The early evidence from mice and men, therefore, suggests that maternal histidinaemia and a central nervous system defect, obvious or subtle, may be related as cause and effect. Clearly, more studies are required before this can be substantiated. We suggest that it become a routine procedure that mothers of children with mental retardation of undetermined cause have their blood histidine (as well as blood phenylalanine) measured. Perhaps all mothers could be examined antenatally by a 'ferric chloride' type of urine test, which would detect both maternal PKU and histidinaemia. Whether or not histidinaemic women should have a low histidine diet in pregnancy will not become clear until further studies have been done.

Summary

A 37-year-old sister of a mentally retarded 27-year-old male with histidinaemia was shown to have the same biochemical condition. She had 5 children aged between 3 and 19 years, all of whom had normal blood histidine levels. The IQ of 4 of the 5 children was assessed and in all 4 the IQ was much less than the mean parental value. The possibility that this was attributable to maternal histidinaemia is considered.

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Minimal rates of oxygen consumption in small-for-dates babies during the first week of life

Scopes and Ahmed (1966) showed that the minimal rates of oxygen consumption in small-for-dates babies remained low during the first 3 days of life but rose abruptly at 4 days and thereafter rates were similar to those of mature babies. During a different study involving metabolic rates (Bhakoo and Scopes, 1971), we had reason to repeat these observations on oxygen consumption in small-for-dates babies with quite different findings.

Material and methods

The birthweights and gestation periods of the 11 babies studied ranged from 1940 to 2700 g and 37 to 40 weeks. Gestational age was calculated from the first day of the mother's last menstrual period in all cases. All babies were below the 10th centile birthweight for gestational age (Butler and Bonham, 1963). The mother's permission was obtained for each study.

Oxygen consumption was measured in an apparatus working on the closed circuit principle as described by Scopes (1965). The study was performed during postprandial sleep over a period of 20 to 30 minutes. The temperature of the environment was kept within the neutral range and was confirmed by measurement of the skin temperature of the exposed abdominal wall. 48 observations were made.

Observations

Table I shows the minimum rates of oxygen consumption in these babies during the first week of life. In the first 12 hours only 2 observations were made. However, the rates of oxygen consumption during this period are the same as the larger number of observations made by Scopes (1965) and by Hill

TABLE I
Minimum rates of O_2 consumption in small-for-dates babies during first week of life

Age	No. of studies	O_2 consumption (mean) (ml/kg per min)	SD	SEM
0-12 hr	2	5.20	—	—
13-36 hr	10	6.50	0.68	0.20
37-60 hr	9	6.54	0.55	0.18
3 dy $\pm$ 12 hr	8	6.85	0.80	0.28
4 dy $\pm$ 12 hr	8	6.65	0.70	0.25
5 dy $\pm$ 12 hr	7	7.00	0.41	0.16
6 dy $\pm$ 12 hr	4	7.9	0.92	0.46

Note: The time intervals are the same as those used by Scopes and Ahmed (1966).

and Robinson (1968) on similar babies at this time of life. Oxygen consumption showed a large rise in the next 24 hours. Between 2 to 6 days, rates were more or less constant. These findings are shown in the Fig. Thus, these small-for-dates babies

FIG.—Minimal rates of oxygen consumption in normal babies, small-for-dates babies fed late (1966), and small-for-dates babies fed early (1970).

behaved like the normal mature neonates. The 3-day lag before a rise in oxygen consumption as seen by Scopes and Ahmed (1966) on small-for-dates babies was no longer shown.

Discussion

There are always difficulties in interpretation of consecutively studied clinical series. The two series compared were in the same unit, using the same techniques, and with an apparently similar population. The findings in small-for-dates babies of the first series (studied in 1964–65) were materially different from those found in the later series and call for an explanation. One of the more obvious changes in the care of the babies between the two series was in the feeding regimen as shown in Table II. It is apparent that not only were the babies in the later series fed early with milk, but also their milk intake was more than twice that of 1966 babies during the first 3 days of life. While 4 out of 17 babies of Scopes and Ahmed's study (1966) developed hypoglycaemia, none of the babies in the later series was hypoglycaemic.

Gentz and Kellum (1971) found that the rise of

TABLE II
Feeding schedule in small-for-dates babies

	1966	1970
First feed	Water 6–12 hr	Milk 1–2 hr
Thereafter ml milk/kg per 24 hr		
1st 24 hr	20	60
2nd 24 hr	40	90
3rd 24 hr	60	120
4th 24 hr	90	150

oxygen consumption (VO_2) in piglets is affected by feeding. If the piglet is starved, rates of VO_2 remain low after birth. Successive feeds are associated with a rise in resting VO_2 until postnatal rise in VO_2 is complete. These changes are not related to changes in plasma volume or albumin absorption. Our data, albeit consecutive, provide evidence that the same effect is seen in the human baby. It is important to restate that we are discussing 'resting metabolic rates'. The babies of the earlier series were capable of increasing their metabolic rate in response to a cool stimulus, at least over a 20-minute period of testing. Nevertheless, the resting rate of these babies was low. Arguing teleologically, it seems that the babies were conserving the limited food reserves. In other situations of starvation, the metabolic rate is not depressed except terminally. However, there is a large rise in the resting metabolic rate in marasmic infants after the introduction of adequate calories into their diet (Montgomery, 1962). Specific dynamic action of food causes only a small rise and could not be responsible for this large rise in metabolism. Thus the suggestion that lack of food depressed the basal metabolic rate in babies of the 1966 series seems to be peculiar to the newborn. The mechanism involved needs further elucidation and may explain differences between various series (e.g. Scopes and Ahmed against Hill and Robinson) on rates of rise after birth.

Summary

In a recently studied series of small-for-dates babies, the postnatal rise in minimal rates of oxygen consumption occurred in the first 36 hours and was quite different from an earlier series. It is suggested that the more liberal feeding regimen of the later series was responsible. Thus, this may represent evidence that in the human newborn baby minimal rates of oxygen consumption are affected by total calorie intake, a fact well established in the newborn piglet.

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Prolonged continuous positive airways pressure for pulmonary oedema due to persistent ductus arteriosus in the newborn

Distending pressure is now recognized therapy for neonatal respiratory distress syndrome (RDS) (Gregory *et al.*, 1971; Chernick, 1973). In most cases the duration of therapy is less than 3 days. This paper describes the prolonged use of continued

positive airways pressure (CPAP) to control drug-resistant pulmonary oedema in 2 babies who initially suffered from RDS, but aged 1 week developed the signs of a persistent ductus arteriosus (PDA).

Methods

RDS was managed in the standard manner (Davies *et al.*, 1972). The Bennett PR 2 ventilator was used when intermittent positive pressure ventilation (IPPV) was indicated and also for administering CPAP through the endotracheal tube (Etches, Houghton, and Moore, 1973).

Case reports

Case 1. A female, birthweight 1190 g at 28 weeks' gestation, was apnoeic at birth. Intubation and positive pressure ventilation were applied but severe RDS developed and the IPPV was continued. Aged 30 minutes on IPPV (pressure 24 cmH₂O, rate 32/min, oxygen 80%) the blood gases were pH 7.16, Pao₂ 56 torr, Paco₂ 52 torr. Her RDS improved and by 7 days the blood gases were satisfactory in 40 to 50% oxygen at ventilator pressures of 16 to 18 cmH₂O and rates of 20 to 30/minute. Periods of spontaneous respiration occurred.

The pattern of her illness now changed, with widespread crepitations in both lungs. Chest x-ray was compatible with pulmonary oedema. The blood pressure was 60/20 with bounding pulses, and a loud systolic murmur heard in the pulmonary area suggested a PDA. She was not infected. Attempts to discontinue IPPV from the 14th to the 17th day failed due to progressive hypercapnia and pulmonary oedema not consistently controlled by digitalis and frusemide (Fig. 1). The frusemide did control an exacerbation of the pulmonary oedema after a plasma and blood infusion at age 14 days, but hyponatraemia developed. Pao₂ remained satisfactory in 35 to 50% oxygen throughout this period. Her weight fell to 950 g and she was never fit enough for cardiac catheterization to confirm the clinical diagnosis. CPAP with 32% oxygen, applied for the first time at age 17 days, controlled the pulmonary oedema for 22 hours. Paco₂ then increased, crepitations

FIG. 1.—Clinical course of Case 1 from 14 to 20 days of age.