THE TURKISH JOURNAL OF
PEDIATRICS
A HACETTEPE BULLETIN VOLUME 17 / Nos. 1-2 / JAN. - APRIL 1975

Editorial

Fetal Malnutrition and its Consequences

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Only during the last two decades have we been aware of the fact that a relatively large number of low birth weight infants are not preterm. The proportion of low birth weights varies in different countries and communities from less than 6% to more than 15%.[1] Of 24,750 successful pregnancies in a maternity hospital in Ankara, the incidence of low birth weight was 8,7%.[2] In another series of 10,000 successful pregnancies the incidence of low birth weight was 8.4%.[3] In Gruenwald's series of 5,000 deliveries this incidence was about 15%.[4] Considering that in the developing countries and in the poorer segments of the developed countries, more than 50% of the infants of low birth weight are "small-for-dates" rather than preterm, this gives an idea of the magnitude of the problem.

The prevailing view of fetal malnutrition holds that cell replication is impaired in utero. Cell replication, of course, depends on protein synthesis. Protein synthesis requires energy as well as sufficient substrate and essential enzymes.

If fetal malnutrition represents an inadequate supply of nutrients to the developing organism, what role does the mother's nutritional status play in fetal development? In the experimental animal, it seems that fetal growth, as well as the development of specific organs, can be impaired by poor nutrition in the mother, especially in the last half of gestation, by protein deprivation.

The term malnutrition is generally used nowadays to describe as completely as possible the clinical features due either to genetic or environmental conditions. All these conditions are of great importance and interest, and their present clinical descriptions will have an enhanced

importance when their etiological factors are better understood. A number of these factors, including maternal malnutrition, placental insufficiency, and antigenic differences, may produce the syndrome of fetal malnutrition. They are therefore a non-specific indication of fetal malnutrition.[5]

The possible etiological factors related to the mother can be summarized as follows.

1. Social class
2. Illegitimacy
3. Age
4. Maternal parity
5. Maternal height and weight
6. Maternal health
7. Maternal nutrition
8. Urinary tract and other infections
9. Smoking
10. Hypertension and Toxemia

The possible etiological factors related to the fetus are shown below:

1. Sex
2. Congenital abnormalities
3. Infection
4. Intracranial factors
5. Other insults

The placentas of growth-retarded infants have been examined, and there is general agreement on the small size of these. The anatomical characteristics of the placenta in "fetal malnutrition" are summarized by Tremblay, Sybulski and Maughn[6] thus:

1. Small for the time of gestation, being of diminished circumference and thin.
2. Fibrotic in texture.
3. Not infarcted.
4. The cord is small in calibre and has few spirals or none and is limp.
5. No microscopic findings to differentiate it from normal (not confirmed by other workers).

All of the above mentioned factors may influence in one way or another the etiology of fetal malnutrition in the broadest sense, and they are of use in alerting the pediatrician to a population at risk, requiring extra attention and often special management. However, for the purpose of studying mechanisms and defining cellular changes, it is obvious that the group is too large. Removing all infants with congenital malformations and known etiologies such as intrauterine infection and chromosomal anomalies from consideration, leaves us with a homogeneous subpopulation who are small at birth, for additional attention.

An important biochemical marker of fetal malnutrition is that "metabolic changes in the leukocyte may be an index of similar changes in the cells of other organs". Studies by Metcoff[7] point out clearly that leukocytes isolated from umbilical cord blood of underweight newborn infants show biochemical changes resembling those found in leukocytes from older children with severe PCM. They also had reduced activities of the energy-generating enzymes pyruvate kinase and adenylate kinase. The leukocytes of mothers delivering these babies possessed the same defects. Moreover, the enzyme activity in the leukocytes of these mothers and their babies differed from those of mothers who delivered premature or full-term babies whose growth was appropriate for their gestational age. The cell size of the leukocyte was increased in the cord blood of babies with fetal malnutrition. Their leukocytes were also similarly increased. These studies suggest that incomplete fetal growth in utero reflects some process occurring in the mother that is manifest in her peripheral blood leukocytes. If this is so, the metabolism of the maternal leukocyte during pregnancy may be a biochemical indicator for fetal malnutrition.

Consequences of Fetal Malnutrition

Far more important than impaired physical growth secondary to fetal malnutrition is indeed impairment of brain development and therefore retarded mental capacity. Medovy[8] reports that "sometimes cell number, sometimes cell size and sometimes both are affected in fetal malnutrition, depending on the agent involved." Since DNA indicates nuclear number in diploid cells, reduced DNA content in an organ can be taken as evidence of decreased cell numbers resulting from impaired cell replication. Malnutrition could interfere with cell replication in brain tissues, thus reducing the content of DNA and lipids, and since enzymes are proteins one would anticipate that impairment of protein synthesis would be associated with impaired enzymes synthesis, as in the case of protein calorie malnutrition.[9] Follow-up studies of the

mental growth and intellectual capabilities of fetally malnourished newborn infants should throw light on this important subject.

Could fetal malnutrition be responsible for a number of non-hereditary metabolic diseases of the newborn? We know only too well that the incidence of urinary calculi is fairly high in countries with low standards of living, particularly where there is a hot dry climate. The majority of these patients are under 5 years of age and from the lower socio-economic classes, with a history of poor animal protein and vitamin intake. But what about urinary lithiasis in the very young? In the last few years at least 5 cases of congenital urinary lithiasis have been observed at Hacettepe Children's Hospital, in whom no idiopathic hypercalciuria, oxaluria, cystinuria or other metabolic causes could be established. Can this be secondary to fetal malnutrition?

All these questions indicate that we are nearer to the beginning than the end of this story.

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