usually within a month be in the satisfactory position of being able to allow him to resume work under conditions which the patient himself will admit are not intolerable. He will then be on small meals, deprived of second helpings and of all raw fruits and vegetables, and of a certain number of cooked foods, such as tough meat and green vegetables which are of an indigestible nature, with small two-hourly feeds to be taken from a pocket flask, and a certain amount of alkaline powder to be taken in addition.

This he has got to go on doing for a long time. The entire absence of symptoms in such cases is a factor which makes carelessness a perpetual temptation, both to the patient and to his medical adviser. We all know the chronic nature and tendency to relapses of these ulcers, but they are so hidden from our view that again and again we tend to become careless. We should think of them in the same way that we think of a chronic ulcer on the leg, and remember that permanent healing cannot be expected in either case without months of careful treatment, in which rest is the all-important factor. In the case of the stomach rest means diminished peristalsis and secretion, and it can easily be obtained by the method here outlined, and there is no excuse for allowing patients to disregard it.

There are certain means of controlling treatment which are highly important. The first is periodic x-ray examination, and since its introduction we have had the experience of seeing deeply penetrating ulcers diminish, and finally become completely obliterated. Nicholas and Moncrieff have reported a series of such cases at Middlesex Hospital during the last twelve months. White, Crohn, Moutier and Porcher, and Maclean, Jones, and Fildes have subsequently made communications to a similar effect. It must be realized that the disappearance of an ulcer, seen by the x rays, is evidence of healing, but not of cure. The best that can have happened during the early months is that the ulcer crater has been bridged over by granulation tissue of a relatively friable nature, and months must elapse before this bridge is converted into a tough, permanent scar.

The other form of control which is most necessary is periodic review of the case as a whole. The moment which, in my experience, decides whether the patient is to be cured or not is at some time at the end of three or four weeks, when, free of all symptoms, he is made to realize the grave potential danger of his position, and the absolute necessity for prolonged after-care. It is, however, a mistake to believe that such prolonged after-care involves any real hardship. Patients of all classes are very willing to continue treatment when once they understand their real position, and the reason why so many relapses have occurred in the past is because the patients have not been made to understand the nature of their disease and the simplicity of the precautions which will lead to cure, if thoroughly applied.

Alcohol and Smoking.

Patients always require instructions about the use of alcohol, and it is difficult to justify extreme rigour in this respect. It would seem that the same rules must be used concerning alcohol as are employed when making choice

among other foods—that is, highly irritating things such as liqueurs or the stronger alcoholic wines must be forbidden, also alcoholic drinks which in their nature are bulky. Beer and cider fall into this latter category and are better avoided, but there does not seem to be any real reason why a glass of light wine should not be allowed at meal times after the early weeks of treatment have been successfully completed.

Smoking falls into a very different category. There is a growing body of opinion which holds the view that nicotine or some other poisons absorbed from tobacco smoke can play a very deleterious part in these cases. Whether cigarettes are worse than pipe tobacco it is difficult to say, but it is a striking fact that duodenal ulcer is commoner among cigarette smokers than among abstainers. As an example, it may be pointed out that in the hospital class of patient duodenal ulcer is scarcely ever seen amongst women, whilst in women in more well-to-do circumstances it is becoming very common, and it may well be that cigarette smoking is the explanation. I always make it a rule to persuade my patients to give up smoking if they can possibly manage it, and many of them say that the very frequent feeds in the early weeks of treatment are of great assistance towards breaking the habit. There is also a strong consensus of opinion amongst patients that they feel rapid relief when smoking is stopped. Accepting this, it must be admitted that nicotine can be at most a contributory factor in the disease.

TREATMENT OF COMPLICATIONS.

Of complications the most frequent is haemorrhage. The treatment of haemorrhage is, in my opinion, always medical, and consists essentially of complete starvation by the mouth, together with the use of sedatives in sufficient amount to produce what is practically a twilight sleep during several days. At the end of that time feeding, which has hitherto consisted simply of rectal salines, may be very cautiously begun with sips of water, albumin water, and glucose water by the mouth, with a slow and gradual progress towards the treatment given to ordinary cases during their first week. Great caution is necessary in these cases, and when convalescence is reached the fact that a dangerous haemorrhage has occurred should always lead the doctor to discuss the possible need of surgical treatment with a greater bias towards excision than if there had been no such complication. Operation at a period when haemorrhage is still threatening the patient's life is, in my opinion, not justifiable. However alarming these cases may be—and admittedly there are few conditions so liable to promote panic amongst those surrounding the patient—operative intervention is always an added risk in a condition which can easily be shown to carry a surprisingly low mortality. Of the last fifty cases of severe haemorrhage or melaena which I have seen, only one patient died, and he died, not through haemorrhage, but from secondary cerebral thrombosis. I have, however, had partial gastrectomy performed on several such cases during convalescence, it having been clear that the ulcer was of a type in which healing under purely medical treatment could not reasonably be expected.

The second common complication—perforation—is one which, of course, calls always for immediate surgical treatment, and it is interesting to observe that such treatment has become more and more conservative in recent years, often consisting of nothing more than the immediate closure of the perforation, with subsequent medical treatment of the case.

Pyloric stenosis and hour-glass deformity of the stomach are usually complications calling for surgical aid. The only word that may be added here is that care must be used to distinguish between deformity due to spasm alone and deformity of a true cicatricial character. Repeated x-ray examination between intervals of medical treatment will always supply the answer to this doubt.

I have not hitherto mentioned the question of malignant transformation occurring in chronic peptic ulcers. So far as I am aware—and it is a problem into which I have made long and careful inquiry—such transformation never takes place. In order to preserve strict scientific accuracy this statement may be qualified by saying that cancerous

change in a chronic ulcer is certainly no commoner than is primary cancer of the duodenum. We all know that rare instances of the latter disease have been reported, but they are so rare that pathologists usually say that they do not occur at all. The fact about the supposed malignant degeneration of gastric ulcers is that cancer of the stomach occasionally arises in the form of a malignant ulcer. These cases are malignant from the outset, although in elderly patients their progress may be slow. When a case with a short history is encountered in a middle-aged or elderly person, who produces an x-ray picture showing a large ulcer, usually not very deep, on the lesser curvature of the stomach, the possibility should always be considered of this being malignant, and if there is any doubt operation becomes desirable.

The subject of complications is in itself a huge one, and any proper discussion of it is bound to bring us to the problem of what may be called "the unsuccessful gastro-enterostomy." It is not my intention to enter into these cases at any length, but it is only right to realize, when one is discussing the alternative lines of treatment in cases of peptic ulcer, that there is no group of patients so calculated to fill both the physician and the surgeon with despair as that group in which a gastro-enterostomy has been performed and the operation has not been a success. Their symptoms are often far more trying than those of any ordinary case. I have seen such patients die of haemorrhage five, eight, fourteen, and even seventeen years after their operation. I have had cases which responded to medical treatment in a dramatic manner; I have had others in which constant relapses occurred; and in all of them I have come to realize that further operation is more difficult and uncertain than in any case where surgery has not previously been undertaken. I read articles by surgeons who write of reconstituting the original state of affairs, but in my experience this is an exceedingly difficult proceeding. I have seen cases where excision of large portions of the stomach and jejunum was successfully accomplished, and in others the shock of this operation has proved too much. There is little doubt that the position of these cases is a very serious one, and what is even more serious is that this operation is being light-heartedly performed by inexperienced surgeons in all parts of the country to-day. The problem, however, is primarily one for discussion among surgeons, and cannot be dealt with here at greater length.

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THE TREATMENT OF ASTHMA,

AND AN IMPROVEMENT OF THE PEPTONED AGAR SERUM.

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ASTHMA is a constitutional condition, being one of a family of allergic disorders, and may be regarded as inherited. The family are all characterized by a state of sensitization. Whatever form the sensitization takes in a parent or grandparent, asthma may result in one or more of the offspring. A child which develops an allergic state on first contact with a foreign protein has been sensitized in the mother's uterus. Many cases of asthma are difficult to trace, and are put down as "acquired," but a remark of Salter¹ may be opportune here.

"It is a curious fact," he says, "that several brothers and sisters in a family may be asthmatic without the parents being so. This would seem to suggest, in respect of disease, a principle with which the breeders of cattle are familiar: that certain combinations produce certain results, and lead to the creation of certain peculiarities . . . just as we sometimes see a family of red-haired children, both the parents of which have black hair."

It will be seen, therefore, how difficult it is to prove that asthma may be acquired. It may be dormant for many years. As Peshkin² correctly says, "the various etiologic protein sensitizations are merely the exciting factors, and not the basic cause of asthma." He also says that protein sensitization does not entirely explain the various manifestations connected with allergy. For instance, "10 per cent. of the children with asthma who were skin-sensitive to various proteins showed no etiological connexion between protein sensitization and asthma."

When it is said that asthma may be due to toxic conditions simply, does not the question arise of how many toxic conditions are found without asthma, and how many cases of asthma there are without any toxic condition? In toxæmia there is usually hyperpiesis, but the opposite is found in asthma. Again, asthma is said to be nervous in origin, that the parasympathetic overacts. Why should it do so? We have the fact brought out by Auer and Lewis³ that anaphylaxis in animals occurs after section of the vagi, and destruction of the cord and medulla. T. Lewis,⁴ in his recent work, says that substances such as egg and fish, in susceptible persons, cause asthma, urticaria, etc. "That these manifestations are brought about also through a mechanism similar to that involved in animal anaphylaxis is open to little doubt, though the manner in which susceptibility is acquired remains unknown." Let us note that in both there is eosinophilia, and that relief is obtained through atropine.

In many asthmatics there are produced in the body substances, pathological but possibly also normal, which produce the attacks. Outside the body, matter or influences of all kinds, antigenic and non-antigenic, are swallowed or inhaled, etc., and act in the same way. The non-antigenic substances arouse asthma by changing the character or metabolism of certain of the proteins. Modifications of all sorts are found. Asthma is sometimes divided up into "kinds"—perhaps ten or more different kinds may be given. There is, however, but one kind, as the constitutions of all persons differ, and thus the various exciting substances differ, and they vary from time to time. One or two instances of the latter I may give.

A lady, aged 43, consulted me in 1925. She said she had very bad asthma from horses and cats, but from no other source. Her skin had never been tested, and in doing so it reacted strongly to horse dander and cat hair, but to nothing else. Her statement was therefore correct, so far. Then she went to France for a month or two, and remained well for a little time. She then wrote me that she had contracted bronchitis and a violent attack of asthma, though she had not been near either horses or cats. This astonished her very much.

In another case, a boy, aged 12, was brought to me from India, and his mother said he never had asthma in the warm weather in India, but on coming to this climate it came on, and it was solely produced by cold. In the warm days of last August violent asthma came on. It was the first time in warm weather.

Many other instances might be given.

Histamine.

Lately a good deal of fresh work has been done on histamine. Last March, Best, Dale, Dudley, and Thorpe⁵ stated that they had recovered histamine from liver and lung, which seemed to justify the expectation that this potent base was widely distributed in the tissues. It was found that 1.58 mg. of pure histamine had been isolated per kilogram of liver and 27.64 mg. per kilogram of lung. For the lungs this is a very high content. It may be released at the moment of death, but they doubt this. "It is conceivable," they write, "that the lung acts as an organ of internal secretion with respect to histamine, or that it merely captures histamine which has escaped into the venous blood." T. Lewis⁶ considers that histamine (or H-substance) is released from the cells of the skin in local injury, and from the tissue cells in general anaphylaxis. "A fundamental fact in the anaphylactic reaction is the liberation of H-substance."

Now histamine in a certain quantity may be released from the cells in anaphylaxis, but that it is held inactive in the normal state is obvious, for, as Dale says, "if suddenly released into the circulation of an animal, it would have a profound shock-like action." On May 27th, 1922, in this JOURNAL I recalled that it had been found by Hanke and Koessler that peptone which was perfectly