factor in such cases and yet allows the infant the longest possible time *in utero* compatible with intrauterine survival.

Cases 15, 17, 20, and 21 had had a previous diabetic pregnancy which resulted in a dead infant. The cause of death on two occasions was cerebral haemorrhage (Cases 17 and 21), but in Cases 15 and 20 the diabetic lethal factor was responsible for the foetal deaths. It follows, therefore, that a diabetic pregnancy which results in the death of the foetus need not be followed by subsequent unsuccessful diabetic pregnancies.

It is well recognized that the diabetic mother has difficulty in breast-feeding her infant. The cause of this is obscure. There is, however, one factor which tends to hinder her. It is that the immature baby does not suck as well as the full-time baby, and hence the earlier the termination of pregnancy the more likely is it that breast-feeding will not be established. One of our patients (Case 24) illustrates this point. In 1949, at another hospital, she was delivered prematurely at the 36th week, by induction of labour, of a baby weighing 7 lb. 8 oz. (3.4 kg.). The baby was difficult to rear in the early weeks and she was unable to breast-feed it after three weeks' energetic trial. Recently she was delivered spontaneously at the end of the 37th week of a baby weighing 8 lb. 11 oz. (3.9 kg.). This baby was at the breast within 48 hours, and breast-feeding was well established during the second week of the puerperium.

The danger of neonatal death in immature infants of diabetic mothers is real. Premature induction of labour increases this danger and produces an infant which is difficult to rear. On the other hand, by allowing the pregnancy to proceed the possibility of difficult labour and disproportion becomes greater as term is approached. In the present series forceps were needed for delivery on seven occasions and caesarean section was performed twice on account of a large infant. The obstetrician's task, therefore, of producing the less immature live infant is increased while that of the paediatrician is decreased.

Conclusion

The foetal salvage rate in this small series (20 out of 24) would appear to justify the course taken of not prematurely terminating the pregnancy. Our improved results are possibly due to the hormone therapy which these mothers have received. It is, however, more likely to be due to the close co-operation between physician, paediatrician, and obstetrician in the care of the diabetic mothers and their offspring.

We should like to record our gratitude to Professor W. C. W. Nixon, director of the obstetric unit, for permission to report these cases, and to the members of the paediatric unit under the direction of Dr. B. E. Schlesinger for their invaluable help in the care of the infants.

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In accordance with an international agreement the Government of the United Kingdom can insist on the international recognition of yellow fever inoculations performed in this country only if: (*a*) they are done at a centre or by a medical practitioner specifically authorized by them for that purpose; (*b*) the certificate is given on one of the international forms specially supplied to such centre or practitioner; (*c*) a vaccine approved by W.H.O. is used for the inoculation. Certificates issued other than in accordance with these conditions will probably not be accepted by foreign health authorities. A list of places where yellow fever inoculation is given free of charge will be found on the back of the notice to travellers issued with all renewals of passports or can be obtained from travel agencies or the Ministry of Health.

TWO CASES OF DIABETES MELLITUS IN INFANTS UNDER 1 YEAR

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Although the onset of diabetes mellitus occurs in 5 to 6% of cases in the first ten years of life, it is rare for the disease to develop in infancy. John (1946) listed 85 cases of diabetes in infants under 1 year. Schwartzman, Crusius, and Beirne (1947), in a more detailed review of the world literature, summarized 57 cases under 1 year and gave details of most of them. The first to survive in order of time was the 27th they describe, and was reported in 1925. Since then only 11 have survived out of the 24 of which adequate details are given. It is not easy to judge how many of these cases had passed into diabetic coma.

In the following two cases which survived, the symptoms began when the patients were under 1 year old.

Case 1

A baby boy aged 13½ months was admitted to hospital on June 18, 1950, with severe glycosuria and ketosis. His brother, aged 10, regularly attended the diabetic clinic, and their parents showed great intelligence and skill in keeping his diabetes stable. Neither of them was diabetic, and there was no known diabetes in either of their families.

The baby weighed 7¼ lb. (3.3 kg.) at birth on May 3, 1949. He did well, weighed 22 lb. (10 kg.) in December, 1949, and was weaned by February, 1950. A few hours after receiving a second dose of antidiphtheria vaccine on March 19 he lost his appetite. He began to vomit solid food and became very constipated. This continued, and by the time of admission he had lost 8 lb. (3.6 kg.). By the middle of May he had become very thirsty, and developed polyuria, and by early June he had become so feeble that he fell over if sat upright. Just before admission his parents tested his urine, and found a full reduction of Benedict's solution.

On admission he had a good colour, but was drowsy and very fretful. The eye tension was lowered, the tongue dry, and the skin dry and inelastic. He was teething, but there was no evidence of infection. His temperature was 96° F. (35.6° C.), pulse 108, and respirations 24. The urine gave full reduction of Benedict's solution and strongly positive Rothera and Gerhardt reactions. The blood sugar was 440 mg. per 100 ml.

He was given either 10 or 15 units of soluble insulin subcutaneously at six-hourly intervals, and at 10.30 a.m. next day the blood sugar was 90 mg. and the ketosis was receding. The next insulin was given 11 hours later, when the blood sugar had risen to 540 mg. per 100 ml. After a short time on six-hourly insulin again it was found that eight-hourly doses (8 a.m., 4 p.m., and 12 midnight) controlled him adequately. The night dose was only two units, but this made all the difference between a blue and orange early-morning urine test. He was not weighed on admission, but was 22¾ lb. (10.3 kg.) 10 days later. He was given 130 g. carbohydrate diet, which he took well. A variety of combinations of insulin were tried in order to eliminate three

injections, and during this time he developed bronchitis and laryngitis and later diarrhoea. These infections disturbed the diabetes to some extent, though he never developed any ketosis. Difficulty was experienced in getting urine specimens, and it was often necessary to wring out his napkins for a test. He was discharged, after nearly three months, on 18 units of globin insulin once daily; he then weighed 27 lb. (12.2 kg.).

He attended the diabetic clinic for the next six months and remained well, gaining weight rapidly. He was kept on globin insulin, though occasionally an additional 2 units of soluble insulin was given at 11 p.m. if a specimen at that time was loaded with sugar.

In March, 1951, he was readmitted with a blood sugar of 300 mg. per 100 ml. and a cough and catarrhal otitis media, which failed to respond to penicillin, but responded to sulphadimidine. The dose of globin insulin had to be increased to 34 units, but this did not control him satisfactorily. He was discharged on 18 units of soluble insulin at 8 a.m. and 12 units at 4 p.m. and 90 g. carbohydrate diet, as he had gained 11 lb. (5 kg.) in six months. On October 25 he weighed 45 lb. (20.4 kg.), was on 100 g. carbohydrate diet, and was having 12 units of soluble insulin at 8 a.m. and 13 units at 4 p.m.

Case 2

A female infant aged 11 months was admitted to hospital on March 1, 1951, at 3 p.m. She was an only child who had had no previous illnesses and was quite well until the day before admission. There was no family history of diabetes, and glycosuria was absent in the parents. On February 28 the child vomited once and was said to look very ill. She was putting her hand to her head; she had previously done this when cutting teeth. Her parents thought she seemed better on March 1, but she was not taking notice of her surroundings. She was sent into hospital by her doctor.

On admission the child looked moribund, and was a bluish-grey colour, with sighing respirations and active alae nasi. A note was made, however, that the clinical picture was not typical of lobar pneumonia, although she had an impaired percussion note at the right base and moist rales at both bases, especially on the right. The throat was clear and the eardrums were normal. There was a black necrotic area of skin on the buttocks. Clinically, there was a moderate degree of dehydration. A definite left-sided facial weakness was noted and ? slight ptosis of the left eye. Deep reflexes were normal, pupils reacted to light, and the fontanelle was not tense. There was no neck stiffness and Kernig's sign was negative. Temperature, 98° F. (36.7° C.).

The diagnosis was in doubt, but as the child was moribund 500.000 units of crystalline penicillin and 1 g. of sulphadimidine were given intramuscularly at once, and the child was placed in an oxygen tent. Lumbar puncture showed a crystal-clear fluid, not under increased pressure, with no increase of cells. A catheter specimen of urine showed a distinct cloud of albumin, with full reduction with Benedict's solution, and the deposit contained some casts and a few epithelial cells.

In view of the large amount of sugar in the urine we wondered if we were dealing with a case of diabetic coma with severe air hunger. Intravenous blood was taken at 8 p.m. for sugar estimation, but before the result was known an intravenous drip of half-strength saline with 5% glucose was set up and 10 units of soluble insulin was injected into the drip. Three minutes later the child opened her eyes a few times, moved her head and limbs, and appeared to be waking. Ten minutes later 10 units of soluble insulin was given intravenously. The result of the blood-sugar estimation had then become known, and was 1,160 mg. per 100 ml.

Her immediate further progress is best summarized as follows. *11 p.m.:* Blood sugar 1,080 mg. per 100 ml. A total of 50 units of soluble insulin had by then been given. Colour improved and respirations less deep. *March 2, 1 a.m.:* Urine still deep orange with Benedict's solution. Child a good colour, respirations quiet, tongue moist, and child moving freely. 35 oz. (1 l.) of fluid intravenously had been given in previous five hours. *2 a.m.:* Urine still deep orange with Benedict's solution. *3 a.m.:* 20 units of soluble insulin given subcutaneously. *5.30 a.m.:* Blood sugar 500 mg. per 100 ml. *9.30 a.m.:* Blood sugar 300 mg. per 100 ml.; blood chlorides 650 mg. per 100 ml. *2.30 p.m.:* Blood sugar 70 mg. The child then had symptoms of hypoglycaemia, which were corrected.

From then on the child improved and the insulin dosage required was worked out. She was eventually discharged well on June 8 on a diet of 1,435 calories (carbohydrate 135 g., protein 86 g., fat 55 g.). Her insulin requirements were 9 units of soluble at 7.30 a.m. and 10 units at 4 p.m. Her weight shortly after admission to hospital (March 10) was 18 lb. (8.2 kg.), and on discharge it was 22 lb. 4 oz. (10.1 kg.).

She has since been seen at the out-patient department on several occasions, and is progressing well. Owing to her rapid gain in weight the carbohydrate in her diet has been reduced to 120 g. and the insulin to 8 units at 7.15 a.m. and 9 units at 4.30 p.m. Her weight on October 18 was 25 lb. (11.3 kg.). A catheter specimen of urine showed no abnormality.

Comments

The highest blood-sugar levels recorded in the review by Schwartzman, Crusius, and Beirne (1947) were 600 mg. per 100 ml. in an infant who survived, and 952 mg. per 100 ml. in one who died.

Case 2 had a blood sugar of 1,160 mg. per 100 ml. before treatment began, the highest figure which we can find recorded in an infant under 1 year.

Newcomb and Farrell (1951), in a review of six cases under 1 year, found fever and pulmonary symptoms in 100%, and "rales and signs of pneumonia" in 66%. They point out that the prevalence of pulmonary signs and symptoms has not been stressed enough. Case 2 fitted into this picture.

We came to the conclusion that soluble insulin at 8 a.m. and 4 p.m. controlled the babies most effectively. Globin insulin alone once a day was satisfactory in Case 1, until the dose rose to over 30 units. One of us (H. S. B.) finds globin insulin once a day most effective throughout the 24 hours in adults, provided the dose remains under 40 units a day. If this amount is exceeded some other combination of insulin is necessary, and it seems that this critical level is lower in infants.

Both babies, when stabilized, showed a marked tendency to gain weight excessively on 130 g. carbohydrate diet. It was found necessary to reduce it after an initial period.

Summary

Two further cases of diabetes mellitus, which began in infants under 1 year old, are described.

The first had a gradual onset, which followed immunization, and was comparatively mild. The second was acute and severe, presenting pulmonary symptoms and signs; her blood sugar was 1,160 mg. per 100 ml., the highest recorded under the age of 1 year.

Both patients survived, and continued well on two doses of soluble insulin daily.

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