THE MANAGEMENT OF DIABETIC COMA

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Many diabetic comas can be prevented by proper education of patients and doctors. They must realize the importance of the warning signs heralding severe ketosis, of increasing the dose of insulin during any infection and of not stopping insulin however much nausea, vomiting or anorexia the patient may have.

Diabetic coma is getting less common; for example, in spite of a rapidly increasing diabetic clinic the admissions to St. Thomas's Hospital for diabetic coma and precoma were 11 in 1932, one in 1938 and three in 1952.

Severe diabetic ketosis, precoma and coma are degrees of the same condition; the principles of treating them are identical. In a patient in diabetic coma, what has to be combatted or corrected? The list is formidable. 1. *Unconsciousness* which may persist after the chemical disturbances have been corrected. 2. *Extreme insulin resistance*. An average maintenance dose of insulin is 40 to 80 units per day; to rescue a patient from diabetic coma requires 1,000 to 2,000 units in one to three days. 3. *Water loss*. To make up for this an average-sized patient will retain about 4½ litres* in the first 72 hours of treatment, to achieve which the total fluid intake has to be some 14 litres. 4. *Loss of electrolytes*. The average case may be short of 500 m.Eq. of sodium, 390 m.Eq. of chloride, 347 m.Eq. of potassium, 39 m.Eq. of magnesium and 1.15 g. of phosphorous; sodium and chloride loss can be made up in 48 hours; the other electrolytes will be restored in eight to 12 days. There is need for caution in giving potassium. 5. *Loss of protein*. There is always a big negative nitrogen balance, for example in one patient with an intake of 77.3 g. of nitrogen in 12 days there was a negative nitrogen balance of 38.8 g. 6. *Disturbance of carbohydrate storage*. With the hyperglycaemia, glycosuria and rapid diuresis, the liver and muscle stores of glycogen are grossly depleted if analogy from diabetic animals holds true. 7. *Fat metabolism disturbance*.

This is shown in the ketonaemia, ketonuria and upset of acid-base balance, with a plasma CO₂ combining power of 20 volumes per cent. or lower. The blood also shows a gross lipaemia, the origin and effects of which are obscure.

How, then, may these various metabolic errors be corrected or combatted?

The *insulin resistance* located in the tissues can only be overcome by very big doses given intravenously. There is a considerable wastage of this via the urine at the beginning of treatment because the diuresis continues; it is quite difficult in the seriously ill patient to give an overdose, especially if glucose is given with the intravenous fluids. As the patient's condition improves, his insulin resistance diminishes and he eventually reaches a constant level of insulin resistance, sensitivity, which determines his maintenance dose. In practice, soluble insulin is used; the technique of physicians varies in detail as to size of dose, frequency and whether part is given intramuscularly as well as intravenously. For example, (a) hourly intravenous doses starting with 200 to 400 units, (b) quarter hourly 25 units intravenously or (c) hourly doses of 50 units intravenously with 50 units intramuscularly. In all cases the dosage diminishes as the patient improves. The main aim is to give as big doses as the patient will stand, so as to cure the metabolic upset as soon as possible. The matter is urgent, and our most powerful tool is insulin. *Severe water depletion* must be overcome by giving it intravenously and quickly, for it is a dangerous condition; the continued diuresis must also be remembered. Once the shock stage is passed and the circulation and kidneys are working normally, it is extremely difficult to give too much; 15 litres are needed to get a 5 litre retention. The empirical point at which to aim is normal skin elasticity, a moist tongue and disappearance of excessive thirst with normal urine output.

Much attention has recently been directed to the correction of electrolyte losses. The most important anions being Na and K, the cations Cl and PO₄. Whether the other ion depletions are of practical importance is not yet known. The

*All the figures of loss of water, electrolytes, etc., are derived from the retention studies made by Nabarro, J. D. N., Spencer, A. G., and Stowers, J. M., *Quart. J. Med.*, 1952, 82, 225.

true figures of electrolyte depletion in any one patient will be unknown, but from the work quoted above a fair approximation of the losses to be made up may be assured. Many fluids for intravenous administration have been devised differing only in the details of their Na, K, Cl, P and lactate concentrations. These have been used empirically in amounts controlled by blood estimations until normal blood concentrations have been attained. To do this as a routine means that first-class laboratory facilities must be available. Fallacies, too, arise in respect of potassium because the serum K concentration does not necessarily reflect cellular potassium; it is the latter that matters, and for this we only have unmeasurable symptoms and T waves in the electrocardiogram by which to assess it.

For the practical physician, however, now that the pioneer work has been done, the matter is easier. Sodium and chlorine must be replaced quickly by using intravenous isotonic saline. By the time that a litre or two of this has been given the circulation is improved and the renal function has recovered enough to have regained the power of maintaining the normal internal environment, although continuing diuresis may result in uneconomical losses. We can therefore give a mixed electrolyte solution until the assumed original losses are made up and the kidneys will balance out any overdose.

We can estimate the amounts we require to give by assumptions based on the exact work on retentions of electrolytes quoted above; two-thirds of the Na and Cl given in 48 hours will be retained with half the K and one-eighth of the P in eight to ten days.

For example, we guess that our patient is short of Na by 500 m.Eq., so in 48 hours we aim to give 750 m.Eq. We guess that he was 350 m.Eq. short of K, so by our intravenous route and by giving 3 per cent. K Cl (= 690 m.Eq. per litre) we aim to get in 550 m.Eq. in eight to ten days. We are likely in this way to give if anything too little; normal renal function will prevent us giving too much. If laboratory facilities are not readily available, one estimation of blood Na Cl K and PO_4 at the end of a week will indicate any further deficiencies to be replaced.

For the purposes of practical management we may safely assume that a patient in deep diabetic coma has the following deficiencies to be made up: Na 500 m.Eq., Cl 400 m.Eq., K 350 m.Eq. and P 1.2 g. If the coma is lighter and consciousness returns in an hour or two, half these deficiencies may be assumed.

The *nitrogen negative balance* is harder to cure as protein intake is bound to be low. It can be

improved by intravenous plasma, which also contains some electrolytes, and by a good protein diet as soon as the patient has an appetite.

Carbohydrate metabolism is corrected by insulin. The hyperglycaemia and glycaemia can be controlled on urine testing, supplemented by blood sugar estimations. The depleted glycogen stores are made up from the intravenous glucose and from the diet. To rescue a patient from diabetic coma it is not necessary to achieve a constantly normal blood sugar concentration, it is sufficient that one hour after a dose of intravenous insulin the blood sugar is between 120 and 220 mg. per 100 ml.; lower levels or completely sugar-free urine are risky.

The *fat metabolite disturbance*, accumulation of β -oxybutyric acid, etc., in the blood, is probably directly due to insulin resistance as well as linked to the carbohydrate upset. The CO_2 combining power of the plasma and the intensity of ketonuria are our direct measures of the severity of the patient's condition. The aim of treatment is to abolish ketonuria as soon as possible. This will happen long before the patient is fully conscious. With recovery the lipaemia disappears. When the ketonuria has been abolished it will be found that the acid-base equilibrium has been restored as shown by a normal CO_2 combining power. In the very rare case only, is there ketonaemia and acidosis, without ketonuria. Hyperpnoea is of course the clinical sign of ketonaemia.

We do not know exactly why a patient in diabetic coma is unconscious, nor why he dies. We do know that there are profound disturbances of protein and fat metabolism as well as of carbohydrate storage throughout the body, especially in the liver and the muscles which include the heart. We know that dehydration and electrolyte depletion are dangerous as in other stuporose states such as heat exhaustion and the crises of Addison's disease; in these electrolyte replacement is also urgent. We know that the central nervous system uses sugar only for its metabolism, and is sensitive to potassium concentration. Small wonder that it is an urgent matter to get the patient back to consciousness. The elderly, presumably arteriosclerotic, brain stands up very badly to prolonged unconsciousness. Older people, even though their chemical condition, as measured by all the available blood and urine estimations, is returned to normal, may never recover consciousness and, after lingering a few days, die.

* A Practical Scheme of Management

The patient is of course in bed with a blanket round him to prevent direct contact with hot water bottles.

Required for intravenous use:

- Isotonic saline.
- 5 per cent. glucose in isotonic saline.
- Plasma.
- Mixed electrolyte solution, 'tissue repair fluid.'

	g.		m.Eq.	
Sodium lactate	2.8	Na	55	} per litre PH
Sodium chloride	1.8	K	23	
Potassium chloride	1.0			
K ₂ HPO ₄	1.0			
Na ₂ HPO ₄	0.14	Cl	45	
Mg Cl ₂	0.25	lactate	20	} 7.4
Glucose	50	P	12	

—Soluble insulin 80 units per c.c.

100 units of insulin are given intravenously at once.

An intravenous drip by a cannula tied into a leg vein is set up and a litre of isotonic saline is run in as fast as possible.

At the end of one hour the patient's condition is assessed by the breathing, pulse, blood pressure, skin condition, level of consciousness and tone of muscles. These are charted hourly. If unchanged a further 200 units of insulin are given and the intravenous isotonic saline continued. If some improvement in the breathing or consciousness has occurred, 100 units of insulin are given and the drip changed to glucose saline. Then hour by hour the patient's condition is watched and insulin, 100 or 50 units, is given until he is properly conscious, and a specimen of urine, obtained by emptying the bladder every two hours, is free of ketones. After the first litre of glucose saline is run in at the rate of a litre in an hour, a pint of plasma is given and the rate of administration dropped to 500 c.c. per hour. Thereafter a litre of mixed electrolyte solution is given alternating subsequently with glucose saline until the patient has been fully conscious and able to drink for four hours, then the intravenous medication may be stopped and the patient encouraged to drink all he wants of fruit drinks and to start eating meals at normal times. The insulin should be dropped to 20 to 50 units intramuscularly four hourly as soon as he becomes fully conscious and is drinking and the urine is free of ketones. This dose should be

continued for 12 hours then reduced to 20 to 50 units eight hourly for 24 hours and then to a maintenance dose b.d. of his dose before coma plus 50 per cent. Watch must be kept of course for hypoglycaemic signs such as profuse sweating or restlessness, but provided that an adequate intake of glucose is maintained, hypoglycaemia is a rare complication of treatment. The only other complications that may arise are (1) bladder infection from the repeated catheterization which should be avoidable by scrupulous technique; (2) cardiac failure as shown by a rising jugular venous pressure. If the latter occurs digoxin may be given into the intravenous drip. The decision as to gastric lavage and emptying the colon can be left to the physician in charge; they are not essential.

It will be noted above that in this scheme no mention has been made of controlling treatment by blood sampling. The above regime can be carried through without any estimations of blood chemistry, using only the urine and clinical observation as guides. If, however, laboratory facilities are to hand, then a more exact chemical control may be obtained by estimations of blood sugar, CO₂ combining power, sodium and chloride, by flame photometric measurements of blood potassium and by serial electrocardiograms. But the matter is urgent and we must get on with the job without waiting for chemical results.

Summary

Recent advances in the treatment of severe diabetic ketosis have lain in the better management and education of diabetic patients; this has resulted in a much lower incidence of this dangerous complication. The improvement has come paripassu with the increase in dietetic carbohydrate allowance to diabetic patients needing insulin. The more exact knowledge of electrolyte disturbances has also improved our treatment. The addition of cocarboxylase and riboflavin, though theoretically useful, has not proved of value in the treatment of human cases of diabetic coma.

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