REFRESHER COURSE FOR GENERAL PRACTITIONERS**DIAGNOSIS AND TREATMENT OF KETOSIS AND HYPOGLYCAEMIA**

BY

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The presence of ketone bodies in the urine should be regarded as the initial stage of a process which, if allowed to progress, may result in diabetic coma. Whenever the urine is found to contain much sugar it should also be tested for diacetic acid, as it is in the early preclinical stage of ketosis that treatment is both simple and effective. Rothera's test with ammonium sulphate, sodium nitroprusside, and strong ammonia should be carried out first. If this is strongly positive, Gerhardt's ferric-chloride test should also be made. Rothera's test is by far the more sensitive, and may therefore be strongly positive when diacetic acid is present in concentrations too small to give a positive result with ferric chloride. An appreciation of this difference between the two tests will enable them to be used to give a rough quantitative idea of the intensity of the ketosis. A positive ferric-chloride test should always be regarded as indicating severe ketosis and the necessity for immediate treatment.

Causes of Ketosis

Ketosis is often present in untreated cases of moderately severe and severe diabetes, its presence being unassociated with any other morbid process. In treated diabetics ketosis may be the result of nothing more than inadequate control of the diabetes, but there is often some complicating factor present which causes an increase in the severity of the disease. This may be an acute infection such as gastro-enteritis, hepatitis, pyelitis, tonsillitis, or pneumonia, or a local condition such as an insulin abscess, carbuncle, or a septic condition of the feet, including gangrene.

Gastro-enteritis rightly heads the list, as it is one of the commonest causes of severe ketosis and diabetic coma. This is because it not only aggravates the diabetes but also produces a state of starvation and dehydration, both of which favour the development of diabetic coma. Added to this, in some cases, is the false assumption that inability to retain food constitutes a reason for withholding insulin, the patient having been taught that an injection of insulin must be followed by food. It is important in this connexion to remember that stopping food and insulin in a severe diabetic is one of the quickest and most certain ways of producing ketosis and diabetic coma. For this reason, if a diabetic receiving insulin is unable to eat his normal diet he should always try to take the carbohydrate portion as milk, alone or with a proprietary milk drink, fruit drinks sweetened with glucose or sugar, bread and milk, toast or biscuits, and the usual dose of insulin. If no food can be retained the patient should take half the usual dose of insulin and get in touch with his doctor.

Sulphonamides, penicillin, or other appropriate treatment should be given without delay in cases of infection, and local collections of pus should be drained whenever this may be done without a general anaesthetic. Major operations on patients with severe ketosis should, if possible, be postponed until the diabetic condition has received appropriate emergency treatment (see below).

Symptoms and Signs of Ketosis

These are anorexia, nausea, vomiting, abdominal pain, shortness of breath, and drowsiness. The only signs are a smell of acetone in the breath, furring of the tongue, and sometimes flushing of the face. All these symptoms and signs may be absent in the presence of a strongly positive Rothera's test, but if this warning is ignored they may develop with alarming rapidity, especially when the patient starts vomiting.

Treatment of Ketosis

The discovery of significant ketonuria indicates the need for insulin therapy or (if the patient is already having insulin) an increase in dosage or some other modification of the existing treatment. In untreated diabetics with moderate ketonuria a single dose of protamine-zinc insulin (P.Z.I.) will often correct the condition, even if it does not control the glycosuria. In severe ketosis, particularly if the ferric-chloride test is positive, the best treatment is the use of two injections of soluble insulin (S.I.), as described in last week's *Journal* (p. 1345).

A third dose may be given before the midday meal if heavy ketonuria persists for more than 48 hours. It is impossible to be dogmatic about dosage, but it is usually safe to start with about 16 to 24 units in the morning and a rather smaller dose in the evening.

When the patient is already taking insulin, treatment will depend on the type of insulin used and the arrangement of doses. For patients receiving a single injection of P.Z.I. the addition of some S.I. before breakfast is often effective, but if this fails to relieve the ketosis a second injection of S.I. may be given before the evening meal.

When a mixed injection of S.I. and P.Z.I. is being taken, the dose of S.I. should be increased by 8 to 12 units, and if ketosis persists an evening dose of 12 to 20 units of S.I. should also be given.

Ketosis in diabetics receiving two injections of S.I. is relatively easy to treat by increasing the dose of both injections and, if necessary, adding 12 to 20 units of S.I. before the midday meal. In all cases care should be taken to see that the daily carbohydrate intake does not fall below 150 g.; if possible, 180 to 200 g. should be given. If the patient is disinclined to eat, the protein and fat portions of the diet may be omitted and the carbohydrate given in the semi-solid or fluid forms described above.

Clinical Ketosis or Pre-coma

When symptoms and signs of ketosis are present the ferric-chloride test will usually be found to be positive, and the condition should be considered as a medical emergency. Treatment consists in giving injections of S.I. and carbohydrate feeds at regular intervals, the following method being both simple and convenient.

The patient's urine is tested four-hourly for sugar (by Benedict's test) and for ketone bodies, and after each test an injection of S.I. is given, the dose depending upon the

general examination should be made, without undue exposure, to exclude any general or local infection, and suitable treatment started without delay.

An injection of 80 to 100 units of S.I. should be given subcutaneously and an intravenous drip set up, if possible into a forearm vein and without cutting down. A catheter specimen of urine should be tested for sugar, ketone bodies, and chlorides, and blood taken for sugar estimation. The stomach should then be washed out with sodium bicarbonate solution. It is convenient to use normal saline for the early treatment of dehydration as it also corrects chloride loss and does not obscure the effect of the initial dose of insulin. The first two litres should be allowed to run in as fast as possible, and if the blood pressure remains very low a third litre may be given in the same way, provided that a careful watch is kept on the bases of the lungs for the onset of pulmonary oedema. Inability to overcome peripheral circulatory failure is the commonest cause of death in diabetic coma, and it is worth while giving 2 pints (1.1 litres) of plasma if saline fails to maintain the blood pressure.

By the time all these things have been done the result of the initial blood-sugar estimation should be known and a decision can be made whether to give more insulin at once or to wait three to four hours for the result of the second blood-sugar test. If the level is very high—over 800 mg. per 100 ml.—a further 80 units or more should be given at once, according to the degree of glycaemia, but for lower levels it is safer to wait and see the effect of the initial dose of insulin. Desperate late cases with a very high blood sugar and an extreme degree of ketosis and dehydration may require many hundreds or even thousands of units of insulin, but they are comparatively rare. The early cases of average severity seldom need more than a few hundred units to remove the ketosis and reduce the blood sugar to a normal level.

There is a tendency at present to give needlessly large and potentially dangerous doses of insulin at very frequent intervals to cases of diabetic coma which could be equally effectively and more safely treated with smaller doses given at intervals of three to four hours. After the second blood-sugar reading has been taken, 4% glucose in 1/5 normal saline should replace normal saline and be given by drip until the patient is conscious and able to take fluids by mouth without vomiting. From this stage onwards the treatment should be the same as that described under "Pre-coma."

Marked tachycardia often persists for several days after the patient has come out of coma, and during this period every care should be taken to throw no unnecessary strain upon the heart. Vitamin B by intramuscular injection in doses of 50 or 100 mg. daily has been advocated, on the assumption that deficiency of this vitamin may be one of the factors responsible for the myocardial weakness.

HYPOGLYCAEMIA

This condition is typically sudden in occurrence, and the patient is well up to the time of onset. The symptoms fall into two main groups. The early symptoms are similar to those produced by an injection of adrenaline, and include pallor, sweating, palpitations, and tremor. The later group are due to failure of oxidation of carbohydrate in nervous tissue, and include higher-centre manifestations such as depression, euphoria, inability to concentrate, deterioration in judgment, and amnesia. There may in addition be central nervous system signs, of which hemiplegia, monoplegia, ataxia, diplopia, and paraesthesiae are the most

common. Hunger is a common symptom, and headache, nausea, and even vomiting are sometimes produced by hypoglycaemia, especially when it is due to P.Z.I. A recurrent morning headache relieved by breakfast is always suggestive of P.Z.I. overdosage. Loss of consciousness may be preceded or accompanied by epileptiform fits, and is a late manifestation of hypoglycaemia in all but those rare cases in which the earlier warning symptoms are entirely absent.

Hypoglycaemic coma should always be suspected when a diabetic taking insulin is known to have been in reasonably good health within a few hours of loss of consciousness. A good history will almost always serve to exclude diabetic coma, but a cerebrovascular lesion such as a haemorrhage, embolus, or thrombosis may present more difficulty, especially if the patient is elderly and has arteriosclerosis.

Patients in hypoglycaemic coma are pale, and the skin is moist; ocular tension and blood pressure are unaffected, respiration resembles that of normal sleep, and there is no acetopnoea. Signs in the central nervous system should not be relied upon in diagnosis, for reasons already given, but are more likely to be present in hypoglycaemic than in diabetic coma. The urine may contain sugar if the bladder has not recently been emptied, but if a catheter is passed the next specimen will be found to be sugar-free. Ketone bodies are absent; if they are present as the result of starvation they are insignificant in amount. The diagnosis may be confirmed by estimation of the blood sugar, which is always low and usually less than 60 mg. per 100 ml. Treatment should never be postponed to obtain the result of the blood-sugar estimation. The differential diagnosis of hypoglycaemia and cerebrovascular accident is rendered simple in most cases by the rapid response of the former to correct and adequate treatment, after which any signs in the central nervous system rapidly disappear.

There is a definite relationship between the time of onset of hypoglycaemia and the type and dose of insulin injected. Thus, small or moderate doses of S.I. tend to produce their maximum effect three to five hours after injection, and larger doses (of 40 units or more) six to ten hours after injection or later. In patients receiving morning and evening S.I., hypoglycaemia is therefore most likely to occur before lunch or tea, and again at bedtime or during the early part of the night, according to the size of dose injected. As P.Z.I. acts most strongly when the patient is fasting, it is most likely to produce hypoglycaemia during the late night or early hours of the morning. Mixed injections of S.I. and P.Z.I. may cause hypoglycaemia before the midday meal, in the late afternoon, and during the night. Globin insulin in some patients resembles S.I. and produces hypoglycaemia before the midday meal, while in others reactions are more common in the late afternoon. If globin insulin is given before breakfast it rarely causes hypoglycaemia during the night.

Prevention of Hypoglycaemia

The time relation between insulin and hypoglycaemia already described makes it possible to anticipate its onset and prevent it by the use of so-called buffer carbohydrate feeds. These should consist of 10 to 20 g. of carbohydrate. For a patient receiving S.I. they should be given at about 11 a.m. and 11 p.m. If a single morning injection of P.Z.I. is being used the feeds are taken at bedtime, and with a mixed injection of S.I. and P.Z.I. at 11 a.m. and on retiring.

Treatment of Hypoglycaemia

First give sugar, glucose, biscuits, bread, jam, chocolate, or some other food with a high carbohydrate value. All diabetics treated with insulin should carry sugar or glucose, and a card stating the nature of their complaint, their dosage of insulin, and the name of the hospital, clinic, or doctor they attend. Such a card can be obtained from the Diabetic Association. Treated early, while the patient can swallow, hypoglycaemia responds very quickly, but care should be taken to give enough carbohydrate to prevent relapse. Three or four lumps of sugar is usually a suitable amount to start with, but more should be given if there is not obvious improvement in 10 to 15 minutes. When consciousness has been lost and food can therefore no longer be given safely by mouth, one of the following methods should be used.

1. *Intravenous Glucose*.—This is the ideal method. If a 60% solution is available a sufficient amount of glucose can be given with a 20-ml. syringe to bring all but the most advanced cases out of coma.

2. *Subcutaneous Adrenaline*.—The injection of 15 minims (0.9 ml.) of 1 in 1,000 solution of adrenaline will raise the blood sugar, produce a return to consciousness, and permit a solution of sugar to be given by mouth.

3. *Stomach Tube*.—This is a safe and good method, and allows a wide choice of carbohydrate food to be made.

The majority of cases of hypoglycaemia recover spontaneously, but some pass into an irreversible state in which they die, and others recover with permanent damage to the brain. It should always be remembered that frequent attacks of hypoglycaemia resemble persistent or recurrent ketosis in so far as they indicate a state of poor stabilization, but, of the two, they are probably the more dangerous. For this reason, whenever there is any doubt about the cause of unconsciousness in a diabetic taking insulin, always give sugar alone first; if the condition is due to hypoglycaemia recovery will result, and if it is due to any other cause, including diabetic coma, no harm will be done.

INTERNATIONAL CONGRESS OF SURGERY MEETING AT NEW ORLEANS

The 13th Congress of the International Society of Surgery, held in New Orleans from October 10–15, was attended by about 500 participants from some 45 countries. All Europe, save Germany and Russia, sent delegates. As usual, France, Belgium, Spain, and Italy were well represented.

Throughout the week the weather was trying, for it was both hot and humid, with some heavy showers. The main activities were centred about the Roosevelt Hotel, which was the headquarters and is not far away from what might be called the medical centre. The huge Charity Hospital with its 3,000 beds is situated there, with the medical departments of the Tulane and Louisiana Universities adjoining.

Each delegate was presented with a useful handbook carrying portraits of the president and the venerable Professor Rudolph Matas, who is still hale and hearty at 89. Professor Matas, honorary chairman of the local committee, is beloved as the doyen of the profession in the South and the lodestar of all medical and cultural activities in New Orleans. The list of sponsors of the Congress was interesting and informative, for it included the State of Louisiana, the City of New Orleans, the Harbour Commissioners, International House, the Association of Commerce, the Public Services Incorporation, and the Universities of Tulane and the Louisiana State. Our own public bodies might take notice of the interest in the Congress shown outside the surgical world.

The people were well aware of our presence and took a lively interest in us, while newspaper publicity was keen and profuse, not only in New Orleans but in the United States generally. Everyone was kind and helpful, and imbued with a refreshing degree of civic pride. The city is spread over a large area, the wide boulevard Canal Street leading to an extensive residential district. The open canals, such a striking feature of the original city, are now covered and bordered with trees. Drainage and water supply are good, and tropical fevers have been banished since 1905, which year marked the conquest of the "yellow jack" scourge and was a landmark of which the medical faculty has much reason to be proud.

The inaugural function took place on the evening of the first day at 8.30 p.m. This was a formal occasion, graced by the presence of the Hon. Walton Butterworth, an Assistant Secretary of State of the U.S.A.; the Hon. Earl L. Long, Governor of the State of Louisiana; the mayor of the city; the officers of the society; Dr. Sandblom, from Stockholm (representing the delegates); and Lord Webb-Johnson, representing the Royal College of Surgeons.

Dr. Arthur Allen, of Boston, vice-president of the society, presided over the meeting. As there were ten addresses to be made, mainly of a general and semi-political character, it was ten o'clock before Professor Grey Turner, the president of the Congress, was called upon to give his inaugural address. The evening was hot and stuffy, and many in the audience must have already reached the point of weariness, if not exhaustion. During the address the president showed by projection pictures of the presidents since the first congress, which was held in Brussels in 1905. His main theme was the training of the surgeon, but in view of the late hour his address had to be considerably curtailed.

Scientific Work

The scientific work began next day. An operating session at Charity Hospital was held from 7.30 a.m. to noon, and the operations were televised to the ballroom of the Roosevelt Hotel. As the galleries for visitors at the hospital provided small accommodation and the floors of the theatres were occupied by many assistants, most delegates had perforce to be content with the television, which was generally agreed to be satisfactory. The screen was 8 ft. by 5 ft. (2.4 by 1.5 m.); the pictures were not in colour, but came out fairly well. Only the immediate operative field could be seen, so that a grasp of the general topography was difficult. There was a running commentary by the operator relayed from the theatres, with some interpolated remarks which were probably not intended to reach the air. The television of other operating sessions was conducted later, when Professors Alton Ochsner, Rives, and others were the operators.

The scientific discussions began on Tuesday afternoon, when Professor Paolucci, of Rome, gave the opening paper on the surgery of the parathyroid. In the discussion Leriche (Paris), Bastos-Ansart (Barcelona), Parsons (New York), Jung and Fontaine (Strasbourg), Mallet-Guy (Lyons), Manzanilla (Mexico), and others took part. Each opener was allowed 30 to 40 minutes and subsequent speakers only five minutes, and it was remarkable how the exertions of the president in the chair managed to keep the speakers pretty well to this schedule. Another feature of the Congress was the installation of the headphone transmission, which worked well enough to give great hopes for its complete success in the future. By adjusting the apparatus each member of the audience could elect to listen to the speaker in the language employed or to hear a translation into French or Spanish. If interpreters familiar with technical terms are available the rendering is naturally better.

The next session, on the surgery of the pancreas, was opened auspiciously by Professor Ian Aird. He was assisted by an excellent series of lantern slides with captions in French. He dealt mainly with operative procedure and gave a detailed account of the exposure of the organ. In the discussion most aspects of the subject were dealt with by speakers from Mexico, Sweden, Bulgaria, North Africa, France, and the United States.

The meeting on post-operative thrombosis and its sequelae was opened by Alton Ochsner and De Bakey, of New Orleans,