presenting feature and caused diagnostic difficulty. In the second patient gastro-intestinal symptoms and urticaria after feeding with cow's milk were followed by refusal of milk which persisted for some weeks after desensitization.

Diagnosis of cow's-milk allergy is mainly clinical. The passive transfer test is a useful aid, but the direct skin test is of little value. Treatment consists in withdrawal of cow's milk and substitution of a suitable alternative, the choice of which is a matter of trial and error. Alternatively, desensitization to the milk is carried out.

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DIABETIC COMA IN INFANCY*

BY

D. W. BEAVEN, M.B., M.R.C.P., M.R.C.P.Ed.
M.R.A.C.P.

Christchurch Hospital, New Zealand

During infancy diabetes mellitus presents as an acute metabolic disturbance.

Both Gaisford and Lightwood (1954) and Paterson (1956) state that diabetes is very rarely seen under the age of 1 year, but Schwartzman *et al.* (1947) collected details of 57 cases in this age group, and Keidan (1955), reviewing the literature, added 22 cases, six of these being transient in the first month of life.

Since that time sporadic cases only have been reported, but details of the following two cases are presented "to augment the knowledge of this group" (Schwartzman *et al.*, 1947). As guidance on the management of diabetic coma in small babies is difficult to obtain, certain aspects of treatment have been discussed. These comments are based on experience in these two cases, on a further two cases in patients under the age of 2 years (not reported here), and on the available literature. Recent experience in the treatment of problems in adult diabetic coma has been utilized and adapted.

Case 1

A full-term female baby born on October 30, 1954 (Birth weight 2.6 kg.), progressed normally until she was first admitted to hospital on July 10, 1955, with irritability, cough, loose bowel motions, and temperature suggesting an infection of the upper respiratory tract. Various investigations were carried out with negative results, and the temperature slowly settled on penicillin therapy. At this time the urine showed a trace of reducing substance on

one occasion, but not on four other occasions. The C.S.F. sugar was 80 mg./100 ml. She was discharged home five weeks later with a diagnosis of recurrent bronchitis.

She was readmitted on October 18, at the age of 11½ months, with a cough and rapid respiration and dehydration, the diagnosis being pneumonia. By next morning drowsiness had increased and a diagnosis of probable diabetic acidosis was made. Blood sugar was 400 mg./100 ml. and serum electrolytes showed a severe primary metabolic acidosis with pH 7.18; CO₂ tension, 22 mm. Hg; blood buffer base, 26 mEq/l.; bicarbonate 7.8 mEq/l.; sodium, 146 mEq/l.; potassium, 3.6 mEq/l.; chlorides, 120 mEq/l. Serum keto-acids were 180 mg./100 ml. Her weight was 18 lb. (8.1 kg.).

Fig. 1.—Details of treatment, showing blood-sugar levels, serum potassium levels, and improvement in acidosis in Case 1.

Soluble insulin was started at 1 p.m., and Fig. 1 shows that an initial insulin dosage of 80 units was required before some control of the blood sugar was obtained. The blood buffer base rose steadily with the correction of the acidosis and with 150 ml. of 1/6 molar sodium lactate solution given intravenously.

The initially rather low potassium fell to 1.7 mEq/l. within 24 hours of starting treatment. During this period calcium gluconate was given intravenously on two occasions for fits of a decerebrate nature with relief of twitchings. On these two occasions the blood sugar was 350 mg. and 110 mg. respectively. (The low serum potassium may have played some part in her slow recovery from drowsiness, but the irritability may have been related to the relative increase in alkalinity.) After the first 24 hours soluble insulin was given according to urine tests three times daily, the total daily dosage being 20–30 units.

Insulin zinc suspension was begun on the fourth day, when solid foods were again taken. The dosage was steadily increased, and she was finally discharged after a respiratory infection on 20 units of I.Z.S. and a 1,200 calorie diet. Before discharge the chest x-ray picture was clear and the ocular fundi were reported normal by the ophthalmologist.

Over the next year she was on a diet averaging 1,200 calories (distributed as protein 40 g., carbohydrate 160 g., and fat 40 g.) and gained 11 lb. (5 kg.), to weigh 29 lb. (13.2 kg.) and measure 34 in. (86 cm.). The height and weight are at the upper limit of normal for her age.

The insulin dosage for this age and weight was 16 units of I.Z.S., and the blood sugars two and a half and two hours after meals were 95 and 105 mg./100 ml.

*Based on papers read before the Annual Meeting of the New Zealand Paediatric Association in 1956 and 1957.

Case 2

A female baby born on December 25, 1954—birth weight 8 lb. 6 oz. (3.8 kg.)—was quite well until the morning of her admission to hospital on December 10, 1955, when she was noticed to be drowsy and "off-colour," with sunken eyes. She became increasingly breathless during the day and was admitted to hospital at 6.30 p.m. with a diagnosis of pneumonia.

On admission she was a dehydrated semiconscious infant with cold extremities, rapid grunting respirations, and a few moist sounds in the left chest; respirations 64 a minute, and pulse 170 a minute. A tentative diagnosis of diabetic coma with respiratory infection was made and an intravenous drip inserted. Blood-sugar results were 1,000 and 950 mg./100 ml., and the serum electrolytes were as follows: blood pH 7.08; CO₂ tension, 19.5 mm. Hg; blood buffer base 24 mEq/l.; plasma bicarbonate, 5.6 mEq/l., which was in keeping with the marked respiratory compensation. Her plasma sodium was 140 mEq/l.; potassium, 4.6 mEq/l.; chlorides, 102 mEq/l.; proteins, 8.7 g./100 ml.; P.C.V., 43%; serum keto-acids, 100 mg./100 ml.

Soluble insulin, 10 units intravenously and 20 units intramuscularly, was given at 8 p.m., and two and a half hours later a further 50 units was given intramuscularly, when there was no fall in the blood sugar. By 4 a.m., with a falling blood sugar (700 mg.), only a further 20 units of insulin was given, and this total of 100 units was sufficient to keep the blood sugar below 200 mg. for the next 30 hours.

Fluids in the first 24 hours for this 20-lb. (9.1-kg.) baby are shown in Table I. At 18 hours these fluids had resulted in a hypernatraemia of 157 mEq/l., and the drip was discontinued at 20 hours, when adequate fluids were being taken by mouth.

TABLE I.—Fluids Given During First 24 Hours of Diabetic Coma

Case 1	8.1 kg.	255 ml. per kg. body weight
" 2	9.1 "	229 " " " " "
Case not reported ..	10.2 "	250 " " " " "

Details of Fluids in Case 2 during First 24 Hours

Type of Solution	Route	Vol. in ml.
1/6 molar sodium lactate	Intravenous	150
Isotonic saline	"	160
5% glucose solution	"	400
5% glucose with 1/5 N saline ..	"	250
" 1/2 normal " saline	Subcutaneous	220
Glucose solutions	Oral	420
Total all routes		1,600

For the next week soluble insulin was given six hourly, according to urine tests, and on the eighth day I.Z.S. and a 1,100-calorie diet were started. This dosage was later reduced to 16 units, but the baby was kept in hospital for a further three months on account of a throat infection, an attack of rubella, and also home circumstances, but was finally discharged on March 22, 1956 on 30 units of I.Z.S. daily and a fairly free diet of about 1,250 calories. Capillary blood sugars morning and evening on this gave figures of 200–250 and 85–150 mg./100 ml.

At home this dosage has gradually been reduced over the past year to 24 units of I.Z.S. daily. At 22 months her weight was 28 lb. (12.9 kg.) and blood sugar 105 mg./100 ml. two and a half hours after dinner.

Discussion

Mortality.—Between 1925 and 1946 the mortality averaged 45–50% for collected cases of diabetes in infants under the age of 1 year, but in more recent series reported by Brodribb *et al.* (1952) and by Keidan (1955) the mortality is nearer 25%.

Presentation.—These two cases and our other young diabetics illustrate a point stressed in the literature—namely, that an erroneous diagnosis of respiratory infection or meningitis is often made. Where there is a relative hypo-

kalaemia with a low blood pH depression of the respiratory centre may result and the typical Kussmaul respiration may be reduced or absent. This finding has recently been reported in a number of adults by Murray (1958), and infants are particularly liable to develop a severe metabolic disturbance. The admission diagnoses in the 12 most recently reported cases of diabetes mellitus under 1 year of age were pneumonia in 4, meningitis in 4, dehydration and infection in 1, "shock" in 1, and diabetes in 1. Newcomb (1951) reported that symptoms pointing to the respiratory system (tachypnoea and fever) were present in all of their six cases in diabetic coma, and signs in the chest were found on auscultation in four of his cases.

The diagnosis may easily be missed, and diabetic acidosis should be considered in any baby with respiratory signs and symptoms and dehydration who does not improve on treatment.

Age of Onset (Table II).—Keidan (1955) has commented on the age distribution at the beginning and end of the first year of life. This may be due to selection of cases, because

TABLE II.—Age Distribution of 79 Reported Cases of Diabetic Coma Under the Age of 1 Year

0–3 Months	4–6 Months	7–9 Months	10–12 Months
29	12	10	28

of greater interest in the neonatal group or because of inclusion in the first three months of all the cases of transient diabetes.

Sex Incidence.—Of the 80-odd reported cases male babies predominate 2:1.

Influence of Heredity.—In Schwartzman's series of 57 cases and Keidan's additional collected 22 cases a positive family history of diabetes mellitus was given in 43% of cases. A history on both sides of the family may be helpful in diagnosis, but in New Zealand and Australia it is often difficult to obtain relevant data about grandparents. Fig. 2 shows the family history in Case 2, with the birth weights where known. The mothers of both these infants had a flattened type of curve on glucose-tolerance testing, suggesting an increased tolerance for glucose, but the significance of this finding is not clear.

FIG. 2.—Family history of Case 2, with birth weights where known.

Management of Coma

Both in these cases and in the older children adequate biochemical control during the first 24 hours is essential. For some time it has been the practice in this hospital for blood to be withdrawn in the casualty or admitting department in all cases of diabetic coma, and also in cases of acidosis in babies.

Correction of Acidosis.—In those cases with a severe keto-naemia the pH, even with adequate respiratory compensation, may fall below 7.2. It appears likely from the work of Kety *et al.* (1948), and also from work on anaesthetic cases by Murray (1958), that depression of medullary centres takes place with low pH figures. Murray has reported three cases in severe diabetic acidosis with absence of Kussmaul respiration because of respiratory centre depression at low pH figures. It has been our practice to use 1/6 molar sodium lactate solution or bicarbonate solution as the initial intravenous fluid whenever severe acidosis is present. Lactate

solution offers some advantage over sodium bicarbonate solution in being more stable and also in providing a glucogenic effect (60 ml. of 1/6 molar sodium lactate per kg. body weight possesses a glucose potential of 0.9 g./kg.). Hartmann and Erganian (1947) recommend 30 ml. of sodium lactate per kg. body weight initially, but in these two cases the average figure was 20 ml./kg. In two other patients between the ages of 1 and 2 years about 15 ml./kg. body weight has been used in the initial 12-hour period. Hartmann and Erganian have also shown that, in comparison with the use of isotonic saline and insulin, sodium lactate solutions will produce a more rapid improvement and so lessen the danger to the cerebral cells of an unduly prolonged low serum pH.

Insulin Requirements.—Reports on the dosage of insulin given to infants in diabetic coma vary from the successfully treated patient of Gans (1954)—5½ lb. (2.5 kg.)—who was given 250 units of insulin in the first 24 hours, to that of Hartmann and Erganian, who recommended 1½ units/lb. (3.3 units/kg.) body weight initially to be repeated in six hours as necessary. Nelson (1954) recommends an initial dosage of 20–30 units at the age of 1 year, and thereafter about half the amount in one to two hours. The insulin dosage used in babies in diabetic coma with severe acidosis is shown in Table III. Thus on body weight an initial

TABLE III.—*Insulin Dosage in First 24 Hours. Babies in Diabetic Coma*

Diabetic Coma			
100 units	8.1 kg.	Case 1	11 months
100 "	9.1 "	" 2	11 "
175 "	10.2 "	—	19 "
110 "	16.0 "	—	29 "

dosage of about 3 units/kg. (or 1½ units/lb.) is advisable, with an additional dosage of 2 units/kg. (or 1 unit/lb.) where the plasma keto-acid level is over 150 mg./100 ml. (Dumm and Shipley, 1946). A gradation of this dosage should be repeated in three to four hours, when the report on further blood-sugar and keto-acid estimations come to hand. There seems to be no advantage in the common practice of hourly injection of insulin. Better control is achieved when insulin is given on the results of these four-hourly blood-sugar and keto-acid estimations.

Hypoglycaemia.—There are many references to hypoglycaemia occurring towards the end of the first 24 hours in the treatment of diabetic coma. We have noticed repeatedly that soluble insulin may have a duration of action up to 36 hours where ketonaemia persists. Even with intra-

FIG. 3.—Showing prolonged action of insulin as observed in Case 2.

muscular instead of subcutaneous injections its action may still last for 24 hours. Fig. 3 shows the prolonged action of insulin in Case 2. Heberden and Friedlander (1955) have mentioned the use of cortisone, sedation, and hypothermia in the treatment of prolonged hypoglycaemic attacks unresponsive to intravenous glucose solutions. They also re-emphasize the cerebral damage which can occur with hypoglycaemic attacks in infants.

Fluids.—The intravenous fluid given initially will largely depend upon the degree of acidosis and the plasma sodium level. The use of 1/6 molar sodium lactate solutions has already been discussed in those cases where severe and dangerous acidosis is present. In one of our recent cases (10.2 kg., 19 months) hypernatraemia was present before treatment, and Case 2 became hypernatraemic during minimal sodium therapy. We believe that this hypernatraemia which occasionally occurs is due to loss of a greater amount of water than sodium and may prejudice the chances of survival in patients in severe diabetic coma. Murray and Beaven (1958) have reported 16 cases of hypernatraemia occurring in diabetic coma, and we suggest that this produces a very severe intracellular dehydration on account of the extreme plasma osmolarity. Where hypernatraemia exists only glucose-containing solutions should be given in the first few hours or until the serum sodium falls. Where initial serum sodium levels are not low, caution is necessary with sodium-containing solutions. The amount of fluid administered in the first 24 hours in three of our cases is shown in Table I, but we are guided by clinical signs of dehydration and serial estimations of packed cell volume, total N.P.N., and plasma proteins. In the treatment of one of these infants and in bigger babies we have used 1/5 or 1/2 normal saline solution with hyalase subcutaneously where the taking of oral fluids has been slow after removal of the intravenous infusion. Plasma can be used as in adults on a body-weight basis where shock does not improve with the correction of the acidosis.

Hypokalaemia.—An initially low serum potassium or an abrupt fall at the four-hour electrolyte estimation should give warning of impending hypokalaemia. In Case 1 intravenous potassium was not given early enough, and fits of a decerebrate nature occurred when the potassium level was 1.7 mEq/l. Low serum potassium levels are particularly dangerous in association with persisting acidosis, as it may further aggravate the depression of the cerebral cells.

Stabilization.—On recovery from coma, stabilization is achieved by means of a fixed calorie diet with soluble insulin given three times daily and I.Z.S. started some time in the first week. At home we have encouraged the parents to try to maintain a low-fat diet which must of necessity be fairly free in other respects. The daily insulin dosage is adjusted according to the previous day's tests.

Follow-up.—One year after discharge both babies were fully re-examined and their diet was adjusted. At the same time several capillary blood-sugar levels were taken to estimate the degree of control. With the onset of diabetes in infancy or early childhood the ultimate prognosis will depend upon a number of factors, not least of which is the intelligence of the parents and how far they are prepared to co-operate with the enthusiasm of their family doctor. Arterial changes and eye complications may develop within a shorter period than in adults, but Wilson *et al.* (1951) present evidence to suggest that good control of urine sugar may possibly delay the onset of arterial complications.

Conclusion and Summary

Two cases of diabetic coma under the age of 1 year are reported.

The comparative rarity of reported cases in this age group is noted and it is suggested that cases may masquerade as meningitis or pneumonia.

The history of familial incidence may be over 40% where accurate information is available.

Some aspects of the management of diabetic coma in small babies have been discussed. These include: the value of 1/6 molar sodium lactate solution; some suggestions on insulin dosage; frequency of hypoglycaemia due to prolonged insulin action; hypernatraemia; and hypokalaemia.

The importance of parental intelligence and co-operation in subsequent management is stressed.

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AETIOLOGY AND TREATMENT OF CONGENITAL DEAF-MUTISM

BY

J. MCKENZIE, M.D.

Lecturer in Embryology, Department of Anatomy,
University of Aberdeen

During an investigation into the problem of congenital abnormalities of the head it was noted that occasionally a child showing obvious maldevelopment of the first visceral arch was also deaf-mute, although the external ear and auditory meatus were normal. Attention was thereby drawn to the possibility of a close connexion between deaf-mutism and abnormal development of the first arch.

The cases described below show little or no obvious evidence of first-arch defect, and the above premise suggested the clinical experiment of determining whether their deaf-mutism was associated with middle-ear (first arch) defect.

Case 1

A boy aged 11 was suspected at the age of 2 years of having middle-ear deafness, "possibly from infection in the first few months of life." When he was first examined it was reported that he did hear—cochleo-palpebral reflex was present but weak. The surgeon had the impression when using tuning-forks that it was a conduction deafness, but was not at all certain. Although six months later (aged 2½) the child showed signs, with pure-tone bone-conduction audiometry, of a severe upper-tone loss in both ears, a tentative diagnosis of air-conduction deafness associated with mental deficiency was made.

At 3½ years co-operation was said to be non-existent during clinical examination; a muscular tic reported a year previously was more pronounced. No final diagnosis was reached, and special schooling was recommended. No other member of the family suffered from deafness or congenital

abnormality, and x-ray examination of the skull was normal. Fig. 1 shows the result of audiometry examination (May, 1957); deafness is shown to be profound, but the marked discrepancy between air-conduction and bone-conduction hearing indicates that at the lower frequencies the deafness is essentially of middle-ear origin, although the upper-tone loss suggests inner-ear deafness.

Case 2

A girl aged 9½ was found most difficult to examine at the age of 2, when the cochleo-palpebral reflex was elicited on very slight stimulus. At 5 years of age the only finding of note was a single islet of hearing at 1,024 cycles revealed by pure-tone audiometry. She was a pleasant, but very shy, timid, little girl, and of her relatives only an aunt of her mother's was reported to have been born deaf;

no further information was available. The patient was consigned to a school for the deaf without further attempts to arrive at the cause or nature of the deafness. At school she was given and wore an air-conduction hearing-aid as a routine, but it was not regarded as being of much help to her. The skull was normal on x-ray examination. Audiometry (Fig. 2) revealed a deafness strikingly similar to that of Case 1.

Cases 3, 4, and 5

Three children aged 12, 9, and 9, respectively (the latter two being twins) were all members of one family suffering from a congenital deafness, which must be hereditary. The mother was born deaf, but the trait could not be traced further back on her side of the family. The father was one of five deaf-mute sons in a family of nine; one of his affected brothers died in a mental hospital, where another was still an inmate; the others and the father of the three patients were normal apart from the deafness. X-ray

FIG. 1.—Case 1. O = Right. X = Left.

FIG. 2.—Case 2.

FIG. 3.—Case 3.