the sort of tuberculosis which should lend itself to a cure when the specific cure for tuberculosis has been found.

2. Simple consumption or simple phthisis pulmonum, called simply by analogy with simple otitis media, simple meningitis, as opposed to a condition due wholly to a specific single cause, such as tuberculous otitis media, cerebro-spinal meningitis, etc. A condition in which histolysis is produced by catarrho-pyogenic organisms; the destruction at first may be slight and unrecognizable clinically or radiographically. All that the patient complains of is slight haemoptysis, or even marked haemoptysis, a cough that will not come to an end, as if due to subacute or chronic catarrhal or suppurative bronchitis; or the patient may complain of severer symptoms, and examination may reveal acute or chronic pneumonia, or cavity formation, or bronchiectasis, or putrid bronchitis, with signs especially in one part of the lung, and there may be progressive wasting and debility. In all cases, whether slight or severe, histolysis of some of the lung tissues has taken place. All signs and symptoms may disappear, never to return; or there may be recurrences, or persistent change takes place, and in the latter case catarrho-pyogenic organisms are "carried" organisms, and may be carried for many years, from the first infection, whatever form it takes. But it is not necessary for the first infection to be accompanied by severe manifestations, or even slight ones. The tubercle bacillus takes no part in encouraging these infections to occur, or in producing any of the signs or symptoms.

3. Tuberculo-consumption, tuberculo-phthisis pulmonum. These terms are somewhat cumbersome, but serve admirably to indicate a condition in which to the above scarcity or plenitude of symptoms and signs met with in simple consumption there is added the presence of tubercle bacilli in the sputum. These organisms may be present in few numbers, only occasionally, even once only in a long series of sputum examinations; they may be discovered in sputum which is only mucoid in appearance, or which is very purulent; they may be absent in the fluid brought up in haemoptysis, or they may be present at the first attack of haemoptysis; they may be discovered because the practitioner has routine examinations made of all sputa; surprise may be caused by finding the organisms in the sputum in a patient who feels quite well and yields no signs, but "hawks" or coughs up scanty phlegm.

There is no escape from the fact that there is no parallelism between the presence of tubercle bacilli in the sputum on the one hand and symptoms and signs on the other, so that it is not to be wondered at that prognosis is so difficult in these cases, and especially when it is known that cases who have never yielded tubercle bacilli in the sputum which may amount to drachms and ounces a day, even on repeated examination, and even in the presence of signs of excavation, or of pneumonia, or of bronchitis, the symptoms being slight or severe, may eventually in the near or remote future yield tubercle bacilli, few or many, in the sputum.

To imply that such conditions of the lung are wholly of tuberculous origin, whether tubercle bacilli are present in the sputum or not, is to ignore pathological studies, because *post-mortem* examination may show that the lung lesions are neither wholly nor in part tuberculous, and experimental study shows that the tubercle bacillus cannot produce all the changes met with in the lungs in these cases.

When tubercle bacilli occur in the sputum they do so as an episode in the progress of a case of simple consumption; this is shown by the fact that the tubercle bacilli are very scanty and are only found on rare occasions, the patient living a long and useful life; the catarrho-pyogenic organisms responsible for the simple consumption have mobilized the tubercle bacilli by opening up a focus of tuberculosis which has been resident ever since early life. In other forms of tuberculo-consumption the tubercle bacilli are present in increasing numbers, because, a focus of old tuberculosis having been opened, the tubercle bacilli have been aspirated into other districts of the lung, and with the help of catarrho-pyogenic organisms have produced the common well known type of disease which destroys so many young adults, but takes toll even after a full, or very full, span of life.

Reflection will show that this view of the nature of the

changes met with when the lower respiratory tract becomes infected by catarrho-pyogenic organisms and tubercle bacilli, and of their interactions one upon another, must influence our views not only as to the meaning of the signs and symptoms of such infections, but will give us more certainty in diagnosis and prognosis, more certainty in treatment; and, in addition, by showing precisely who are the patients who are responsible for the dissemination of tuberculosis in a community, will reduce the expense to the individual and to the nation of treating without discrimination large numbers of people as if they were suffering from some form of tuberculo-consumption, when in reality they are suffering from an infection which is much more serious than it is thought to be—namely, that brought about by catarrho-pyogenic organisms.

This view simply requires, on the part of our profession, the examination much more frequently, and infinitely more continuously and thoughtfully, of the sputum for tubercle bacilli.

A reversion to the use of the term "consumption" or "phthisis pulmonum," with the qualifications above suggested, is by no means a reaction in itself. We must still believe that the tubercle bacillus is the cause of tuberculosis, but we need no longer believe that all the changes present in the lungs of a case yielding tubercle bacilli in the sputum are due to the tubercle bacillus. We may believe that cases of simple consumption exist, and are in no way dependent upon early or late tuberculosis of the lungs, but upon catarrho-pyogenic infection; the proof of this latter position is that critical examination of the lungs in such cases at *post-mortem* inquiry, and the modern radiographic study during life of these cases, show the existence of cases of simple consumption which yield signs and symptoms identical with those of tuberculo-consumption, but differing from the latter condition during life by the absence of tubercle bacilli from the sputum.

THE EFFECTS OF PANCREAS PREPARATIONS BY THE MOUTH UPON CARBOHYDRATE METABOLISM.

BY

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EVER since the important part taken by the pancreas in carbohydrate metabolism was proved experimentally in 1889, attempts have been made to treat diabetes mellitus by administering the fresh gland, or preparations made from it, by the mouth. On the whole the results have been disappointing, although a few observers have claimed individual successes. The striking and often dramatic effects obtained with insulin diverted attention for a time from other forms of treatment, but the unavoidable disadvantage of a method which necessitates daily injections over long periods, it may be for the remainder of the patient's life, has recently revived interest in this question; again, satisfactory results have been reported by some, while others have met only with failure. Experimental work, rendered possible by the discovery of insulin, has offered an explanation of this divergence of experience and suggested that there are types of cases in which the regular ingestion of pancreas may be of benefit.

The effects of insulin are usually gauged by the fall in the percentage of sugar in the blood which rapidly follows its subcutaneous or intravenous injection, and it has been generally assumed that because no such change occurs when it is administered in other ways it has no influence upon carbohydrate metabolism. This is not necessarily the case, however, for insulin promotes the deposition of glycogen as well as influencing the utilization of sugar by the tissues; possibly the two functions are distinct, so that one may be lost while the other is retained. In order to test this possibility Mr. Howard and I carried out a series of experiments upon rats and guinea-pigs. They were based upon the well known fact that the fall in the sugar content of the blood induced by injecting insulin can be counteracted by injecting adrenaline as long as there is stored glycogen

in the tissues, since adrenaline promotes the formation of sugar from glycogen, whereas insulin has the reverse effect. If, then, insulin given by mouth, for example, has no influence upon the percentage of sugar in the blood of itself but is still capable of preventing the rise which would otherwise result from an adrenaline injection, it follows that the insulin, or at least a part of it having antiglycogenolytic properties, has been absorbed into the circulation.

Six rats and nine guinea-pigs were first tested for their response to subcutaneous injections of insulin and adrenaline, separately and in succession. The average fasting sugar content of the blood in the rats was 0.11 per cent.; after the injection of two units of insulin it had fallen to 0.06 per cent. by the end of the first hour; while half an hour after 0.25 c.cm. of adrenaline had been given subcutaneously it had risen to 0.17 per cent. When two units of insulin were injected and followed a quarter of an hour later by 0.25 c.cm. of adrenaline, an average blood sugar of 0.11 per cent. was found in half an hour, one hour, and again in an hour and a half. Similar results were obtained with the guinea-pigs, an average fasting blood sugar of 0.09 per cent. being reduced to 0.05 per cent. by the injection of two units of insulin, and increased to 0.15 per cent. by 0.25 c.cm. of adrenaline. When the two were given in the same doses in succession the rise which should have resulted from the adrenaline did not develop, nor did the same fall occur as when the insulin alone had been given, an average level of 0.07 per cent. being obtained in one and a half hours, suggesting that the dose was not quite as well balanced as in the rats and that there was a relative excess of insulin. Investigation of the respiratory quotient of these animals showed that an injection of two units of insulin induced an average rise of 6.5 per cent. in the rats, and 15.5 per cent. in the guinea-pigs, while 0.25 c.cm. of adrenaline given subcutaneously resulted in an increase of 8.3 per cent. in the former and 8.8 per cent. in the latter. Successive injections of the same dose brought about no change in one rat and one guinea-pig; in the remainder there was a rise of 3.2 per cent. in the rats and 5.5 per cent. in the guinea-pigs.

The same animals were then given two units of insulin by the mouth every hour for three hours, and it was found that no alteration in the sugar content of the blood or in the respiratory quotient resulted. On repeating this experiment but injecting 0.25 c.cm. of adrenaline subcutaneously a quarter of an hour after the last dose, the pronounced rise in the sugar content of the blood when adrenaline had been given alone did not occur, the average for the rats in half an hour working out at 0.12 per cent. and in an hour at 0.11 per cent., while in the guinea-pigs 0.09 per cent. was found at the half-hour and hour. Two of the rats and one of the guinea-pigs showed a slight rise in the respiratory quotient—2.6 per cent and 1.3 per cent. respectively, but both figures are probably within the limits of experimental error. It is therefore evident that when insulin is given by the mouth to rats and guinea-pigs it loses its power of bringing about the characteristic drop in the sugar content of the blood resulting from subcutaneous injection, but is absorbed and retains its property of counteracting the effect of adrenaline.

Further observations upon rats suggested that this property is not due to a chemical neutralization of adrenaline by insulin but is dependent upon their exerting opposing influences on carbohydrate metabolism, for when an injection of 0.25 c.cm. of adrenaline was given subcutaneously, followed immediately by a mixture of the same amount of adrenaline with two units of insulin hourly for three hours by the mouth, the percentage of sugar in the blood was not affected and the respiratory quotient was unaltered in four of the rats and showed an average increase of only 1 per cent. in the remaining two. It should be mentioned that preliminary experiments had proved that adrenaline by the mouth has no effect on the blood sugar or on the respiratory quotient.

Rats are peculiarly suitable for feeding experiments as they greedily eat anything; no difficulty was experienced therefore in feeding six rats with large quantities of fresh guinea-pig pancreas. Although as much as a whole gland

was taken by each of the animals on one occasion, frequent examinations of their blood at intervals up to four hours showed no fall in the blood sugar, which averaged out at 0.12 per cent., compared with the average fasting value of 0.11 per cent. The respiratory quotient was unchanged in five and showed an increase of 2.5 per cent. in one, but as there was no rise in the blood sugar this slight increase may have been an experimental error. When these rats were given half a fresh guinea-pig's pancreas by the mouth and 0.25 c.cm. of adrenaline was injected subcutaneously a quarter of an hour later the percentage of sugar in the blood was not increased and the respiratory quotient was unaltered in four, while in two there was an average rise of 2.5 per cent. It is, of course, impossible to estimate the insulin content of the pancreas administered in these experiments; but it is evident that half a fresh guinea-pig's pancreas neutralized the effect exerted by 0.25 c.cm. of adrenaline on carbohydrate metabolism more completely than two units of insulin in spite of the fact that by itself it had no more influence upon the sugar content of the blood.

We have carried out a similar series of experiments with a number of commercial preparations of pancreas advertised as being efficacious in the treatment of diabetes, employing samples kindly supplied to us by the makers. None of these was found to reduce the sugar content of the blood like insulin when administered orally or by subcutaneous injection, so that, evidently, they cannot be used to supplement or replace the entire internal secretion of the pancreas and promote sugar utilization by the tissues. That this is the case, at any rate as regards oral administration, is further shown by there being no appreciable change in any instance in the respiratory quotient when they were given to rats in doses advised by the makers for human beings:

Proportions of Rats showing an Increase in the Respiratory Quotient (R.Q.).

	R.Q. Increased.	R.Q. Average per cent. Increase.
Insulin 2 units subcutaneously	6 out of 6	6.5
Adrenaline 0.25 c.cm. subcutaneously	6 " 6	8.3
Insulin and adrenaline subcutaneously	5 " 6	3.2
{ Insulin, oral, 2 units hourly for three hours	0 " 6	—
{ Do., and adrenaline subcutaneously 0.25 c.cm.	2 " 6	2.6
{ Raw pancreas, oral (half guinea-pig's pancreas)	1 " 6	2.5
{ Do., and adrenaline subcutaneously 0.25 c.cm.	2 " 6	2.5
{ Mackenzie Wallis's extract, oral, 1 gr. hourly	0 " 6	—
{ Do., and adrenaline subcutaneously 0.25 c.cm.	1 " 6	1.3
{ Trypsogen, oral, 1 tablet hourly for three hours	2 " 7	3.3
{ Do., and adrenaline subcutaneously 0.25 c.cm.	2 " 7	1.3
{ Trypsogen with gold and arsenic, oral, 1 tablet	2 " 7	3.1
{ Do., and adrenaline subcutaneously 0.25 c.cm.	7 " 7	3.1
{ Insulase, oral, 5 gr. hourly for three hours	2 " 7	1.3
{ Do., and adrenalin subcutaneously 0.25 c.cm.	3 " 7	1.3
{ Pancreatin (old stock), oral, 1 tablet for three	1 " 7	2.6
{ Do., and adrenaline subcutaneously 0.25 c.cm.	7 " 7	11.0
{ Pancreatin (new), oral, 1 tablet for three hours	0 " 7	—
{ Do., and adrenaline subcutaneously 0.25 c.cm.	7 " 7	7.6
{ Foetal pancreas (Harrower), oral	0 " 7	—
{ Do., and adrenaline subcutaneously 0.25 c.cm.	6 " 6	3.9
{ Pancreas tail (Harrower), oral	1 " 7	1.3
{ Do., and adrenaline subcutaneously 0.25 c.cm.	6 " 6	6.1
{ Pancrehepatine, oral, 1 tablet hourly for three	1 " 6	2.6
{ Do., and adrenaline subcutaneously 0.25 c.cm.	3 " 6	2.2

Several, although not all, of these preparations appeared to have the power of neutralizing the effect of a subcutaneous injection of adrenaline, like insulin or fresh pancreas; for when an average human dose was given by the mouth and 0.25 c.cm. of adrenaline was subsequently injected there was no rise in the respiratory quotient in at least the majority of the animals, and when

an increase occurred it was considerably less than when adrenaline had been injected alone (see table). Judged by this criterion, Mackenzie Wallis's preparation, trypsinogen, especially when prepared without gold and arsenic, and to a less extent insulase and pancrehepatine, would seem to contain an antiglycogenolytic fraction which is absorbed from the alimentary tract, and, so far as one can tell without means of accurately comparing the dosage, is as active as in raw pancreas. It is probable that the age of the preparation influences its efficiency in this respect, for a sample of pansecratin which had been kept in the laboratory for over a year was found to have no power to neutralize the effect of adrenaline, whereas a fresh sample used immediately after its receipt from the maker gave a better result.

If raw pancreas and pancreas preparations taken by the mouth act in human beings as they do in rats it would seem that they cannot be relied upon to replace the internal secretion of the pancreas entirely when it is deficient or absent, for although glycogen storage may be improved by their administration, the utilization of sugar by the tissues is not affected and the progress of the disease will not be materially influenced; when, however, there is merely a relative deficiency of the antiglycogenolytic factor due to the abnormal activity of some influence which, like adrenaline, prevents glycogen storage, the excessive formation of sugar from glycogen can apparently be controlled and prevented by an adequate dosage of one or other of these substances. In other words, it seems probable on experimental grounds that true pancreatic diabetes, dependent upon organic or functional deficiency of the gland, is not likely to benefit from the treatment to any appreciable extent, but that "non-pancreatic" glycosurias in which the functions of the pancreas are being normally or nearly normally carried out and there is merely a relative deficiency of the internal secretion will probably be improved and may even be cured, if suitable restriction of the diet is practised at the same time, especially in the earlier stages.

My clinical experience with various pancreas preparations, and especially with Mackenzie Wallis's extract and trypsinogen, tends to confirm these conclusions, for I have found that when their administration is confined to cases where analysis of the blood shows that defective glycogen storage is responsible for the glycosuria the results of adequate and prolonged treatment are satisfactory, but that it is useless, or worse than useless, to waste time on oral treatment where examination of the blood gives decisive evidence of an absolute deficiency of the internal secretion of the pancreas; in such cases insulin subcutaneously is required, either as a temporary expedient while the pancreas is recovering its functions, or permanently when there is organic disease of such extent that an adequate diet cannot be metabolized without. As a rule the non-pancreatic forms of diabetes or glycosuria are met with in the later years of life, and it is interesting to note that most of the cases in which treatment with raw fresh pancreas is reported to have been beneficial have been middle-aged or elderly. In some there has been a family history of diabetes or glycosuria—a more common occurrence in the non-pancreatic than in the true pancreatic forms in my experience.

The first case in which diabetes was successfully treated by the oral administration of fresh pancreas was described by Cowles in 1911.¹ The patient, a middle-aged man, is said to have consumed an average of over three fresh pancreases daily, and as a result his appetite improved, his thirst disappeared, a gain in strength and weight occurred, the quantity and specific gravity of the urine fell, and the sugar diminished, although he was never quite sugar-free. The diet was not much restricted, only sugar being forbidden. Eventually the patient discontinued the treatment, the symptoms returned, and he subsequently died after developing a large carbuncle on his neck. *Post mortem* the pancreas was found to be represented by a fibrous cord about one-fourth the size of the normal gland. In this particular instance there was undeniable evidence of serious organic disease of the pancreas, yet large doses of raw pancreas by the mouth were

found to be beneficial. The explanation probably lies in the nature of the disease, which was evidently a chronic interstitial pancreatitis, and this leads me to a brief consideration of the reason why the sugar-utilizing fraction of insulin when given by the mouth does not usually gain entrance to the circulation, like the antiglycogenolytic fraction.

The starting point of Banting's work upon insulin was his conviction that the failure of previous experimenters to preserve the antidiabetic hormone in extracts of the pancreas was due to the presence of the associated proteolytic enzymes by which it was destroyed, and his success arose from the adoption of methods of extraction by which their action was avoided. It seems probable, therefore, that the inactivation of insulin and pancreas preparations taken by the mouth is due to the action of trypsin in the intestine, and that this is the case is further suggested by the results of experiments upon healthy rats which Mr. Howard and I have recently performed. We have found that when means are taken to minimize tryptic action in the intestine the effects of insulin given by the mouth, upon both the blood sugar and the respiratory quotient, approximate more nearly to those resulting from the injection of insulin the more completely the action of trypsin is prevented—results which incidentally suggest that it may be possible eventually to overcome the present disadvantages of oral administration and make it applicable to all forms of diabetes. These results also offer an explanation of the success of the raw pancreas treatment in Cowles's case, for when the external secretion of the pancreas is absent or deficient, as analysis of the faeces shows it is if the gland is sclerotic, the inactivation of insulin, or the internal secretion contained in fresh pancreas, will not take place or will be less complete than when a normal amount of trypsin is entering the intestine; consequently the effect upon carbohydrate metabolism will be greater, particularly as regards the sugar-utilizing factor. It is probable, therefore, that fresh pancreas and active pancreas preparations given by the mouth will improve carbohydrate metabolism in some forms of pancreatic diabetes as well as in the non-pancreatic varieties, under suitable conditions; but as my examinations of the faeces from a very large number of diabetics have shown that an excess of the external secretion of the pancreas is much more commonly met with than a deficiency, more especially in young people and in the earlier stages of the disease, there still remains a very considerable proportion in which no benefit can be expected, at least as the treatment is at present carried out.

REFERENCE.

¹ *Boston Medical and Surgical Journal*, 1911.

THE ULTRA-VIOLET RAYS IN DERMATOLOGICAL PRACTICE.

BY

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FROM time immemorial the value of sunlight has been recognized in the treatment of disease, but it is only recently that, in this country at any rate, physicians have been able to ensure a constant supply of ultra-violet rays. The mercury vapour and the carbon arc lamps were at once recognized as providing a remedy of high potential value, and were tested against various diseases. Exaggerated claims were made for these lamps before a sufficiently long clinical trial had been given them, but they have now been used over a period of some months in the treatment of many different dermatological conditions, and experience has shown in which success may be looked for.

The action of the lamps is both general and local. The general action is that of a powerful stimulant. Young persons respond more readily to this general action than do the old, but patients are few, especially if they live in a town, who do not obtain great benefit. The improve-