hyaline degeneration is present in these cases—as is probable—it would seem that this degenerative change is not due to the diabetes itself but to associated vascular lesions. In any case we are of the opinion that widespread arterial degeneration can produce the whole clinical picture within a short space of time.

With regard to Group 2, where incidental 'oedematous nephritis occurred in diabetes, the differential diagnosis is practically impossible during life. The clinical picture is the same, with the exception of occurrence earlier in life and perhaps the absence of retinal haemorrhage.

Prognosis.—The onset of albuminuria, apart from that associated with a precomatose state in diabetic patients, is usually of serious import and must be taken as a warning of impending renal complications. When retinitis and oedema occur the outlook is bad, and within two years death usually supervenes from uraemia, cardiac failure, or a combination of both. It is doubtful whether, in the present state of knowledge, any steps can be taken to defer these changes or to deal effectively with them when they occur.

Summary

Twenty-four cases of renal failure occurring in diabetic patients are described.

Classification shows four groups, including those associated with the Kimmelstiel-Wilson lesion.

Pathological details and photomicrographs illustrate the paper.

We are indebted to Mr. Norman Mowat for preparing the composite photomicrographs and to Mr. George Cheyne for technical help.

REFERENCES

- Anson, L. J. (1938). *Sth. med. J.*, **31**, 1272.
 Bell, E. T. (1946). *Renal Diseases*. Kimpton, London.
 Derow, H. A., Altschule, M. D., and Schlesinger, M. J. (1939). *New Engl. J. Med.*, **221**, 1012.
 Herbut, P. A. (1941). *Arch. Path.*, **31**, 501.
 Horn, R. C., and Smetana, H. (1942). *Amer. J. Path.*, **18**, 93.
 Kimmelstiel, P., and Wilson, C. (1936). *Ibid.*, **12**, 83.
 Laipply, T. C., Eitzen, O., and Dutra, F. R. (1944). *Arch. intern. Med.*, **74**, 354.
 Mauser, C. L., Rowe, A. H., and Michael, P. P. E. (1942). *Ann. intern. Med.*, **17**, 101.
 Newburger, R. A., and Peters, J. P. (1939). *Arch. intern. Med.*, **64**, 1252.
 Porter, W. B., and Walker, H. (1941). *J. Amer. med. Ass.*, **116**, 459.
 Segal, S., and Allen, A. C. (1941). *Amer. J. med. Sci.*, **201**, 516.

DIABETIC COMA

BY

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From Jan. 1, 1940, to Jan. 1, 1946, Root treated 188 cases of diabetic coma in the New England Deaconess Hospital, with 6 deaths; and from Jan. 1, 1946, to Jan. 1, 1948, he treated 55 cases with no deaths. He has published a very full description of his methods of treatment (Root, 1945). My authority for the recent statistics is a personal communication from him. Few physicians or clinics have published their death rate in diabetic coma, and no recorded results are so good as this.

My essay in discipleship is prompted by the wish to make this line of treatment more widely known, for it has received sadly little attention from writers of textbooks in Europe, and some of the textbooks that are deservedly popular in this country advocate methods which include those very sins of commission and omission which Root has shown to be responsible for failure to save the more severe cases of coma. The chief sin of omission is not to appreciate the urgent need for large doses of insulin and the fact that insulin-resistance increases as the condition

progresses. The chief sins of commission are the early administration of glucose and the use of the oral route for the administration of fluids.

This paper is based on bitter personal experience, for I have made many mistakes myself, and have learnt what happens when sufficient insulin is not given soon enough, when gastric aspiration is omitted or fluids are given by mouth, and when glucose-saline is given intravenously instead of simple normal saline.

Undoubtedly much of the credit for the good results of Root and his colleagues must be given to their personal skill and to the 24-hour laboratory service maintained in their hospital. But even the worst cases can be saved by physicians of less experience and in the absence of blood analysis. Root (1945) states: "No plan of treatment based on mathematical calculations of the blood sugar and carbon dioxide will take the place of constant bedside observation of the patient and adjustment of treatment to the patient's changing condition."

Nomenclature and Diagnosis

The accepted meaning of the word "coma" is a state in which the patient does not respond to any external stimulus. In this sense of the word the term "diabetic coma" is a misnomer, for it is only very rarely that the patient when first seen is in a state of true coma; usually the mental state is one of mild, moderate, or severe confusion with marked drowsiness.

The term diabetic coma is in fact by general agreement applied to severe *rapidly progressive* diabetic ketosis, and its diagnostic features are increasing drowsiness and confusion (ending eventually in true coma) with increasing hyperpnoea, dilatation of the stomach, and eventually circulatory failure due to electrolyte and water depletion. The biochemical findings are characteristic. It is readily induced even in the controlled diabetic by acute infections or alimentary tract disturbances. It is not so much a complication of diabetes as the end-stage of diabetes, and the treatment of coma is the treatment of diabetes—namely, insulin.

The condition is easy to recognize, a mistake being in fact almost impossible. One essential feature which distinguishes it from other causes of coma in diabetics is that in diabetic coma "unconsciousness" does not supervene till after a progressive and characteristic illness lasting as a rule several days. The diabetic who is found "unconscious" without any preliminary illness may be a case of hypoglycaemia or he may have had a stroke, but he is certainly not a case of diabetic coma.

Summary of Treatment

In most cases it is possible to bring about a striking improvement in from three to six hours, and during this period constant hard work at the bedside is necessary. The only factor in bringing about this improvement is insulin. Two other measures are important—gastric aspiration and the intravenous administration of normal saline.

The chief point in treatment is to ensure, even at the risk of giving more than may be needed, that the patient gets enough insulin within the first three hours. Of course in many cases some infective process is present and must be treated too.

Insulin Dosage

There are four points of fundamental importance. The first is that it is the insulin which cures diabetic coma: though other measures are necessary they are not curative. The second point is that insulin resistance increases so long

as the coma remains inadequately treated; the longer the delay in administering an adequate dose the greater the dose required to cure the patient. The third point is one which is familiar to all physicians who treat diabetic coma, but is not sufficiently emphasized by textbooks. The beneficial effect of an adequate dose of insulin is clinically manifest as a rule in less than 15 minutes; if a single dose of insulin fails to produce an obvious improvement within about 15 minutes it may be inferred that the dose was grossly inadequate. The fourth point is also one which has not been emphasized strongly enough—that, if what may later prove to be an unnecessarily large dose be given, a lapse into hypoglycaemia is not to be feared until after the clinical improvement that is bound to follow a more than adequate dose has taken place.

The required dose varies greatly. In general, the longer the patient has been ill and the graver his state the higher the required dose, but it is impossible to know in advance how much will in fact be required: one gives repeated doses and watches the effect. In an early case—that is, when the patient can give a clear account of himself—start with 100 units, and if there is no obvious improvement in half an hour give 100 units every half-hour until an improvement is obvious. Even in early cases a single dose of 100 units is usually not enough. If the patient is already drowsy and confused give the same initial dose of 100 units, but do not wait longer than a quarter of an hour before giving the second 100 units, for in a mentally confused patient the early good effect of an effective dose is very obvious. If the patient is inaccessible (“unconscious”) start with 500 units, and be prepared to give more if no improvement is seen at the end of half an hour. When the patient is a child a lower scale of dosage may be adopted, and very often hitherto untreated diabetics in coma need less insulin than long-established insulin-treated cases.

If at any stage a striking clinical improvement has occurred and steady progress is maintained, no further insulin need be given, but the moment any suspicion arises that the improvement is not continuing more insulin must be given. If a clinical relapse occurs—that is, if the patient after a short improvement tends to revert to his original drowsiness—*very much more* insulin must be given.

If at the end of the first hour a very obvious improvement has not been produced it must be assumed that the dose of insulin so far given was not merely inadequate but grossly inadequate. It must be remembered that, although some severe cases recover on a few hundred units, dosages of about 1,000 units have sometimes to be given, and even 2,000 units have occasionally been required. Very large doses are particularly likely to be necessary for patients who have before admission been given glucose accompanied by insufficient insulin.

If no improvement has occurred by the end of the first hour doses of 100 units should be given as often as every ten minutes till improvement begins. The chief and most easily detected early signs of improvement are in the mental state and the hyperpnoea.

The less experienced a physician is in the treatment of diabetic coma the more generous should his dosage of insulin be; he must start treatment with the resolution that, whatever happens, he will not allow his patient to die from underdosage. A steadily falling blood sugar is a good indication that the dose so far given is adequate, and a physician who has to treat diabetic coma without blood-sugar estimations should make a point of erring on the generous side with his dosage. An even more trustworthy sign of adequacy of dosage is a steady mental improvement and diminution of hyperpnoea, but the less experienced

physician may find it difficult to be sure that the expected improvement has started; if he is in doubt he should play for safety by giving more insulin, and thus he may expect to find later that he has given much more than was really needed.

So when diabetic coma is treated without blood-sugar control or by relatively inexperienced physicians some cases of hypoglycaemia may be expected to occur, but hypoglycaemia is a minor complication and very easy to deal with. Usually it does not occur until the patient is able to take food by the mouth, but in any case it is easily corrected by an ampoule of concentrated glucose solution intravenously. So far as I know there is no record of a patient ever having passed from diabetic coma into a fatal hypoglycaemic attack.

At the end of three hours there should be marked improvement. The hyperpnoea should have stopped, the blood-sugar should have fallen to near normal, and in many cases the urine will be sugar-free. The pulse rate will nearly always still be rapid. In some cases there will be very much less acetone in the urine, but the rate of improvement in Rothera's test is variable. If the urine was originally copious and pale it should have become less copious and more concentrated. If the urine was scanty or absent (as in extreme cases with grave circulatory failure) the administration of saline should have begun to produce a normal urinary secretion. If the patient is unable to pass urine one must never hesitate about catheterizing at hourly intervals in order to obtain a specimen.

If at the end of the first three hours a striking change for the better has not taken place the sands are running out, and the dosage of insulin must be condemned as very grossly inadequate and very much more be given.

In nearly every case at the end of the first six hours the patient is ready to eat and drink and is asserting his improvement with delight. In the young patient everything should now go smoothly, provided that a watch is kept for hypoglycaemia. In elderly or debilitated patients difficulties in the restoration of the water and electrolyte content of the body fluids may arise.

Relapse into diabetic coma is very rare indeed, but the dosage of insulin required during the few days after recovery is very variable. Many cases, after being sugar-free and almost acetone-free, soon develop glycosuria and slight ketonuria again and need large doses for the next few days, but others may not need any insulin at all for twelve or twenty-four hours after their recovery.

Gastric Aspiration

In almost every case of diabetic coma admitted to hospital the stomach is dilated, and unless this is dealt with the physician will lose some of his cases no matter how skilful his treatment in other respects may be. In many cases the condition gives rise to abdominal pain, but in others there is no complaint of pain at all. Examination of the abdominal wall does not as a rule give any hint of the presence of this dilatation.

As soon as the initial dose of insulin has been given a stomach-tube should be passed no matter how strongly the patient may object. Usually at least a pint of contents can be aspirated, and in all cases of severe coma they are black; in the less advanced cases they are brown or pink, but sometimes at an early stage they are not tinged with blood at all.

When gastric aspiration is omitted the following sequence of events may occur. Improvement on insulin and intravenous saline takes place and the patient seems to be on the

road to recovery. Then, as his mental state improves, just as in a patient recovering from an anaesthetic, he becomes restless, vomits a few ounces of black or coffee-coloured fluid, and within a few minutes marked dyspnoea with numerous rales sets in, the pulse becomes quick and feeble, and the patient dies in cyanosis. Post-mortem examination shows gastric contents in the respiratory passages.

Unless the patient is mistakenly allowed to drink before he has recovered it is not usually necessary to aspirate the gastric contents a second time, but a second aspiration is occasionally called for. A return of abdominal pain or a rising pulse rate should suggest the need for a second aspiration.

It should be remembered that the disturbance of the alimentary tract is not confined to the stomach. The intestine is often incapable of absorbing a rectal drip, and a rectal saline may be retained in the bowel for some hours before being returned.

Saline

Almost every case of moderately severe diabetic coma needs (if an adult) from 2 to 4 litres of normal saline in the first few hours. If the blood pressure has fallen to a dangerously low level 2 litres given quickly will as a rule restore it, but much more may be needed. In rare cases with complete anuria even larger volumes have been given with success. Root emphasizes that in such cases intravenous saline should be given until urinary excretion begins.

It is not easy to know which cases will need intravenous saline and which will recover without it. Except in cases of marked circulatory collapse it is not an urgent matter, but once the patient has reached hospital it is wise to give it if the case is of even moderate severity. The needle used should be of a bore large enough to allow a rapid flow, but in cases with circulatory failure it may be necessary to cut down a vein. Another difficulty sometimes met with is vein spasm. In such cases a pump of the rotating cam type which milks the fluid down the tube can be used to start the flow; once spasm has been overcome it is no longer needed. In gravely collapsed patients subcutaneous saline should be started at once in order that no time shall be lost while search for a vein is being made.

The rate of flow should be fast enough to deliver the initial 2 litres in about an hour. In some cases it may be possible to stop then, but as a rule it is safer to leave the needle in for a few more hours and continue to administer at least enough saline to make good the continuing urinary loss until clear clinical signs of recovery appear. There is no risk of overloading the circulation by the initial 2 litres, but in elderly diabetics with myocardial inadequacy and potential left-ventricle failure there is a grave risk of delivering fluid too rapidly after the initial extreme sodium and water depletion has been corrected. In children the rate of flow must be much slower than in adults.

Root's statistics strongly support his claim that normal saline is the only intravenous injection needed in diabetic coma. Other authors have asserted that alkalinizing solutions are necessary or that plasma should be used. Any physician who has seen elderly diabetics pass the first critical six hours and become sugar-free and ketone-free only to die a few days later from circulatory failure must worry, as I have done, about the adequacy of his treatment. But, in view of the very large volume of saline given by Root to some of his cases with ultimate success, the probability is that when others fail to restore the blood volume it is the physician's judgment which is at fault and not the composition of the solution used.

Recently it has been pointed out that recovery from diabetic coma is followed by a fall in blood potassium and

blood phosphate levels, and it has been suggested that this fall may be the cause of deaths occurring some hours or days after the cure of the ketosis.

There is, in effect, definite evidence that a serious potassium depletion may occur in some cases, and the clinical picture appears to be recognizable. If marked asthenia follows an apparent clinical recovery the possibility should be suspected and potassium chloride (or some other potassium salt) given in 0.5-g. doses every half-hour. Recovery has been recorded as a result of this line of treatment (Holler, 1946; Nicholson and Branning, 1947).

Glucose

For some years Root and his colleagues have preached against the administration of glucose in diabetic coma. Their arguments have been so widely accepted, and they have made so many converts among those who formerly administered glucose as a routine, that it must be admitted that they are right.

There is of course no danger in administering glucose if after a successful treatment by insulin a low blood sugar or sugar-free urine suggests that hypoglycaemia is to be expected, but glucose given at an earlier stage is dangerous. Admittedly many cases of coma which have been given glucose and sufficient insulin have recovered, but nevertheless glucose given at an early stage exposes the patient to special added risks which may just turn the scale against him.

Glucose-saline must not be given instead of normal saline by the intravenous route. One litre of glucose-saline contains 50 g. of glucose—that is, enough glucose to raise the already very high blood sugar to well over 1% if the injection is given at the usual rate. As a result the urinary excretion of water and of glucose tends to rise rapidly, and the degree of both water and sodium depletion may be increased. Almost as serious is another result—that the physician is deprived of two very valuable aids to his assessment of progress, the falling blood sugar and the gradual return of the volume and colour of the urine to normal. Finally it has been shown that continued administration of glucose may in the end favour the onset of anuria.

The notion that glucose is a part of the treatment of coma entails another danger—that the physician may order his patient to drink glucose solution and thus increase the degree of dilatation of the stomach. In my experience this is a very common mistake, and the ill effects are very obvious.

The General Practitioner and Coma

Few of us can hope to be in a position to claim, like Root, that we have cured 55 consecutive cases out of 55, but all of us should be able to cure every moderately early case. The following suggestions should facilitate early administration of insulin, the point above all others which is decisive.

Every patient on one of the slow insulins should stock a couple of bottles of plain insulin for his doctor's use in emergencies, for the doctor called to a diabetic's house may not think it necessary to pack insulin in his bag.

Every hospital which is prepared to treat diabetic coma should make it known to all local practitioners and to all its diabetic patients that an acutely ill diabetic is always admitted without even telephone notice, whether it has a vacant bed or not. The relatives of all diabetic patients should know that when a diabetic takes to his bed or seems in any way unwell he should be shifted at once to hospital.

The doctor called to a case of coma should always give at least 100 units at once before even ordering the ambulance. If the patient is inaccessible ("unconscious") he should give

500 units, but in such patients he should aspirate the gastric contents, as extreme gastric dilatation is sure to be present and the patient may improve enough to vomit in the ambulance and inspire his vomit.

Any physician who has ever treated diabetic coma in the patient's own home must agree that, though of course one may succeed, the difficulties are so great and the unpleasant surprises so numerous that home treatment should rarely if ever be undertaken.

Summary

The line of treatment of diabetic coma given by Root and his colleagues in Boston is advocated.

The essential point is large insulin dosage at an early stage. Physicians less experienced than Root and working in less well-equipped clinics should deliberately err on the side of giving larger doses than the experts, for there is no danger in giving too much and every danger in giving too little.

Gastric aspiration must be carried out as routine in every case and nothing be given by the mouth during the critical first few hours.

Intravenous saline is needed by many cases and by all the severe cases, sometimes in very large quantities. The syndrome of potassium depletion must be rare, but the possibility should be kept in mind.

Glucose must not be given by any route until clinical recovery has begun, but after this it may safely be given to prevent hypoglycaemic attacks.

REFERENCES

- Holler, J. W. (1946). *J. Amer. med. Ass.*, **131**, 1186.
 Nicholson, W. M., and Branning, W. S. (1947). *Ibid.*, **134**, 1292.
 Root, H. F. (1945). *Ibid.*, **127**, 557.

TREATMENT OF CHRONIC VARICOSE ULCERS BY LUMBAR SYMPATHECTOMY

BY

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Chronic varicose ulcers heal slowly, relapse easily, and remain a source of constant annoyance to those they affect. Some tend to heal in summer, some with or in spite of the application of lotio rubra, scarlet red, sulphonamide, or penicillin powders, some following protection by Unna's paste or "elastoplast"; some respond to sclerosing treatment of the causative veins or after Trendelenburg's operation with high and low ties, some even requiring skin-grafting. Yet many, even after this gamut of medical and surgical treatment, remain a chronic antisocial disability to their unfortunate owners.

Case 1

A man aged 49 was admitted to Southend General Hospital on Sept. 9, 1946, with a history of varicose veins in his left leg associated with a large left varicose ulcer for 27 years. He had had a flesh gunshot wound in this leg below the knee in 1917, without peripheral nerve injury. In 1937 a left saphena varix had been excised. In spite of a wide range of local treatment the ulcer never healed even after lengthy periods of rest in bed. The Wassermann reaction was negative.

On June 8, 1946, two varices were excised from the left femoral triangle and several others from the left popliteal fossa. On reporting to the out-patient department on Aug. 17 he complained of the ulcer, which was larger than before,

together with pain and swelling in the left leg. There was thrombophlebitis of the branches of the saphena magna vein. On Sept. 9, there being no improvement, he was admitted. The ulcer, situated just above the medial malleolus, measured 5 by 3 cm.

The leg was elevated and the ulcer covered with tulle gras. Sulphadiazine, 14 g., was given orally for two days. The swelling rapidly subsided and the phlebitis regressed, but the ulcer remained the same. Its cure became the next problem, for it greatly handicapped him in his work as a painter.

On examining him afresh what impressed us most was the coldness of the limb, together with its cyanotic appearance compared with his normal right leg. The cutaneous circulation was obviously poor. It occurred to us that, if only the blood supply to the skin could be improved, healing of the ulcer might occur spontaneously. The ulcer maintained its existence as a result of the state of stagnant anoxia which surrounded it. Almost it was an "anoxic ulcer." Arguing on the analogy that head wounds, with a rich blood supply, heal quickly and remain healed, we decided to try the effect of a lumbar paravertebral block of the sympathetic nervous system in improving the cutaneous circulation. Following the infiltration of 100 ml. of 0.5% procaine solution along the left side of the lumbar vertebral column there was a remarkable improvement in the colour and warmth of the limb which persisted for 24 hours. As we did not have a skin thermometer the exact temperature rise could not be measured, but the patient had no doubt at all that his left leg was warmer.

Operation.—After considerable thought, in view of the attendant risks of any operation, we suggested that his ulcer might be "cured" by left lumbar sympathectomy. So far as we were aware at that time, this had not been tried for varicose ulcer before. It was an experiment, and we could not guarantee the result. The patient accepted. On Sept. 27 left lumbar ganglionectomy was successfully performed, the second, third, and fourth lumbar ganglia being removed. In the left leg there was an immediate rise in temperature, which has persisted.

Fourteen days after operation the ulcer was healed for the first time in 27 years. When seen on June 7, 1947, he was extremely fit and well; the skin was healthy, the scar soft. He said he felt ten years younger. On Sept. 11 his leg was still healed. No pulse difference was detected in the femoral, anterior, or posterior tibial vessels of the right and left legs. To prevent swelling he wears a below-knee elastic stocking. On May 13, 1948, he reported that the ulcer was still soundly healed.

Case 2

A married woman aged 57 was admitted on Dec. 31, 1946, with a left varicose ulcer which had persisted for 15 years, it being the result of a left "white leg." Three years after onset of the ulcer she developed "phlebitis" in her left leg following injection treatment for varicose veins. On Nov. 13, 1945, one vein was tied below the left knee, with slight improvement in the ulcer and surrounding weeping eczema.

Physical examination showed a fit corpulent woman. On the medial surface of the left leg were two chronic ulcers, each 4 by 2.5 cm., surrounded by a large area of weeping eczema and pigmentation extending half-way up the leg, which was cold and blue. There were no large varicose veins now. Her Wassermann and Kahn reactions were negative, and her urine was normal. She was finding the leg an increasing source of annoyance. After a left paravertebral block there was marked vasodilatation.

On Jan. 3, 1947, a left lumbar sympathectomy was performed. By Jan. 16 the ulcer had healed for the first time in 15 years. The patient was discharged with instructions to apply calamine lotion to the varicose eczema and to keep the skin protected with a crepe bandage. When seen on June 7 her ulcer was soundly healed and the skin healthy. She said that eczema still occasionally bothered her. When seen on Sept. 11 the eczema, which was some distance from the healed ulcer, was weeping. The ulcer had healed leaving a thick scar, which later might well be excised and skin-grafted. No elastic support had been worn, but one was on order. On May 18, 1948,