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SOME RECENT ADVANCES IN MEDICAL DIAGNOSIS AND TREATMENT *

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Medicine has made such gigantic strides in the last few years that to cover the field would be a task beyond my powers. I shall limit myself to those recent advances with which I am chiefly familiar. Most of these relate to the digestive tract.

Sialography

The radiographic demonstration of the ducts of the parotid and submaxillary glands has been made possible by the injection into them of substances opaque to x rays. Payne (1931) described in detail the introduction of lipiodol into the parotid duct. By this means the outline of the main duct and its branches can be demonstrated and, when infection occurs, various abnormalities such as spherical dilatation, comparable to that seen in bronchiectasis of the lung, can be demonstrated. The same writer (1933), describing nineteen cases of *recurrent pyogenic parotitis* fully investigated by examination of the saliva and also by sialography, summarizes the symptoms and signs of this by no means uncommon disease. It usually starts with a feeling of fullness in the region of one parotid and then slight swelling. Attacks may be initiated by a meal. The gland gradually enlarges, reaching its maximum within a few hours up to twenty-four, and subsides over a course of several weeks. During subsidence a foul taste may be experienced, and examination may reveal muco-pus oozing from the duct. After a period of relief the whole process is repeated. It is interesting to note that the ratio of females to males is 8 to 1. So far as physical signs are concerned the gland is easily palpable, not uncommonly tender, and, with acute exacerbation of the disease, fever, increase of swelling, and well-marked tenderness are present. The saliva, instead of being clear, contains numerous flakes consisting of shreds of mucus with pus cells, epithelial cells, and micro-organisms. I have notes of seven patients whom I have seen with this disease, and five of them have apparently recovered completely as the result of massage to the parotid, directed especially along the line of the duct, and also diathermy. In one case of submaxillary gland infection its removal resulted in entire disappearance of symptoms. In the submaxillary gland case and three of my parotid patients the outstanding symptom was, in point of fact, that of *soreness of the tongue*, and owing to the great frequency with which one meets this

most troublesome symptom in practice the possibility of a chronic infection of one or other of the salivary glands should certainly be borne in mind.

Gastric and Peptic Ulcer

One cannot obtain a clear idea of the advances made in the diagnosis and treatment of these conditions without briefly reviewing the last twenty years, or even more. It was Moynihan who was responsible for describing the symptoms of duodenal ulcer and placing that condition on the medical map as a diagnosable entity. In 1921 Bennett and Ryle published the result of their investigations of a hundred healthy students by means of a fractional test meal, and thus applied a further stimulus to gastro-enterology. They showed that 20 per cent. possessed a degree of free acidity which fell outside the mean curve. Of this 20 per cent. half were hyperchlorhydric and half were hypochlorhydric or achlorhydric. It was about this time that they and other workers popularized the alkali treatment of gastric and duodenal ulcer. MacLean, Jones, and Fildes (1928) wrote on the cure of gastric and duodenal ulcers by intensive alkaline treatment. They referred to the already well-known fact that suitable alkalis, rest, and diet would cause a disappearance of symptoms, and produced various radiographs showing the disappearance of ulcer craters. The investigations of these patients were not, however, repeated after a long enough interval to justify the assumption that they were cured.

We now know that a great number of methods of treatment will result in the apparent cure of an ulcer if judged purely by x-ray appearances. I have produced equally striking effects with histidine in patients who have had no other treatment, but am quite satisfied that, in spite of the relief of symptoms, the ulcers were not cured. This drug, which has been used largely in the form of a preparation called "larostidin," is injected intramuscularly daily for fifteen to twenty doses. Numerous and conflicting reports have appeared as to its value. The general opinion of critical observers is that it seems to have some effect in aiding the healing of ulcers, but it is not permanent, and certainly the preparation cannot replace the more orthodox methods of therapy. I began to doubt its efficacy when I followed up histidine-treated patients for a few weeks subsequent to the discontinuation of treatment. In every case a relapse was noticeable, not only from recurrence of symptoms but also from x-ray

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appearances within five weeks. No doubt the mere fact of relapse is a strong point in favour of the histidine having done some good, but, on the other hand, it is highly improbable that anything approaching healing could have been produced with such an early return of all the signs and symptoms. There is no evidence that ulceration in the human being is due to a deficiency of histidine, and there seems, in point of fact, no convincing experimental work to justify its use. If a series of patients are treated with an intensive alkali and dietetic regime and compared with those treated with histidine it will be found that there is very little difference in the immediate recovery percentage. On the other hand, the histidine-treated patients relapse more readily and far more rapidly than those treated by diet and alkali. Gastroscopey has already taught us that large craters as seen by *x* rays seldom seem so deep when observed by direct vision. The apparent depth is produced not only by swelling of the mucosa but by contraction of the underlying muscularis.

Associations of Gastro-intestinal Disease

The remarkable discoveries of Minot and Murphy relative to the treatment of pernicious anaemia, and the more recent work of Castle in explaining the association of achylia with this hitherto fatal disease and with sub-acute combined degeneration of the cord, have given a tremendous forward impulse to the study of gastro-intestinal disease and its relation to more remote systems of the body. I drew attention (Douthwaite, 1936) to an interesting group of hitherto unexplained cases of polyneuritis, sometimes of extreme severity, all of which appeared to be associated with disease of the stomach leading to achlorhydria or achylia, and termed these gastrogenous polyneuritis. In view of Castle's recent work it may well be that they are actually examples of European beriberi, for it has been shown that in conditions of gastritis and achylia the absorption of vitamin B₁ may be deficient, and that an adequate supply of this substance is capable of curing certain types of neuritis, especially alcoholic neuritis, even though the original aggravating factor is still operative.

Faber (1927) preached unheeded for many years the doctrine of chronic gastritis. He studied stomachs preserved by the injection of 10 per cent. formalin solution through the abdominal wall into the peritoneal cavity and into the stomach, and, following that investigation, he advanced the study of gastric pathology by the recognition of chronic gastritis and also of the acute variety. Whether one has to assume that all cases of achylia are the result of chronic gastritis is to my mind quite another matter. This has been accepted as a teaching during the last few years on incomplete evidence, for although it is clear that chronic gastritis might well be expected to produce atrophy of the mucosa in time, it is by no means certain that all conditions in which gastric atrophy is present have been preceded by an inflammatory state—in short, by gastritis. One must be cautious before jumping to this conclusion, particularly when it is borne in mind that the incidence of achlorhydria and achylia rises steadily with age. It seems on the face of it unlikely that an inflammatory condition of the stomach would attack the populace with such regularity. On the other hand, if achylia is due to a gradual degeneration, such as occurs in other structures with advancing years, the findings would be understandable. The point is of importance because if Hurst's view is correct, that gastritis is the precursor of achylia, and gastritis always precedes the

development of carcinoma of the stomach, except in ulcer cancer, it should be possible materially to reduce the incidence of stomach cancer. If, on the other hand, achylia is frequently not the result of inflammatory changes, the whole supposed association between achylia, gastritis, and carcinoma becomes at once subject to considerable doubt. Morley (1937) quotes Robertson's and Wilkinson's cases of cancer of the stomach where test meals taken at intervals have shown the presence of a carcinoma and a free acidity which has steadily diminished. This would suggest that the cancer was responsible for the fall of acid. The most that can be said at present is that, although on theoretical grounds it is probable that the gastritis-cancer sequence is true in a proportion of cases, it must not be regarded as an invariable association, even apart from those cases of cancer which do sometimes arise in chronic gastric ulcer.

Non-ulcerative Haematemesis and Melaena

In using the term "non-ulcerative" I mean to imply that the cases about to be described are those in which profuse haemorrhage has occurred and shown itself either as melaena or as haematemesis, or both, and in which there has been no preceding history of ulcer and where the most careful investigations have completely failed to reveal the presence of an ulcer after the haemorrhage. Furthermore, the subsequent history of these patients has been quite unlike that generally associated with peptic ulcer.

My attention was first drawn to the possibility of severe haemorrhage occurring in the absence of a readily demonstrable disease in the stomach or duodenum by a patient under my care at Guy's Hospital who had been twice admitted on account of recurrent severe haematemesis. He gave no history of indigestion. Melaena persisted for two or three days only and then cleared up. Several *x*-ray examinations revealed no disease. A fractional test meal showed achlorhydria and a great excess of mucus in every specimen. The case was presumably one of gastritis. With rest in bed, a non-irritant diet, and gastric lavage he rapidly improved. A further test meal revealed a return of free hydrochloric acid and no excess of mucus. There has been no recurrence of symptoms after five years.

A man aged 50 was seen by me three years ago on account of severe haematemesis and melaena, again with no preceding history of indigestion. Physical examination was negative, except for haemoglobin of 52 per cent. and heavily infected teeth. He was treated with soft diet and rest in bed, but had a further severe melaena. His doctor then called in a surgeon, who performed a laparotomy and found no abnormality. The patient recovered in spite of this. A test meal revealed exactly the same state of affairs as in my previous case.

A third man, 60 years old, was under my care in hospital with recurrent small haematemeses but no pain. A fractional test meal again showed a picture of severe gastritis and absence of free hydrochloric acid, and blood in every specimen. In fact, it looked very much like the test meal of a carcinoma of the stomach. Repeated *x*-ray examinations were negative. Stomach washouts were heavily tinged with blood for four or five weeks, but ultimately complete recovery took place.

The next three patients were those with hyperchlorhydria. In one there was a history suggesting a duodenal ulcer, but this was not demonstrated by the most careful and repeated *x*-ray investigations, and the profuse melaena for which he came in cleared up in two days. The other two patients are of considerable interest, since both of them were doctors and reliable witnesses. The first consulted me because he had noticed black stools and had felt giddy. He said that he had been perfectly well until a few hours after being at a cocktail party, where he had had only one cocktail but had eaten a large number of salted almonds. His theory was that these had scratched his mucosa. Investigation in a nursing home revealed the hyperchlorhydria so common in doctors. *X*-ray

examination four days after the melaena showed a normal stomach and duodenum. Occult blood had left the stools in three days. The patient has been back at his busy practice for over two years since, and has taken no precautions: he has smoked and has taken alcohol without any further trouble.

The last example was that of a doctor who, on account of supra-orbital neuritis, kept himself going in his practice by taking aspirin. This had been proceeding for ten days when one morning he awoke with pain and took two aspirin tablets without water or milk, as had been his custom hitherto. A quarter of an hour later he felt a slight epigastric pain; the same day, four or five hours later, he felt faint and had colic, and soon passed stools containing a little visible blood and a large amount of tarry material. The value of this instance is that he had his alimentary tract examined by x rays and a fractional test meal and a blood count done four or five days before this occurred, and, apart from a hyperchlorhydria, he was shown to be normal. The investigations were purely precautionary, as he had reached middle life (41 years). After the melaena, which lasted for three days, his haemoglobin was 58 per cent. In spite of this he carried on at work, and made a complete recovery. When radiographed twelve days after the bleeding, again no abnormality was found. He had never had any symptoms of indigestion, and has had none since, although two years have elapsed.

The last two cases, I believe, illustrate the susceptibility of the gastric or duodenal mucosa, especially in the presence of a high acid, to what are regarded as minor sources of irritation—in the one alcohol, or possibly salted almonds, in the other free acid liberated from aspirin.

Clearly, it is of practical value to realize that profuse haemorrhage may occur as the result of chronic gastritis on the one hand, or comparatively slight trauma in the presence of hyperchlorhydria on the other hand, otherwise these patients might well be condemned to irksome and superfluous restrictions. The more our knowledge of the stomach increases, the greater does the value of special methods of investigation increase. It is only by these that we can be certain of such diagnoses as gastritis and mucosal atrophy. Many people presenting test meals of a type suggesting gastritis have no symptoms whatsoever. In the past it has been assumed that gastritis was present if there was hypochlorhydria or achlorhydria, associated with an excess of mucus. On the other hand, the finding of hyperchlorhydria, which is seldom associated with an excess of demonstrable mucus, was not thought necessarily indicative of gastritis. Too much importance has been attached to what has been regarded as an excess of mucus in the past. The less the acid secreted, the more will the mucus appear to be, although there may be no true absolute increase. Conversely, in highly acid specimens, mucus, when present, is masked and is very difficult to detect. The most obvious appearances of gastritis, as seen through the gastroscope, are usually to be found in a hyperchlorhydric stomach in which test meals reveal no mucus. In short, a hypertrophic gastritis that is very liable to superficial erosions and bleeding will give a test meal of hyperchlorhydria more often than not. If in cases of achlorhydria or hypochlorhydria there is apparently a great excess of mucus, so much so that it is difficult to obtain specimens through the tube, and if in addition blood or pus cells are detected microscopically in the test meal deposits, and again if the test meal has an unpleasant smell, it is probably correct to assume that chronic gastritis is indeed present.

The value of the *gastroscope* lies mainly in three directions: (1) Giving a clear view of the gastric mucosa, from which one can say with some degree of certainty that gastritis is or is not present. (2) Indicating whether an ulcer which has apparently healed, according to occult

blood tests and x-ray examination, has in fact healed or not. Usually it has not, and it requires many more weeks of treatment after the signs are absent before sound healing has occurred. (3) To determine whether an ulcer is malignant. A malignant ulcer can occasionally be recognized as such, when x rays have failed, by observation of its irregular edge.

X Rays.—The combination of the use of small quantities of barium emulsion smeared over the stomach and duodenum and the development of apparatus which allows of aimed exposures, if necessary with compression, makes such an advance in radiographic technique that, given enough experience in interpretation, there is seldom any possibility of error in the diagnosis of peptic ulcer, or genuine as opposed to imaginary disease of the appendix. The only common mistake is to diagnose gastritis too readily, but this aspect will gradually be checked by the extended use of the gastroscope.

The most important contribution to gastro-enterology which has been made in recent years is provided by Magnus and Ungley (1938). Immediately after death from *pernicious anaemia* the stomachs were fixed by the introduction of formalin through a stomach tube. Microscopy showed that the characteristic lesion was one of atrophy of all the stomach coats in the region of the fundus and the body mucosa. The pyloro-duodenal region, which was hitherto supposed to be responsible for the production of the intrinsic factors necessary for the health of blood and spinal cord, was quite normal. Furthermore, *there was nothing to suggest that inflammation—that is, gastritis—had preceded the atrophy*. Gastroscopy confirms the localization of the trouble.

Fifteen years ago, when the orthodox treatment for gastric and duodenal ulcer was prolonged rest in bed and two-hourly feeds of milk and milky foods until the stools became free of occult blood, I abandoned this procedure in favour of a liberal though soft diet, allowing milk, cereals, bread-and-butter, honey, fish, and egg, and purée of fruit and vegetable, after one week of rest in bed on milk only. I have had no reason to regret it. I had not the strength of my convictions when dealing with cases of haematemesis until reading of the most impressive series produced by Meulengracht (1935), who gave patients exhibiting haematemesis and melaena a liberal diet, including even meat, provided the food was soft and the solid food was served as purée, with the most excellent results. He points out quite rightly that it is desirable that the stomach should not be empty of food and thus contain free gastric juice, which may be highly acid and therefore detrimental to the ulcer which is bleeding. Furthermore, the prolonged starvation of the patient, and even deprivation of an adequate amount of fluid, which was so common in the past could only give rise to anxiety, restlessness, and diminishing recuperative powers. His method of feeding has now become fairly general in our hospitals, and the claims have been fully vindicated.

Regional Ileitis

Localized inflammation of the small intestine has recently been holding the centre of medical attention. Crohn, Ginzburg, and Oppenheimer (1932) reported thirteen cases in which it was in the terminal foot of the ileum. It appeared to begin in the ileo-caecal valve, and produced ulceration and destruction of the mucosa with thickening and inflammation of the other coats and considerable narrowing of the lumen. Abscesses and fistulae were reported. Since that time it has become clear that the condition may occur not only in the ileo-caecal region

but also at other points in the course of the ileum. Microscopically the lesion is seen to consist of a benign granuloma, often presenting giant-cell systems, and thus giving rise to the mistaken assumption that the condition was one of tuberculosis. This has been disproved not only by microscopical examinations but also by guinea-pig tests. The symptomatology is a varied one, but with adequate care it is probable that many cases can be diagnosed before operation. The picture may be like that of ulcerative colitis, with diarrhoea, pain, and fever; or again, perhaps more frequently, there is central abdominal pain and recurrent distension of the abdomen, gradually giving rise to a permanent picture of chronic intestinal obstruction. By this time a mass can often be palpated in the right iliac fossa or elsewhere in the abdomen. Loss of weight and anaemia are also fairly constant features. A sudden attack of pain, with tenderness and some rigidity in the right iliac fossa, has often led to the removal of a completely harmless appendix. This should be taken as a warning against the employment of minute incisions for the removing of an appendix, when a larger one would have brought into view the diseased area of the bowel. If found in the early stages the treatment is satisfactory, and consists of resection of the affected portion. X rays will help in the later stages by showing a filling defect and partial obstruction of the ileum.

Intrathoracic Disease

The biggest advance in the diagnosis of pulmonary disease is due to the more general appreciation of the value of the bronchoscope. The discovery of a small carcinoma of a bronchus is thus made possible; it may explain the presence of a lung abscess, the persistence of a cough, or even the sudden development of auricular fibrillation or flutter in a hitherto healthy patient. Why this remarkable association exists is still a matter of doubt. Now that surgery no longer shudders at the removal of a lung such early diagnosis is of very real importance.

Tomography allows of the taking of x-ray pictures of the lungs in different planes, while the other planes are sufficiently suppressed as not to interfere with a clear visual examination of the area inspected. This is particularly helpful in relation to cavities, whether tuberculous or those arising from non-tuberculous abscesses.

O'Shaughnessy's cardio-omentopexy for angina pectoris and persistent disability from cardiac infarction is the outstanding achievement of present-day surgery. The balanced judgment of physician and surgeon in choosing suitable cases of coronary disease is an essential to success.

Pharmacological Advances

Of *prontosil* and its derivatives so much has been written lately that it would be pointless for me to do more than pay homage to this remarkable drug, the uses of which I have summarized in a recent paper (1937a). The haemolytic streptococcus, the *Bacillus coli*, the gonococcus, and probably the meningococcus are all susceptible to its influence, the first, however, far and away the most constantly so. Likewise of *gold* in the treatment of rheumatoid arthritis I shall say little, except to emphasize the fact that it is of much greater value in treatment than any preparation used hitherto; but it also carries with it many dangers, to which I have already made reference (Douthwaite, 1937b).

Eumydrine (atropine methylnitrate), the dose of which is a sixtieth to a thirtieth of a grain, is a valuable anti-

spasmodic, and less poisonous than atropine sulphate. It appears to have revolutionized the treatment of congenital pyloric stenosis in infants and converted it into a medical rather than a surgical problem, to the benefit of the infants.

A valuable addition to our pharmacological resources is *zinc-protamine-insulin*. The object of this preparation is to produce an insulin which is absorbed slowly and will therefore have its action spread out more evenly throughout the day, and thus approximate as closely as possible to the normal production of insulin by the pancreas. The action starts in about nine hours and reaches its maximum in fifteen to twenty hours after injection. A single administration of ordinary insulin and the zinc preparation in the morning may thus suffice for daily treatment.

The success of *measles convalescent serum* was so great that in an epidemic it was often impossible to obtain supplies. This difficulty has been overcome in the most surprising way by the finding of an effective anti-measles *placental extract*. A dose of 5 c.cm. at the first sign of pyrexia, headache, or Koplik's spots will either prevent the rash entirely or render the disease of trivial severity. Smaller doses given earlier in the incubation period will have a similar effect. When we think of the frequency and severity of complications and sequelae of measles it is clear that this discovery is of the greatest benefit to mankind.

Endocrines.—The development of endocrinology has already led to therapeutic results that are little short of startling. One can safely predict the profound effect it will have on medicine of the future, for we are no longer employing foreign substances to influence body activities but rather the very essences of the mysterious life forces. Already we can alleviate the mental and physical disturbances of the menopause with oestrin: we read of virility given to eunuchs with testosterone; and before long I hope we shall have means to control the obesity of pituitary or hypothalamic dysfunction. Yet we must progress cautiously and sift the evidence of efficacy with care lest endocrinology fall into the disrepute so justly meted out to wholesale vaccine therapy and other vogues. Nowhere is this more important than in dealing with male impotence acquired after a period of normal function. So often the cause lies in the mind, and its cure is suggestion. Parkes (1938) clearly summarizes the work on the efficacy of hormones in relation to absorption rate, and reveals the remarkable fact that the more complete purification of the essential extract results in reduced effectiveness on administration. This is due to the hormone being too rapidly absorbed. To counteract this tendency such combinations as testosterone propionate or oestradiol benzoate have been devised.

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