mechanisms which have been thought at one time or another to limit the life-span of the red cell in health—metabolic failure, removal from the circulation by phagocytic cells, the action of the spleen, fragmentation in the circulation, actual lysis in the circulation—have all been shown to be important factors under the abnormal circumstances which we call disease.

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CONGENITAL TEMPORARY DIABETES MELLITUS

BY

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The literature of diabetes mellitus in infancy reveals a certain amount of confusion, largely attributable to the fact that the aetiology of diabetes remains unknown. It is well recognized that in adults the term diabetes mellitus includes more than one disease. It is perhaps insufficiently appreciated that the same is true of the infant. Two types can now be separated. In older infants insulin-sensitive diabetes mellitus with ketosis and acidosis necessitates the lifelong use of insulin, and it is not distinguishable from the common type of diabetes of later childhood and early adult life. There is, however, another type, with onset at or shortly after birth, which is also insulin-sensitive but is not accompanied by ketosis, and which appears to be capable of spontaneous recovery. The first such case was described by Kitselle in 1852 in his own newborn son, who died after a short period of polyuria, polydipsia, glycosuria, and emaciation. Once recognized, this disease has a rather characteristic clinical picture. We now report four cases in the hope that recognition of other cases will be encouraged. There is reason to believe that a lack of awareness has led to mistaken diagnoses and the preventable deaths of some affected infants. Case 1 was previously reported by Wylie (1953) before it was appreciated that spontaneous recovery from the diabetes could occur.

Case 1

A female infant was admitted to the Royal Hospital for Sick Children, Glasgow, on May 15, 1952, aged 17 days. She was the first child of healthy, young, unrelated parents. There was no family history of diabetes. She was born at term according to the expected date of delivery. Birth weight was 5 lb. 5 oz. (2.41 kg.). There was no asphyxia, cyanosis, or other upset; she fed eagerly, but after 17 days her weight had fallen to 3 lb. 15 oz. (1.78 kg.). There had been no vomiting or diarrhoea.

On admission she was profoundly wasted and severely dehydrated, with a depressed fontanelle and overriding of the sutures. Her skin and facies were pale and had a remarkable and characteristic lined appearance of "old age," whereas her eyes showed a liveliness of consciousness which is quite unusual in the severely dehydrated infant (Fig. 1). There were no clinical signs of local disease. An electrocardiogram was normal. The blood revealed evidence of gross haemoconcentration; haemoglobin 17.5 g./100 ml.; red cells 5,290,000/c.mm. The urine showed a trace of protein and abundant sugar. Chromatography confirmed that the sugar was glucose. The blood-sugar level was 666 mg./100 ml. At no time was ketonuria detected.

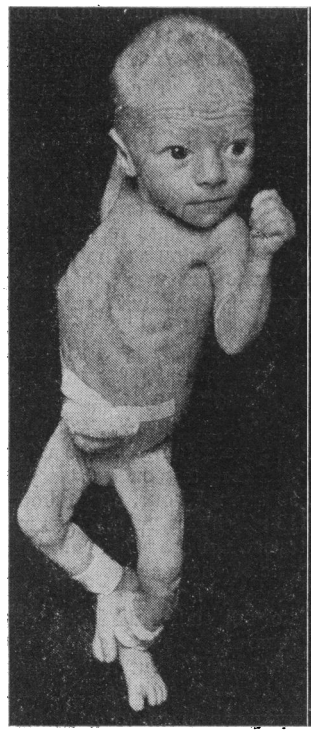

FIG. 1

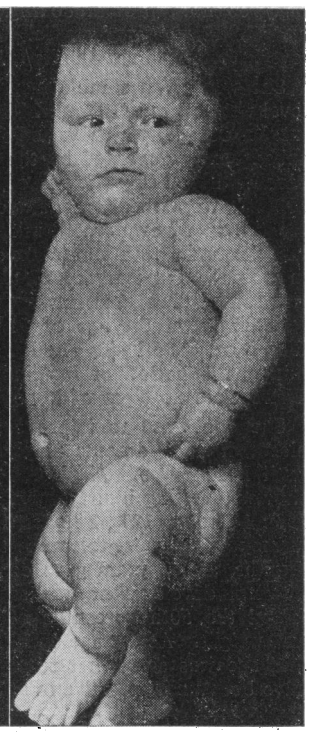

FIG. 2

FIG. 1.—Case 1. Note marked emaciation and overriding of skull sutures which contrast with alert expression. FIG. 2.—Case 1. At the age of 5 months infant shows obesity and moon-face.

She was given 5% glucose in N/4 saline by intravenous "drip," and soluble insulin 10 units intramuscularly every four hours. After 12 hours the blood sugar had fallen to 102 mg./100 ml. Thereafter insulin dosage, 5–10 units, was regulated by blood-sugar estimations. She fed well on half-cream national dried milk. After 48 hours the serum potassium level was 3.58 mEq/l., and potassium chloride 0.125 g. was given twice daily by mouth for five days. In spite of a steadily increasing calorie intake with four-hourly 5-unit doses of soluble insulin the blood-sugar levels varied widely (from 20 to 500 mg./100 ml.), and she had many hypoglycaemic episodes. However, she gained weight rapidly. At the age of 5 weeks the haemoglobin level was 9.1 g./100 ml. and she was transfused with 75 ml. of group A rhesus-positive blood. She was discharged home on June 24 on soluble insulin 5 units four-hourly before her feeds.

Further hypoglycaemic attacks necessitated reduction of the insulin dosage to 3 units four-hourly on July 15. Rapid gain in weight continued. On October 7, aged 5 months, she weighed 16 lb. 4 oz. (7.37 kg.), which was 116% of the expected weight for her age. She looked obese and moon-faced (Fig. 2). A glucose-tolerance test on January 7, 1953, showed: fasting blood sugar, 81 mg.; ½ hour, 182; 1 hour, 196; 1½ hours, 222; 2 hours, 235 mg./100 ml. On May 5 the insulin was reduced to 2 units four-hourly because of further hypoglycaemic attacks. On May 28 a glucose-tolerance test showed: fasting blood sugar, 105 mg.; ½ hour, 161; 1 hour, 223; 1½ hours, 208; 2 hours, 157; 2½ hours, 88 mg./100 ml. The insulin was reduced to 2 units thrice daily. Her weight was 24 lb. 7 oz. (11.1 kg.), 120% of the expected weight for her age. She remained symptomless from that time although continuing to look moon-faced and obese. On November 11, aged 18 months, the insulin was withdrawn. A glucose-tolerance test on this date showed: fasting blood sugar, 53 mg.; ½ hour, 174; 1 hour, 192; 1½ hours, 213; 2 hours, 166; 2½ hours, 172 mg./100 ml. Her urine contained only sugar during the glucose-tolerance test.

After withdrawal of her insulin her weight slowly approached normal levels. On July 30, 1954, aged 2½ years, it was 27 lb. 1½ oz. (12.3 kg.), 101% of her expected weight, and her height was 30 in. (76 cm.), 91% of her expected height. A glucose tolerance test showed: fasting blood sugar, 25 mg.; ½ hour, 123; 1 hour, 93; 1½ hours, 84; 2 hours, 73; 2½ hours, 77 mg./100 ml. She began to walk at 16 months and to speak at 18 months. However, it slowly became obvious that she was a high-grade mental defective, and at the age of 8½ years she was transferred to a special school for educationally subnormal children.

In 1957 her parents had another (male) child, who seems normal in all respects.

Case 2

A female infant was admitted to the Royal Hospital for Sick Children, Glasgow, on December 8, 1955, at the age of 7 days. She was the first child of healthy, young, unrelated parents. There was no family history of diabetes, but a cousin of the mother was an epileptic. She was born at term according to the expected date of delivery. Owing to previous miscarriages the mother was treated with ethisterone linguets 25 mg. daily during pregnancy. Birth weight was 4¼ lb. (1.93 kg.). Delivery was by forceps. There were no signs of birth trauma: She sucked well, but in spite of an adequate fluid intake her weight loss was excessive.

On admission she was profoundly wasted, her weight being 3 lb. 13½ oz. (1.74 kg.). The fontanelle was depressed and the sutures were overriding. The only abnormal local sign was some enlargement of the clitoris which might have been due to the ethisterone taken by the mother. During the next four days she fed eagerly without vomiting. However, on December 12 she weighed 3 lb. 3 oz. (1.35 kg.) and started to vomit frequently. On this date one of us (J. H. H.) recognized the same lined, pale, and aged appearance with apparent mental alertness previously noted in Case 1. On questioning, the nurses reported the presence of polyuria. The urine was loaded with sugar. It also contained a trace of protein and numerous casts. There was never any ketonuria. The sugar was confirmed to be glucose by chromatography. The blood-sugar level was 1,292 mg./100 ml. She was too ill to be photographed, but her appearance 48 hours later (Fig. 3) was still very similar to that in Case 1.

She was given soluble insulin 5 units three-hourly seven times daily before her feeds of half-cream national dried milk, which she continued to take eagerly. After 24 hours the blood sugar had fallen to 114 mg./100 ml. After 48 hours her weight had risen to 3 lb. 12 oz. (1.70 kg.) and the insulin was reduced to 3 units seven times daily. As in

Case 1, the blood-sugar levels varied widely (from 12 to 144 mg./100 ml.) and the insulin dosage was progressively reduced until 1 unit was being given seven times daily on December 21. The next day the feeding interval was altered to four-hourly, after which insulin requirements varied from 1 to 2 units before feeds. In spite of several low blood-sugar levels the infant showed only occasional episodes of limpness, which were quickly relieved with oral glucose. On January 10, 1956, she weighed 6 lb. 1½ oz. (2.76 kg.) and an attempt was made to withdraw the insulin.

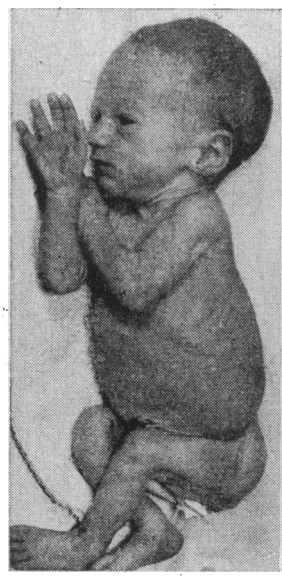

FIG. 3

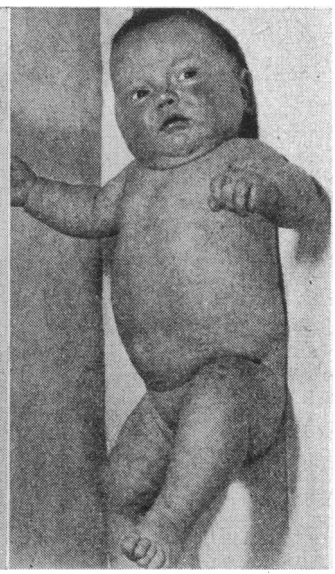

FIG. 4

FIG. 3.—Case 2. Note similar appearance to that in Case 1 (Fig. 1) with marked emaciation and alert expression. FIG. 4.—Case 2. At the age of 3¼ months infant looks obese and moon-faced.

On January 11 her weight had fallen to 5 lb. 6½ oz. (2.45 kg.) and there was again depression of the fontanelle with overriding of the sutures. She was quickly returned to her former satisfactory condition by restarting insulin. She was discharged home on January 16 on insulin 1 unit six times daily.

Her mother increased the insulin to 2 units before some feeds because she noted polyuria and slowing down of weight gain from time to time. She also reported that 3 units produced sweating just before the next feed. There were no losses of consciousness or convulsions. By March 20 the insulin had been reduced to 2 units four times daily. Her weight was then 12 lb. 8 oz. (5.7 kg.), 105% of her expected weight at the age of 15 weeks, and she looked obsese and moon-faced (Fig. 4). On April 29 insulin was completely withdrawn without adverse effects. Thereafter her weight gain slowed down and at 10 months she weighed 18 lb. (8.2 kg.), 93% of her expected weight.

She appeared to develop normally until April, 1958, when she had a transient loss of consciousness. On September 5, 1958, aged 2¾ years, she had a frank right-sided convulsion which lasted one hour. She was then found to have a slightly spastic right leg. An E.E.G. showed a focal spike discharge over the left mid-parietal region. A trial of primidone had to be abandoned because of ataxia, but she remained free from further seizures on ethotoin ("peganone") 250 mg. b.d. Psychiatric examinations in April, 1959, and subsequently revealed her to be of low average intelligence. She was re-examined in February, 1960, because of failure to grow. Her height was 34½ in. (87.6 cm.), 86% of her expected height. She was, however, normally proportioned. Radiographs showed ossification to be at the lower range of normal. A buccal smear was chromatin-positive.

The parents have subsequently had two normal children.

Case 3

A female infant was admitted to the Eastern General Hospital, Edinburgh, on December 20, 1957, at the age of 12 days. She was the second child of young, healthy, unrelated parents. The first child was healthy. There was no family history of diabetes. She was born spontaneously at an estimated 36 weeks' gestation. Her birth weight was 4 lb. 11 oz. (2.13 kg.). In spite of feeding well her weight on the 12th day was 4 lb. 5 oz. (1.96 kg.).

On admission no specific abnormality was detected. She fed eagerly. On January 7, 1958, aged 30 days, her weight was 5 lb. 3 oz. (2.35 kg.). Thereafter she began to lose weight in spite of an adequate intake and in the absence of vomiting or diarrhoea. On January 9 she suddenly collapsed, there was abdominal distension, and she cried as if in pain. Dehydration was present. Her temperature rose to 100.2° F. (37.9° C.) but there were no signs of infection. She seemed to improve temporarily, but on January 11 her weight was 4 lb. 11 oz. (2.13 kg.). Her urine was then found to contain 4 g. of glucose per 100 ml., but it was free of ketones. The blood-sugar level was 800 mg./100 ml. Chromatography, fermentation, and osazone tests showed the sugar to be glucose. Other values were serum sodium 134.8 mEq/l.; potassium 6.02 mEq/l.; chloride 102.4 mEq/l. The cerebrospinal fluid had a sugar content of 253 mg./100 ml.; protein 80 mg./100 ml. Cultures of blood and C.S.F. remained sterile. The serum and urine amylase levels were less than 8 units/ml. and 2 units/ml. respectively.

She was given soluble insulin, 5 units. The blood-sugar level was 350 mg./100 ml. 2½ hours after the first dose. The insulin dosage, which varied from 4 to 7 units a day, was subsequently governed by the sugar levels in the urine and blood. Blood-sugar levels of 173, 236, 260, and 247 mg./100 ml. were recorded between January 12 and 14. The feeds were of evaporated milk. The response to treatment was dramatic, with correction of dehydration and rapid gain in weight. On January 27 a change was made to insulin zinc suspension, but insulin therapy was withdrawn on January 28 at the age of 51 days. Her weight was then 6 lb. 8 oz. (2.95 kg.). The lowest blood-sugar level recorded during the period of insulin therapy was 33 mg./100 ml. There were no signs of hypoglycaemia at any time.

She continued to improve after insulin was withdrawn, although small amouts of glucose were found in the urine until February 8. A glucose-tolerance test on February 7 showed: fasting blood sugar, 50 mg.; ½ hour, 90; 1 hour, 193; 1½ hours, 127; 2 hours, 113; 2½ hours, 58 mg./100 ml. Subsequent glucose-tolerance tests when aged 7 months, 18 months, and 2 years gave completely normal results. Her physical development was satisfactory and she has maintained the 50th percentile of normal standards for height and weight. At the age of 3½ years it had become apparent that she was somewhat retarded mentally, but her parents have been uncooperative in attempts at objective assessment.

The mother has subsequently given birth to a healthy male infant.

Steroid Studies.—Six 24-hour collections of urine at different ages were tested for the output of 17-ketosteroids

TABLE I.—*Case* 3. *Excretion of Urinary Corticosteroids*

	Age	Weight	Volume of 24-Hour Urine	24-Hour Excretion of	
				17-Keto-steroids	17-Hydroxy-corticosteroids
Case 3	44 days	2·72 kg.	294 ml.	0·88 mg.	3·2 mg.
	53 ,,	2·95 ,,	225 ,,		3·1 ,,
Controls	28 days	2·72 kg.	170 ml.		1·9 mg.
	30 ,,	2·15 ,,	226 ,,		1·67 ,,
	28 ,,	2·24 ,,	110 ,,		0·48 ,,
	11 ,,	1·93 ,,	102 ,,		1·2 ,,
	12 ,,	2·15 ,,	115 ,,		1·2 ,,
Case 3 after recovery	3 months	3·57 kg.	225 ml.	0·92 mg.	1·96 mg.
	7 ,,	7·03 ,,	258 ,,	0·7 ,,	1·9 ,,
	18 ,,	11·31 ,,	155 ,,	1·1 ,,	1·5 ,,
	23 ,,	12·02 ,,	293 ,,		3·0 ,,

and 17-hydroxycorticosteroids (Tompsett and Smith, 1955). The results are shown in Table I.

Case 4

A female infant was born in the Glasgow Royal Maternity and Women's Hospital on July 22, 1961, the first child of young, healthy, unrelated parents. She was born three weeks after the expected date of delivery and had a birth weight of 4 lb. 1 oz. (1.84 kg.). There was no family history of diabetes, although the mother was found to have glycosuria on three occasions during her pregnancy. A glucose-tolerance test on June 13 was normal.

On admission to the premature-baby unit the infant was thought to show the appearance of post-maturity (placental insufficiency) with dry and wrinkled skin. She was put to the breast after 36 hours and sucked eagerly. By August 1, in spite of 15 fl. oz. (425 ml.) of breast milk daily, her weight had fallen to 4 lb. 1 oz. (1.84 kg.) after a previous rise to 4 lb. 5 oz. (1.95 kg). At this time her resemblance to Cases 1 and 2 was noted. Her urine was found to be loaded with sugar, confirmed by chromatography to be glucose. There was no ketonuria. The blood sugar was 750 mg./100 ml.

She was placed on six four-hourly feeds of half-cream national dried milk with 4 units of soluble insulin before each. She rapidly recovered from her dehydration. The blood-sugar level fell to 100 mg./100 ml. in 30 hours. On August 11 she weighed 5 lb. 12 oz. (2.61 kg). The insulin was stopped and replaced by tolbutamide 125 mg. twice daily. The glycosuria immediately returned, blood sugar rose to 576 mg./100 ml., and in 48 hours her weight had fallen to 5 lb. 2½ oz. (2.34 kg). When the tolbutamide was withdrawn and insulin restarted, 4 units six times daily, rapid gain in weight was resumed. The insulin requirements slowly fell and on September 7 a change was made to a single dose of insulin zinc suspension 8 units daily. She was discharged home on September 15 at the age of 8 weeks, weighing 9 lb. 4 oz. (4.19 kg). At no time were hypoglycaemic attacks observed.

She continued to grow rapidly although her blood-sugar levels varied from 235 to 359 mg./100 ml. The insulin was omitted from September 28 although her blood-sugar level was 318 mg./100 ml. She weighed 10 lb. 8oz. (4.76 kg.). By October random blood-sugar levels were always normal and she continued to thrive. A glucose-tolerance test on November 2 showed: fasting blood sugar, 59 mg.; ½ hour, 97; 1 hour, 162; 1½ hours, 151; 2 hours, 95 mg./100 ml. On January 25, 1962, aged 6 months, she weighed 16 lb. 15 oz. (7.68 kg.), 113% of her expected weight. Although unable to sit up unsupported she showed a lively interest, reached for toys, and vocalized normally.

Steroid Studies.—Four 24-hour collections of urine between August 3 and 7 were tested for the output of 17-ketosteroids and 17-hydroxycorticosteroids (Appleby *et al.*, 1955). The results are shown in Table II. Further separation of 17-hydroxycorticosteroids by chromatography on Bush C showed no 3 oxo-Δ^4 compounds, indicating that all the 17-OHCSs were reduced or hydrogenated and that the 17-OHCSs were mainly metabolites of compound F (hydrocortisone).

TABLE II.—*Case 4. Excretion of Urinary Corticosteroids*

Age	Volume of 24-Hour Urine	24-Hour Excretion of	
		17-Keto-steroids	17-Hydroxy-corticosteroids
12 days	81 ml.	0·17 mg.	0·34 mg.
13 ,,	74 ,,	0·08 ,,	0·46 ,,
14 ,,	50 ,,	0·09 ,,	0·39 ,,
15 ,,	48 ,,	0·12 ,,	0·29 ,,

Discussion

Each of our four patients showed marked hyperglycaemia and glycosuria, with rapid loss of weight in the absence of diarrhoea or vomiting, and dehydration in spite of an adequate intake of fluid and calories. Although the disease varied greatly in severity in the four patients it was markedly sensitive and responsive to insulin. These facts would seem to justify a diagnosis of diabetes mellitus. The absence of ketosis is well known to be a feature of the insulin-resistant type of diabetes encountered in obese adults of middle age, but it was unexpected in our insulin-sensitive patients. On the other hand, it is well recognized that the newborn infant does not react with ketosis to other stresses such as starvation or high intestinal obstruction. The unique finding in neonatal diabetes mellitus is the spontaneous recovery if the infant can be kept alive long enough. This demands accurate diagnosis followed by prompt treatment with insulin. The failure of tolbutamide in therapy was demonstrated in Case 4.

Diagnosis

The difficulty of collecting urine from small newborn infants, especially females, has almost certainly led to cases of neonatal diabetes being missed, and to death being wrongly certified as due to such causes as prematurity, post-maturity, inanition, or marasmus. An important observation is that all our four patients had birth weights below 5½ lb. (2.5 kg.), although, in fact, three (Cases 1, 2, and 4) were born at or after full-term. Engleson and Zetterqvist (1957) stressed the appearance of post-maturity or placental dysfunction (Clifford, 1954) in their two patients. Several other reported cases were certainly or probably post-mature (Ramsey, 1926; Stradqvist, 1932; Arey, 1953; Keidan, 1955). It would seem wise, therefore, to ensure examination of the urine or blood for sugar content in every infant of low birth weight who is born after a normal or unduly long period of gestation. We have been impressed by the characteristic appearance of these diabetic infants at the stage of dehydration (Figs. 1 and 3). In addition to the usual signs of dehydration, the infants had a peculiar pallor and lined, aged appearance which was associated with a remarkably "open-eyed" alert facies. This contrasts strongly with the semicomatose state and glazed eyes which are usual in severely dehydrated infants. Polyuria is also present, but is not easy to recognize in the newborn.

Prognosis

The follow-up of the surviving cases so far reported is given in Table III. Complete recovery from the diabetic condition appears to be invariable, and permanent sequelae have not previously been recorded. It should be noted, however, that in most cases the period of

TABLE III.—*Recorded Cases of Congenital Diabetes Mellitus with Recovery*

Authors	Sex	Birth Weight (kg.)	Highest Blood Sugar (mg./100 ml.)	Duration of Glycosuria or Treatment	Period of Follow-up
Ramsey (1926) ..	M	2·20	263	1 month	25 years
Lawrence and McCance (1931)	F	3·75	600	7 days	3 months
Strandqvist (1932)	M	2·20	420	14 ,,	9 ,,
Nawrocka-Kanska (1952)	M	2·70	268	12 ,,	1 year
Arey (1953) ..	M	2·20	555	6 weeks	5 months
Keidan (1955) ..	F	2·78	245	17 days	10 ,,
Engleson and Zetterqvist (1957)	M	2·78	720	3 months	3 years
	F	2·02	560	200 days	1 year
Present authors (Cases 1–4)	F	2·41	708	18 months	9 years
	F	1·93	1,292	4½ ,,	5 ,,
	F	2·13	800	28 days	3 ,,
	F	1·84	750	2 months	6 months

follow-up has been relatively short. By contrast, the three of our four patients (Cases 1, 2, and 3) followed up long enough for psychomotor assessment have shown evidence of cerebral abnormality. Two (Cases 1 and 3) are mentally retarded. One (Case 2) is mentally much below the level of intelligence of her parents, and in addition suffers from a spastic monoplegia and has had epileptic seizures associated with a focal abnormality in the electroencephalogram. The brain damage in Cases 1 and 2 might have been attributable to the hypoglycaemic periods which were frequently recorded during the early stage of insulin therapy. In Case 3, however, no such pathogenesis existed. It is not yet clear whether the likelihood of residual brain-damage could be related to the duration of the diabetic state. Table III shows that this has varied greatly. Indeed, in two cases recovery took place without the use of insulin (Nawrocka-Kanska, 1952: Keidan, 1955).

Aetiology

Little can be deduced from the meagre information available in the literature. It was, unfortunately, not possible to estimate the plasma insulin-like activity in any of our patients. There have been few satisfactory reports of the state of the pancreas in infants who have died of neonatal diabetes. A necropsy was performed 14 hours after death on one patient who died in the Royal Hospital for Sick Children, Glasgow. Gross hypoplasia of the pancreas was found (weight 1.06 g.). Microscopical examination showed a great diminution in the number of islets of Langerhans (Devine, 1938). It seems impossible that the pancreas in any of our patients was in a similar hypoplastic state, because clearly each was capable in time of producing enough insulin to meet the infant's requirements. On the other hand, Baird and Farquhar (1962) have produced evidence that normal newborn infants have a remarkably poor glucose tolerance and low plasma insulin-like activity. It is not inconceivable that this could be aggravated by the anoxia attendant upon placental dysfunction resulting from post-maturity.

Infection has been a feature in some of the published cases (Ramsey, 1926: Lawrence and McCance, 1931; Lewis and Eisenberg, 1935: Limper and Miller, 1935; Stradqvist, 1932: Arey, 1953; Keidan, 1955), but was more probably a complication than a cause of the diabetic state. The case described by Jeune and Riedweg (1960) was more probably an example of a transient glycosuria and hyperglycaemia due to infection. In none of our patients was there any clinical or laboratory evidence of infection. Keidan (1955) postulated a hypothalamic influence in his case because the cerebrospinal fluid was xanthochromic with a raised protein content. A similar finding was noted by Nawrocka-Kanska (1952). In one of our patients the cerebrospinal fluid contained an unusually high level of protein (Case 3). There were, however, no other signs of hypothalamic disturbance, and a transient cerebral cause is difficult to accept.

Engleson and Zetterqvist (1957) suggested an adrenocortical disturbance. Jeune and Riedweg (1960) found normal levels of corticosteroids in both plasma and urine in their somewhat doubtful case. We estimated the urinary excretion of 17-ketosteroids and 17-hydroxycosticosteroids in two of our patients (Cases 3 and 4), but by different methods and in different laboratories. In Case 3 there seemed to be a moderate increase of 17-hydroxycorticosteroids above the normal levels for the method. In Case 4 the corticosteroid excretion levels were well within the normal range of a large number of healthy infants previously studied by the same techniques. The somewhat moon-faced appearance noted in Cases 1 and 2 (Figs. 3 and 4) during the stage of recovery was reminiscent both of Cushing's syndrome and of the infants of diabetic mothers. Baird and Farquhar (1962) have shown, however, that the infants of diabetic mothers owe their characteristic appearance to an increased deposition of fat due to excessive production of insulin. Our patients were therefore probably obese owing to the administration of insulin possibly beyond the period when this was really necessary. In the presence of an insulin-sensitive diabetes it is difficult to accept overactivity of the adrenal cortex as an aetiological factor.

Summary

Four cases of congenital diabetes mellitus are described. The predominant features were insulin-sensitivity in the absence of ketosis and ultimate complete recovery from the diabetic state. In three of the four cases residual brain damage was noted. It is suggested that this condition may not be excessively rare and that increased awareness of the somewhat characteristic clinical picture would lead to more frequent recognition of the disease.

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A British Standards Institution Committee which has been giving careful consideration to types of conical fittings for hypodermic needles has unanimously agreed that the Luer fitting should be adopted generally in the United Kingdom because of the greater strength of the metal and the better grip attained between the nozzle and the needle. This committee has been preparing another standard in the British Standard series of specifications for hypodermic equipment. B.S. 3522: 1962 "Hypodermic Surgical Mounted Needles (Luer Fitting)." This specifies requirements for a range of sizes of hypodermic stainless steel needles, mounted with the Luer conical socket, and having points as follows: (1) regular points with a bevel of 12 degrees nominal, (2) short points with a bevel of 18 degrees nominal. Copies of this standard may be obtained from the B.S.I. Sales Branch, 2 Park Street, London W.1. (Price 5s each. Postage extra to non-subscribers.)