Nutrient stores in human foetal livers

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1. Liver composition and hepatic nutrient stores in foetuses born to mothers belonging to a low socio-economic group of the population were determined.

2. The contribution by the liver to body-weight and the concentration of water and nitrogen in liver at different gestational ages were relatively constant.

3. Total iron and copper contents of the liver were in the normal reported range but the ferritin content was considerably lower in the present investigation.

4. Hepatic stores of vitamin A, vitamin B_{12} and folate were lower than the values that have been reported elsewhere.

5. It is suggested that inadequate stores of iron, vitamin A, vitamin B_{12} and folate in these infants may predispose them to the early development of some deficiency diseases.

The liver is known to be a major site where many nutrients such as iron, vitamin A, vitamin B_{12} and folate are stored. Most of these nutrients are transferred from the mother to the foetus by a process of active transport across the placenta. Studies on experimental animals have demonstrated that the extent of hepatic stores in the young may be considerably influenced by the level of dietary intake of these nutrients by the mother during pregnancy. Such information in the human is scanty.

Among the important nutritional problems seen in India in older infants and young children belonging to the poor sections of the population are deficiency of vitamin A and Fe-deficiency anaemia. Megaloblastic anaemia in infants due to vitamin B_{12} and folate deficiency has also been reported. The results of several studies have shown that the concentration of most vitamins in the breast milk of poor Indian mothers is considerably lower than in that of well-nourished mothers of the West (Belavady, 1963). While this could be an important cause of the widespread prevalence of signs of vitamin deficiencies in the community, it is also likely that the low hepatic stores with which the infants are born has a contributory role. An investigation was therefore undertaken to determine the hepatic stores of vitamin A, vitamin B_{12}, folate, Fe and copper in the foetuses whose body composition was reported earlier (Apte & Iyengar, 1972).

EXPERIMENTAL

Livers of thirty-eight foetuses, whose body composition was studied, were removed, washed and weighed. Samples of 1–3 g fresh liver were taken from the right lobe for determination of non-haem Fe, vitamin A, vitamin B_{12} and folate. The remaining liver was cut into small pieces in a Petri dish and dried in a hot-air oven at 90° for 8–10 d; samples of the dried powder were used for determination of nitrogen, Fe and Cu contents.

Analytical methods

Non-haem Fe was determined by Kaldor's (1954) method, vitamin A by the spectrophotometric method and folate and vitamin B_{12} by microbiological assay with *Lactobacillus casei* and *Euglena gracilis* respectively.

Total N was determined by the micro-Kjeldhal method, total inorganic Fe was estimated by Wong's (1928) thiocyanate method and Cu by the method described by Gubler, Lahey, Ashenbruker, Cartwright & Wintrobe (1952).

RESULTS

The body-weights and liver weights of the foetuses were found to increase with advancing gestational age. However, the liver weight expressed as a percentage of body-weight was relatively constant at about 4·4% irrespective of gestational age (Table 1).

Table 1. *Nitrogen and water in human foetal liver*

(Mean values with their standard errors; figures in parentheses are the numbers of livers analysed)

		Liver wt			
Age of foetus (weeks)	Body-wt (g)	g	Liver wt as % of body-wt	Water content (g per 100 g liver)	N content (g per 100 g liver)
< 28 (7)	733·4 ± 120·04	38·01 ± 12·000	4·76 ± 0·651	81·91 ± 0·706	1·89 ± 0·083
28–32 (10)	1225·7 ± 64·07	53·05 ± 3·143	4·37 ± 0·124	80·86 ± 0·956	1·95 ± 0·122
33–36 (5)	1454·4 ± 132·55	63·80 ± 5·757	4·38 ± 0·233	83·58 ± 0·387	1·80 ± 0·030
37–40:					
Body-wt < 2250 g (4)	1850·0 ± 162·02	84·75 ± 9·499	4·23 ± 0·269	81·30 ± 0·794	2·08 ± 0·029
Body-wt < 2250 g (12)	2635·3 ± 97·90	121·42 ± 10·611	4·43 ± 0·242	81·01 ± 0·584	1·96 ± 0·074

The concentration of water and N in the livers studied also remained relatively constant during intra-uterine growth (Table 1). The total Fe content of the livers increased with advancing gestation. However, when related either to body-weight or to liver weight or expressed as a proportion of total body Fe, the liver Fe remained relatively constant at all gestational ages. Non-haem Fe, the storage form of Fe (ferritin and haemosiderin) followed the same pattern as that of total Fe. The total and non-haem Fe content of the liver and the proportion of non-haem Fe to total Fe were significantly higher in full-term infants weighing more than 2250 g than in those weighing less than 2250 g (Table 2).

The total Cu content of the liver increased with advancing gestation, but when expressed per g liver remained relatively constant at all gestational ages (Table 2).

The mean vitamin A concentration in the liver ranged between 16·2 and 30·6 μg/g at different gestational periods. However, at the same gestational age wide variations were seen between foetuses in the concentration of vitamin A. Fourteen of twenty-eight livers had concentrations below 10 μg/g.

Table 2. *Iron and copper in human foetal liver*

(Mean values with their standard errors; figures in parentheses are the numbers of livers analysed)

Age of foetus (weeks)	Total iron in liver (mg)	Fe content		Fe (mg per g of fresh liver)	Total-non-haem Fe (mg)	Non-haem Fe (as % of liver Fe)	Cu content	
		mg/kg body-wt	As % of total body Fe				mg	mg/100 g fresh liver
< 28 (7)	12·8 ± 2·78	15·0 ± 2·01	29·9 ± 3·99	0·31 ± 0·031	6·5 ± 1·98	50·8 ± 12·17	1·5 ± 0·28	4·6 ± 0·55
28–32 (10)	17·2 ± 2·05	14·8 ± 1·75	27·9 ± 3·76	0·33 ± 0·041	8·1 ± 1·94	50·2 ± 7·62	2·1 ± 0·28	3·9 ± 0·46
33–36 (5)	20·2 ± 2·37	14·4 ± 2·21	25·3 ± 3·23	0·29 ± 0·029	8·4 ± 0·60	48·5 ± 4·12	2·2 ± 0·47	3·5 ± 0·69
37–40:								
Body-wt < 2250 g (4)	21·6 ± 3·05	11·7 ± 0·76	21·3 ± 1·63	0·27 ± 0·023	10·3 ± 3·43	48·6 ± 8·53	3·9 ± 0·76	5·9 ± 0·43
Body-wt > 2250 g (12)	48·5 ± 6·61	18·3 ± 2·26	31·5 ± 3·06	0·39 ± 0·045	29·9 ± 6·50	57·9 ± 6·20	5·0 ± 0·53	4·1 ± 0·34

Table 3. *Vitamins in human foetal liver*

(Mean values with their standard errors; figures in parentheses are the numbers of livers analysed)

Age of foetus (weeks)	Vitamin A content		Folate content		Vitamin B_{12} content	
	μg/g	μg	μg/g	μg	ng/g	μg
< 28	20·6 ± 7·23 (6)	1280·0 ± 630·00	1·6 ± 0·49 (8)	96·5 ± 45·56	62·7 ± 16·00 (8)	2·3 ± 0·71
28–32	30·6 ± 12·45 (5)	1445·0 ± 1181·90	2·7 ± 0·70 (6)	95·9 ± 19·00	104·3 ± 17·14 (4)	5·6 ± 1·12
33–36	16·2 ± 6·20 (6)	999·0 ± 445·10	1·5 ± 0·33 (6)	104·6 ± 23·26	85·3 ± 10·08 (5)	6·5 ± 0·95
37–40	20·3 ± 10·40 (12)	1937·0 ± 1041·60	2·4 ± 0·21 (13)	261·7 ± 18·37	80·6 ± 12·15 (10)	8·9 ± 1·32

The mean concentration of folate and vitamin B_{12} in the liver ranged from 1·5 to 2·7 μg/g and from 62·7 to 104·3 ng/g respectively. There appeared to be no correlation between the gestational age on the one hand and the concentration of either vitamin A, folate or vitamin B_{12} on the other (Table 3).

DISCUSSION

The results indicate that the contribution by the liver to body-weight and the concentration of water and N in the liver during different gestational periods were relatively constant. These observations are at variance with those of Widdowson & Dickerson (1960), who reported a progressive fall in water and increase in N content. It is possible that these differences reflect differences in total body composition already reported (Apte & Iyangar, 1972).

The total Fe content of the liver showed wide variation, as reported by Bruckmann & Zondek (1939), Lintzel, Rechenberger & Schairer (1944) and Widdowson & Spray (1951). The values for total liver Fe obtained in the present study are lower than those reported by Bruckmann & Zondek (1939) but higher than that found by Widdowson & Spray (1951) and similar to those reported by Lintzel *et al.* (1944). Liver Fe as a percentage of total body Fe was distinctly higher than that reported by Widdowson & Spray (1951), the proportion being quite constant at various gestational periods. Ferritin, the storage form of Fe in the liver, accounted for 50% of total liver Fe, a value lower by nearly 35% than that reported by Bruckmann & Zondek (1939), indicating reduced Fe stores.

The Cu contents of liver observed in the present investigation are in line with those reported by Bruckmann & Zondek (1939) and Widdowson & Spray (1951).

The vitamin A concentration in liver tended to increase during the early part of the third trimester, followed by a fall as pregnancy advanced, though the changes were not statistically significant. This observation is similar to that of Skurnick, Heikel & Westerberg (1944), who observed an increase in the concentration of vitamin A in the foetal liver in the earlier part of gestation, followed by a fall. The concentrations of vitamin A in full-term foetuses observed in the present study were considerably lower than those reported for foetuses studied in Finland by Skurnick *et al.* (1944), in England by Marrack (1948–9) and in the USA by Lewis, Bodansky & Shapiro (1943). This may be a reflection of deficient intakes of vitamin A by the mothers. It has been reported earlier from these laboratories that the serum concentration of vitamin A in pregnant women belonging to the poor socio-economic group progressively falls with increasing gestation and that at term levels are as low as 60 i.u./100 ml (Venkatachalam, Belavady & Gopalan, 1962). The concentration of vitamin A in blood of infants born to such mothers was found to be rarely above 40 i.u./100 ml.

Reports on the concentration of folic acid in foetal liver are very scanty. This may partly be due to the assumption that water-soluble vitamins cross the placental barrier with relative ease and that a high concentration of the vitamin can be maintained in the foetuses even if concentrations in maternal tissues are low. A recent report on the folate content of foetal liver has indicated that liver folate concentrations per unit weight are more closely related to the weight of the foetus than to the gestational age (Hussain & Wadsworth, 1968). The folate concentration of 2·4 μg/g liver observed at term in the present study is only 50% of the value reported by Hussain & Wadsworth (1968). As with vitamin A, studies carried out at these laboratories have shown that almost 70% of pregnant women during the last trimester have folate levels below 3 ng/ml in serum and below 90 ng/ml in red cells – suggestive of folate deficiency (Iyengar, 1971). The low stores of the vitamin in the foetal livers may therefore be a reflection of the maternal situation.

The mean value for liver stores of vitamin B_{12} was 9 μg, a value considerably lower than that reported by Baker, Jacob, Rajan & Swaminathan (1962) and by Rappazzo, Salami & Hall (1970).

The results obtained in this study therefore suggest that inadequate stores of Fe, vitamin A, folate and vitamin B_{12} with which infants belonging to the poor income groups are born predispose them to diseases associated with these deficiencies.

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