

## Short reports

### Congenital absence of islets of Langerhans

A male infant with congenital diabetes mellitus died on the 3rd day of life. No recognizable islet cells were found in the pancreas at necropsy. A male sib probably died from the same condition, which is hitherto undescribed.

#### Case history

The infant was born after an uneventful pregnancy of 39 weeks' gestation and a normal vertex delivery. His mother was quite sure of her dates, but the child weighed only 2.13 kg, measured 39 cm in crown-rump length and 50 cm in crown-heel length, and had a head circumference of 33 cm. He was wasted and covered in meconium, and had an Apgar score of 6 at 1 minute. Within a few hours he had respiratory distress and it was uncertain whether this was due to meconium aspiration or hyaline membrane disease but air entry and chest x-ray were normal. Blood gas analysis at the age of 5 hours gave  $P_{O_2}$  64 mmHg (8.5 kPa),  $P_{CO_2}$  30 mmHg (4.0 kPa),  $pH$  7.35, standard bicarbonate 18 mmol/l (18 mEq/l), and base deficit 7 mmol/l (7 mEq/l) indicative of a mild metabolic acidosis.

He was treated with vitamin K, penicillin, kanamycin, and 10% dextrose (3 ml/h), and small amounts of sodium bicarbonate. However, at the age of 12 hours, though apparently better and accepting small tube feeds of half-cream milk, he still had deep respirations at a rate of 60-80/min. Repeated acid-base estimations showed an increasing metabolic acidosis and at 24 hours  $P_{CO_2}$  was 19.5 mmHg (2.6 kPa),  $pH$  7.24, standard bicarbonate 13 mmol, and base deficit 18 mmol/l. In spite of further sodium bicarbonate the picture was virtually unchanged at 36 hours. At this time the urine was found to contain large amounts of sugar and acetone. Dextrostix indicated a blood sugar level above 22 mmol/l (396 mg/100 ml), subsequently measured as over 40 mmol/l (721 mg/100 ml). The infant was then given 2 units of insulin before transfer to the University Hospital of Wales. On arrival he was both acidotic and dehydrated with hypotonia, rapid deep respirations, and a poor pulse

volume.  $pH$  was 7.21,  $P_{CO_2}$  18 mmHg (2.4 kPa),  $P_{O_2}$  86 mmHg (11 kPa), standard bicarbonate 11 mmol/l, and base deficit 20 mmol/l. Blood glucose was now 28 mmol/l (505 mg/100 ml). He was given a further 2 units of insulin and rehydration was begun but he suddenly collapsed and died, aged 40 hours.

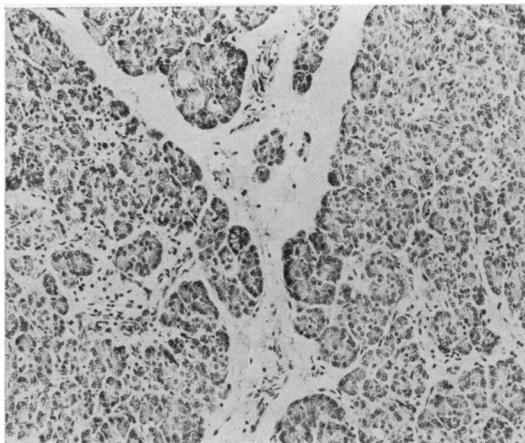
#### Postmortem and histological examination

The body appeared dehydrated and lacked adipose tissue. The trachea and the lungs, which together weighed 33 g, contained blood and showed patchy collapse, haemorrhagic consolidation, areas of hyperdistension, and contained numerous epithelial squames. The dilated heart (weight 12 g) showed slight fatty change and a probe-patent ductus arteriosus. There was some blood in the stomach and small intestine and the liver (weight 90 g) was enlarged and showed fatty change. The thymus showed cellular depletion and the brain (weight 367 g) was somewhat oedematous, but well myelinated.

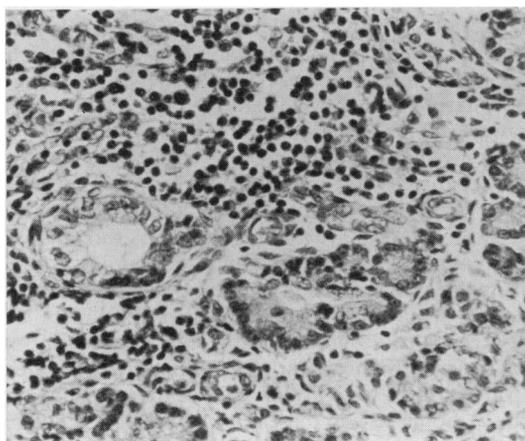
The pancreas appeared normal in size and consistency. Sections through the head, midbody, and tail showed normal exocrine elements, though the ducts appeared to be dilated, containing some eosinophilic material. The perilobular connective tissue was prominent, but recognizable islets of Langerhans could not be found (Fig. 1). A number of bizarre, well capillarized lymphoid aggregates of various sizes were present within the parenchyma (Fig. 2). Some cells in these appeared finely granular, suggestive of endocrine cells, but special staining for  $\alpha$ - and  $\beta$ -cells and for argyrophilia was negative. In addition, there were spaces within the parenchyma containing a few loose 'connective tissue cells', which might represent former islets. Insulin was estimated in the pancreatic tissue which was found to contain only 54 IU/g while two normal control pancreases removed from infants dying at 24 and 28 hours each contained in excess of 2000 IU/g.

#### Family history

The first child of these parents was a male, born 8 years previously, weighing only 1.6 kg, at term, though by dates he was of 41 weeks' gestation. He was noted to be very wasted and had an initial



**Fig. 1** Low power photomicrograph of the pancreas showing exocrine elements together with several spaces containing loose connective tissue. (Haematoxylin and eosin.  $\times 80$ .)



**Fig. 2** High power photomicrograph of a well capillarized lymphoid aggregate with some finely granular cells, but no recognizable  $\alpha$ - or  $\beta$ -cells. (Haematoxylin and eosin.  $\times 240$ .)

Apgar score of only 1 which improved to 5 at 5 minutes. The clinical notes from that time are not extensive, but it was noted that the abdomen had a doughy feel, a comment which would have also been appropriate for the infant described above. Respirations were rapid (80/min) and irregular, the pulse rapid (160/min), and the baby looked pale and shocked. He lived for only 48 hours and vomited altered blood before he died. Though he was pale, Hb was 13.5 g/dl. The most

interesting necropsy feature was the fact that the liver was fatty, but no sections of the pancreas were made.

Between this pregnancy in 1966 and the child described here born in 1974, the mother gave birth to 2 normal girls in 1967 and 1969. The mother, born in 1946, and the father, born in 1945, are unrelated. They are both healthy with a normal glucose tolerance test performed after the last pregnancy.

### Discussion

This infant had congenital diabetes consequent upon extreme involution, or complete absence of pancreatic islet cells. The slight trace of insulin present in the pancreas at necropsy was probably derived from the insulin administered therapeutically and contrasted with the abundance of insulin found in the 2 control pancreases. The relatively few bizarre lymphoreticular aggregates and the 'spaces' may represent remnants of islets, and may indicate an extreme form of the normal involutionary changes in the islets seen in the newborn fetus (Emery and Bury, 1964). Alternatively, the appearance somewhat resembles those of insulinitis of juvenile diabetes recorded by Stansfield and Warren (1928) and LeCompte (1958). However, it is unlikely that an intrauterine viral infection would have affected two pregnancies separated by two normal ones. A viral or toxic aetiology, or even an autoimmune one, is a possibility which is impossible to rule out at this stage but which does not have any convincing evidence to support it. As two male sibs appear to have been affected, the condition is in our opinion most likely to have been caused by an autosomal recessive or an X-linked abiotrophy or degeneration. No similar case reports have been traced.

### Summary

A small-for-dates male infant who developed acute metabolic acidosis shortly after birth had diabetes and died aged 40 hours. At necropsy there was an absence of any recognizable islets of Langerhans though lymphoreticular aggregates were found. This was the fourth child of healthy unrelated parents whose first child, also a male, died at 48 hours under similar circumstances. It is suggested that both boys had the same underlying pathology and this might be a previously undescribed recessive or x-linked inherited condition.

We are grateful to Dr. N. G. Sanerkin who carried out the necropsy on the first sib; to Dr. M. Addison,

who performed the insulin estimations on the pancreas; and to Professors I. Doniach and E. Williams for helpful advice.

#### References

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## Measurements of systolic blood pressure in the preterm baby by the transcutaneous Doppler method

Comprehensive care of the sick small baby should include regular estimation of blood pressure (BP) by a technique which should be reliable and free of risks. Though a number of indirect methods exist in monitoring BP in the newborn, accuracy of such procedures remains largely undetermined. However, introduction of the transcutaneous Doppler ultrasound (Black *et al.* 1972; Kirkland and Kirkland, 1972) in measuring BP showed that the method was fairly accurate and correlated well with direct intra-arterial measurements (Elseed *et al.* 1973). Using the Doppler method we have estimated systolic BP in preterm babies during the first 7 days of life to determine within-patient variations and standard deviations.

#### Material and methods

Thirty-five babies were studied. All were well. Birthweights ranged from 1000-2500 g. None developed clinical features of respiratory distress. Systolic BP was taken in the upper limbs, after feeds when babies were quiet or asleep, twice daily during the first 7 days of life from 9.00 a.m.-11.00 a.m. and 3.00 p.m.-5.00 p.m. The instrument used was Model No. 802, Parks Electronic Ltd., cuff size 4 cm. 14

measurements were made on each of 35 babies, i.e. 490.

#### Results

Mean systolic BP is shown in the Table. In the analysis the groups have been treated as representing a

Table Mean systolic blood pressure

No. of babies	Birthweight (g)	Mean systolic pressure (mmHg)	Standard error (mmHg)
10	1000-1500	74.0	2.5
9*	1501-2000	69.5	2.6
16	2001-2500	71.8	1.9

\*One baby omitted: this baby was excluded from some of the later analysis as its readings were felt to be a very extreme set of observations. Here it does not alter the estimates significantly. No weighting was used, since 14 observations were available on all the babies. The differences between the groups are not significant at the 5% level. Thus, overall, systolic BP in this group of babies has a mean of  $71.9 \pm 1.3$  mmHg, SE).

random sample from a 'population' of babies with birthweights in the appropriate ranges. (All babies were born in Peterborough during the time over which the data were collected. The group means are considered as estimates of the means in the appropriate 'populations', and estimated standard errors have been calculated, on that basis, using the analysis of variance.

The day from birth appears to have an effect on systolic pressures. An analysis of variance was carried out using all the data, with the model:

$$Y_{IJK} = \mu + \alpha_I + \beta_J + \gamma_K + \delta_{IJ} + \eta_{IK} + \epsilon_{JK} + \zeta_{IJK}$$

where I (I = 1 ... 35) represents 'baby', J (J = 1 ... 7) represents 'day from birth', K (K = 1 ... 2) represents 'time of day'.

The variance ratio, against the residual (i.e. baby  $\times$  day  $\times$  time) for baby  $\times$  day was 1.70 ( $P \approx 0.005$ ) and for baby  $\times$  time was 1.85 ( $P \approx 0.025$ ). The variance ratio (against the baby  $\times$  time interaction) for time was 2.72 ( $P \approx 0.1$ ). Thus the baby  $\times$  day and baby  $\times$  time interactions seem significant.

Three main sources of variation have been isolated (estimates based on the Table omitting one observation). (i) Between babies—estimated standard deviation 6.4. (ii) Variation due to the differing patterns over days—estimated standard deviation 6.9. (iii) Residual, within-baby variation—estimated standard deviation 11.6.

The effect of birthweight has been examined. There does not seem to be any clear relationship between birthweight and mean blood pressure.