Foetal growth retardation

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THE INTERNATIONAL DEFINITION of a premature infant is a live born infant with a birth weight of 5½ lb. (2.5 kg.) or less. The inadequacy of this definition was obvious for various reasons; one of these was that it did not separate a small group of babies, who were small for the particular gestation involved. These babies were labelled variously as pseudo-premature, intrauterine growth retardation, dymaturity, etc. Butler and Bonham (1963) described them as "small for date babies" and defined them as babies who are two standard deviations below the expected weight for the particular gestation.

Clinically, these infants are usually thin, long with wrinkled, dry, peeling meconium-stained skin and with an unusual lively alert appearance. They usually have well-developed grasp and sucking reflexes.

Sometimes it is difficult clinically to separate SFD babies from premature babies. Calculation of gestation can sometimes be difficult because one is dependent on date of last menstrual period. Neurological testing was introduced as a method of estimating gestation. Robinson (1966) found that neurological reflexes could be used with some degree of accuracy to estimate gestation and with the knowledge of gestation, one can decide whether an infant is small for date.

The recognition of these "small for date babies" was important as the perinatal mortality in this group was high. Butler and Bonham (1965) found that in 1958 in England 69/1,000 "small for date babies" born at 36 weeks' gestation or over died during labour or in the neonatal period.

The major causes of death were intrapartum asphyxia, pneumonia, and massive pulmonary haemorrhage (Table 1). These babies are easily chilled because of the lack of subcutaneous fat. There was also an increased incidence of hypoglycaemia.

Gruenwald (1963) described the characteristic necropsy finding.

There was a lack of subcutaneous fat, the liver thymus and lungs were relatively small, but the body length and heart weight were relatively big for the particular weight of the infant. Brain weight was found to be much heavier than expected. Also the brain, liver ratio (normal = 3:1) was increased to 6:1 and liver glycogen was found to be low.

Placental findings varied. In women, who had toxaemia, there was infarction of the placenta with obliteration of vessels to placenta. In others, there was a reduction in placental size. Primary placental abnormalities have also been described.

Etiology

With the recognition of the clinical features and pathological findings, it was necessary to try to understand the possible etiology of these "small for date babies."

Foetal growth is theoretically dependent on:—

i) Nutrition: both quantity and quality.
ii) State of maternal circulation to the placenta.
iii) State of the placenta
iv) State of the foetal circulation
v) The genetic potential of the foetus

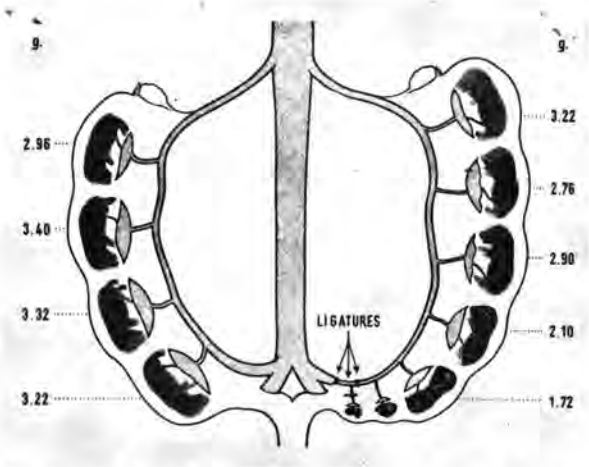

Fig. 1: **Foetal growth retardation produced by ligating one horn of the uterine artery (J.S. Wigglesworth Journal of Path and Bact. 1964.)**

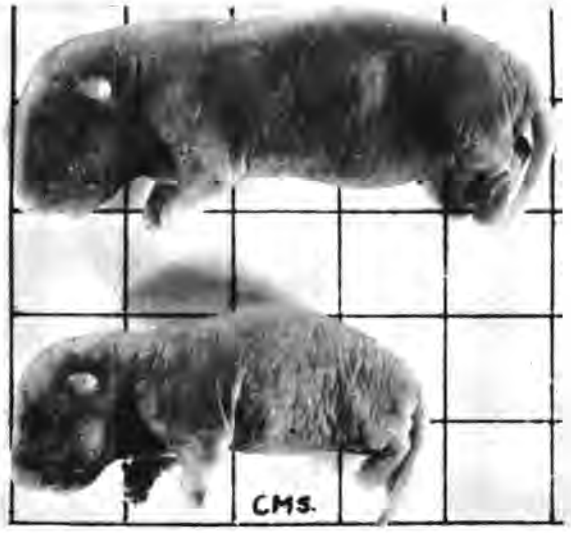

Fig. 2: **Foetal growth retardation produced by starving pregnant rats in the last three days of pregnancy.**

vi) The ability of the foetus to assimilate the nutrients supplied.

The effect of nutrition on foetuses has been extensively studied in animals. Wallace L.R. (1945), working on ewes, showed that when pregnant ewes were fed on a low plane of nutrition in the last six weeks of pregnancy, the lambs were 40% below the expected weight.

These nutrition experiments have been done on rats with similar results. (Benjamin W. Beg 1965), Wigglesworth J.S. & Paramaesvaran N. (1968 unpublished) starved pregnant rats in the last three days of pregnancy. The foetuses were delivered by Caesarian section a day before delivery. The foetuses were found to be grossly retarded. (Fig. 2) The brain was little affected but the liver was grossly retarded. Using a biochemical method to analyse DNA content of the liver and brain and then using these figures to work out the total cell count, it was found that the retardation was due to both a reduction in cell size and cell number (Table 2).

The part played by the maternal circulation to the placenta was studied by Wigglesworth J.S. (1964) on rats. The blood supply to foetuses in a rat is derived from both the uterine and ovarian artery. (Fig. 1). The uterine artery to one born was ligated on Day 16 of pregnancy. The foetuses were delivered by Caesarian section a day before delivery. The foetuses on the ligated side were growth retardated, the severity becoming less as one moved away from the site of ligation.

Butler, W.H. & Wigglesworth, J.S. (1966), also studied the effect of maternal liver damage on the foetuses. Aflatoxin BI was injected into pregnant rats on Day 16. Aflatoxin BI inhibits protein synthesis in the liver. This means reduced aminoacids for foetal growth.

Foetuses were growth retarded, but showed no effect of the drug themselves. Maternal liver showed histological damage.

DISCUSSION

In man, the part played by nutrition is thought to be small. It has been found that even in starvation, the weight reduction of foetuses was only about 200 gm.

It is known that maternal hypertension and toxaemia of pregnancy are associated with "small for date babies." Pathological findings show arterial

Table 1

MORTALITY RATES PER THOUSAND FROM RESPIRATORY AND CEREBRAL CAUSES OF "SMALL FOR DATE" BABIES (BORN AT 36 WEEKS GESTATION AND OVER (BUTLER 1965)

	'Small for Date babies.'	Normal for date babies
Intrapartum asphyxia	23.8	4.4
Pneumonia	10.7	0.8
Massive pulmonary haemorrhage	9.5	0.1
Cerebral birth trauma asphyxia	5.0	2.1
Hyaline membrane	4.5	0.1
Intraventricular haemorrhage	1.6	0.0
Total deaths	68.5	8.8

Table 2
STARVATION EXPERIMENT ON PREGNANT RATS

	CONTROL	STARVED	PROBABILITY
FOETAL WT.	5.866 gms.	4,437 gms.	– 24.4%
BRAIN WT.	224.7 mgms.	205.5 mgms.	– 8.55%
TOTAL CELL COUNT	139.8×10^6	138.2×10^6	– 1%
LIVER WT.	441 mgms.	278 mgms.	– 37.0%
TOTAL CELL COUNT	321.6×10^6	245.9×10^6	– 23.6%

obliteration with infarction of the placenta. This corresponds well with the ligation experiments of Wigglesworth, J.S. (1964). Gruenwald (1963) also found primary placental abnormalities associated with these "small for date babies." This indicates that vascular causes, resulting in reduced nutrients to the foetus, play an important part in growth retardation.

There is an inverse relationship between litter size and birth weight both for polytoccous animals and man. There is a progressive decrease in weight in twins, triplets and quadruplets. The stage when the foetus gets retarded in man is thought to occur when the total weight of foetuses is 7 lb. (McKeown & Record (1952)). Therefore, this retardation in multiple pregnancies occurs earlier in triplets than in twins.

The foetal growth retardation occuring in multiple pregnancies could be the result of a vascular as well as a nutritional cause. Maybe, both factors play a part.

A rarer cause of foetal growth retardation in twin pregnancies is the intrauterine transfusion syndrome where blood passes from one twin to the other causing one to be anaemic and small, and the other well developed.

Foetal weight varies with the different races. Socio-economic factors must play an important role here. We also know that the average foetal weight increases with parity and decreases with age (after 30). The above factors suggest that maternal environment is another very important factor influencing foetal growth.

Although the genetic potential plays an important role in deciding adult height, foetal growth is not much influenced. But congenital disorders, both chromosomal and others, can influence foetal growth. We know that in the congenital Rubella Syndrome, growth retardation is present.

In conclusion, it is obvious from the clinical and experimental studies done on foetal growth retardation, that the etiology must be multifactorial. But because of these studies, one is now able to recognise these babies, sometimes predict their birth and so be able to give them the special care and attention they need. This may help reduce the high perinatal mortality that occurs in this group. But there is still a lot to be known before one can prevent the occurence of "small for date babies."

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