PERINATAL CIRCUMSTANCES IN DAR ES SALAAM, TANZANIA

STUDIES ON SOME PHYSIOLOGICAL ASPECTS IN THE TROPICS

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"How is it that poor men's wives, who have no cold fowl or port wine on which to be coshered up, nurse their children without difficulty, whereas the wives of rich men, who eat and drink everything that is good, cannot do so, we will for the present leave to the doctors and mothers to settle between them".

Anthony Trollope (1847)

to Maria, Rinske
and Jan Doede

CONTENTS

INTRODUCTION

The effect of mild to moderate maternal undernutrition on intrauterine and subsequent growth and development in man remains largely unknown. Little is known of the physiological and particularly the metabolic aspects of the maternal/fetal relationship under these circumstances. The great difficulty is to construct an experimental situation suitable for investigation in man. In animal the construction of an experiment is simpler and as a result much of our recent knowledge is mainly derived from animal studies. These have shown that maternal nutritional restriction during pregnancy may reduce the size of the offspring and may retard subsequent postnatal growth. Morphological and histochemical alterations of fetal organs have been documented while the rate of cell multiplication in brain is diminished.

Food restriction in man studied during wartime, resulted in lower birth weight, although the reduction was not more than 100-200 grams on the average. No increase was found in perinatal death, nor could any association be observed with premature delivery. In an evaluation of the influence of restricted maternal nutrition on human development of the offspring 20 years after the Dutch hunger winter 1944-1945, no deleterious effect, could be demonstrated. "We must ask ourselves how important it is, in terms of future performance, to weigh a few hundred grams more or less at birth" (Béhar, 1975).

Maternal undernutrition prevails in the developing countries and thus it is generally only in these countries that the opportunity arises to study the effects of a limited dietary intake during pregnancy and early infancy on the mother and her offspring. Community surveys carried out in Tanzania have shown widespread undernutrition among pregnant women when compared to dietary allowances recommended by FAO/WHO (1973).

In this thesis our own and collaborative studies on some physiological and metabolic characteristics are reported for the Tanzanian pregnant woman and her offspring during the last stage of pregnancy and are presented in *chapter one* to *chapter five*. These data are related to studies from Western countries in an attempt to define the possible effects of environmental circumstances in which these babies are born and whether they contribute to the future health of the children.

The determination of anthropometric standards, as given in *chapter one*, for the neonatal population of Dar es Salaam, Tanzania, was required in order to quantitate fetal growth and to enable us to assess abnormal fetal maturation or growth for that particular society. Local *intrauterine growth* curves for weight, crown-heel length and head circumference are presented together with curves of weight/length, weight/head circumference and weight/length x head circumference ratios in *chapter one, section A*. The high incidence of low birth weight infants among the population studied, prompted us to evaluate the factors associated with low birth weight. The results of this study are described in *chapter one, section B*.

Two studies on *protein* metabolism are presented in *chapter two*. In order to gain some knowledge of protein metabolism during pregnancy in the mother and fetus under so called "unfavourable" nutritional conditions, we studied the concentrations of essential and non-essential amino acids in cord blood of normal term Tanzanian infants and in the serum of their mothers immediately after delivery. The results of these studies are compared with Western standards and presented in *chapter two, section A*. Since the fetus synthesises its proteins, with the exception of IgG, from amino acids which have been transferred across the placenta, we were interested in the levels of total protein, albumin, IgG, IgM and IgA in paired Tanzanian maternal/fetal blood samples among preterm, small-for-dates and term infants. In addition this information could be of importance to assess the humoral immune status of the Tanzanian newborn infant, who will most likely be exposed to numerous infections postnatally. Results of these studies are presented in *chapter two*, *section B*.

Attempts to gain information on the factors influencing *lipid metabolism* during pregnancy, fetal life and postnatal life resulted in the two studies reported in *chapter three*. In *section A* of this chapter, serum lipids, total cholesterol and triglyceride in maternal/cord blood pairs are presented from infants of normal and low birth weight in Dar es Salaam, Tanzania. In *section B (chapter three)* the results of a study on the changes in fatty-acid composition of body fat before and after birth are presented, together with the fatty-acid composition of breast milk fat in a sample of the population of Dar es Salaam.

A study on body weight changes during pregnancy in Tanzanian women is presented in *chapter four*.

In a study presented in *chapter five* emphasis was placed on the collection of anthropometric data of breast-fed Tanzanian infants. These postnatal standards and those obtained "antenatally" (*chapter one*, *section A*) were combined to construct a perinatal growth chart. The same study summarises some of the metabolic characteristics of the mother and her normal term infant immediately after delivery. These data are related to studies from Western countries. The references are given at the end of each study. A summary in English and Dutch is presented at the end of this thesis.

N.B. In this text the Caucasian population pertains to the white race with their "Western" feeding habits.

Chapter one

STUDIES ON INTRAUTERINE GROWTH

A. *Intrauterine growth of liveborn Tanzanian infants**

Local standards are presented of intrauterine growth curves for weight, crown-heel length and head circumference, together with curves for body measurement ratios of weight/length, weight/head circumference and weight/length x head circumference for the population of Dar es Salaam, Tanzania. The incidence of low birth weight infants (< 2500 g) found in this study was 15%. The effects of reduced fetal growth on anthropometric measurements are discussed. A comparison is made with similar growth standards composed for a community with a completely different socioeconomic and nutritional status (Usher and McLean, 1969). Results show that from 28 to 34 weeks of gestation, weight gain was reduced for Tanzanian fetuses, whereas length and head circumference were relatively less affected. However, the velocity of growth seems to be relatively rapid from 34 to 38 weeks of gestation. Details, inclusive the references, are described in paper 1, which is reprinted in the addendum.

* These studies were done in collaboration with R.L. Mbise and have been published in Tropical and Geographical Medicine, 31: 7-19, 1979.

B. *Factors associated with low birth weight in the population of Dar es Salaam, Tanzania**

This study was undertaken to evaluate the environmental, fetal and maternal factors associated with the birth of a low birth weight infant. The incidence of low birth weight was higher among infants belonging to parents of a low socio-economic status and among female infants. Primiparity, short stature of the mother, a multiple pregnancy, toxaemia of pregnancy were some of the factors influencing the growth velocity of the fetus, leading to an increased incidence of small-for-dates infants. Low maternal age and antepartum hemorrhage mainly affected the duration of gestation, which led to a preponderance of infants borm preterm. However, in 66% of the mothers with low birth weight infants no associated maternal complication of the pregnancy could be detected. Details and references of this study, reprinted from Tropical and Geographical Medicine, are presented in paper 2 in the addendum.

* These studies were done in collaboration with R.L. Mbise and have been published in Tropical and Geographical Medicine, 31: 21-32, 1979.

Chapter two

STUDIES ON PROTEIN METABOLISM

A. *Free amino acid levels of mother and child immediately after delivery in Dar es Salaam, Tanzania**

Although animal experiments have shown that undernutrition of pregnant animals may produce growth retardation of the offspring (Widdowson, 1968; Widdowson, 1971; Winick, 1975) and that undernutrition during the stage of intensive cell multiplication causes an irreparable deficit in cell population of organs (Winick, 1971), the effect of undernutrition on the fetus during human pregnancy is still uncertain (Smith, 1947, Thomson, 1959; Stein *et al*, 1975).

Information on the contribution of amino acids to the supply of nitrogen to the human fetus under different nutritional conditions is limited to the period during or just after delivery due to the technical and ethical problems involved (Pohlandt, 1978; Hayashi *et al*, 1978).

Although the intake of energy and proteins during pregnancy in Tanzania has been found to be lower (Maletnlema and Bavu, 1971) than the recommendations of WHO/FAO (1973), the speed of growth of the fetus under these circumstances has been shown to be more than adequate during the last stage of pregnancy (Boersma and Mbise, 1979).

The object of this paper is to present data on the concentrations of essential and non-essential amino acids in cord blood of normal term Tanzanian infants and in venous blood of their mothers immediately after delivery. This could provide information about certain aspects of the

*These studies were done in collaboration with W. Blom and A.W. Massawe and have been accepted for publication in Biology of the Neonate.

metabolism of mother and fetus under these "unfavourable" nutritional conditions. These data were compared with values reported from Sweden (Lindblad and Baldesten, 1967).

METHODS

Age, marital status and past obstetric history were recorded from 300 pregnant Tanzanian women who were delivered in one of the public hospitals in Dar es Salaam, Tanzania. For details regarding local health facilities, population and geographical circumstances see previous studies (Boersma and Mbise, 1979 and Mbise and Boersma, 1979).

Standing height of mothers was taken by a non stretchable tape measure to the nearest 0.5 cm. Just after delivery anthropometric measurements were taken from the newborn infant. Gestational age of the newborn infant was calculated using the method of Dubowitz *et al* (1970). At delivery the umbilical cord was carefully cleaned before collection of approximately 10 ml of whole cord blood. Milking of the cord was avoided as it causes hemolysis. Immediately after birth 5 ml of venous blood was taken from the cubital vein of the mother. Both samples were left to clot at room temperature ($\pm$ 25°C) for approximately half an hour. Serum was than separated by centrifugation and stored and transported at -20°C until analysed.

From the whole population 20 randomly selected mothers of term appropriate for gestational age infants* and their offspring were studied in more detail. Only normotensive, apparently healthy mothers without any clinical deficiency symptoms were included. The urine of these mothers was negative for protein and glucose and a thick blood smear was negative for malaria. The mean $\pm$ S.D. and range of various anthropometric data and total proteins of these 20 mothers and their offspring are presented in *Table I*.

*Term appropriate for gestational age is defined by an infant who is born within 38-42 weeks of gestation and whose birth weight fell within the range of $\pm$ 1 SD for gestational age, using the local standards (Boersma and Mbise, 1979).

Table I. Mean $\pm$ SD and range of various anthropometric and clinical data together with total proteins of the 20 mothers and their appropriate for gestational age infants studied.

Data	*Mean*	*SD*	*Range*
Mothers			
Age, years	25.1	4.7	17-36
Height, cm	153.9	7.5	140-165
Parity	3.5	1.8	1-7
Systolic blood pressure, mm Hg	115	6.9	110-130
Diastolic blood pressure, mm Hg	76	5.0	70-80
Total protein, g/100 ml	6.6	0.7	5.7-7.9
Infants			
Weight, g	3,051	292	2,670-3,680
Length, cm	49.2	1.3	47-52
Head circumference, cm	34.3	1.3	32-37
Gestational age, weeks	39.8	0.7	38-41
Total protein, g/100 ml	6.9	0.5	6.0-7.8

The birth weight, crown-heel length and head circumference of these infants (11 males and 9 females) are plotted on the local intra-uterine growth chart (Boersma and Mbise, 1979) as shown in *Figure 1*. All infants were born by normal uneventful crown vaginal delivery after an uncomplicated pregnancy. The Apgar score at one-minute after birth was more than 8 in all infants included in this study. Quantitation of amino acids was performed on an automatic analyser (Technicon TSM I) using the two column method of Spackman *et al* (1958) at the laboratories of Sophia Children's Hospital, Rotterdam, The Netherlands. Serum was deproteinised by adding 1 volume of 3% sulfosalicylic acid. As an internal standard nor-leucine was added to the serum samples. The samples were discarded if hemolysis had occurred.

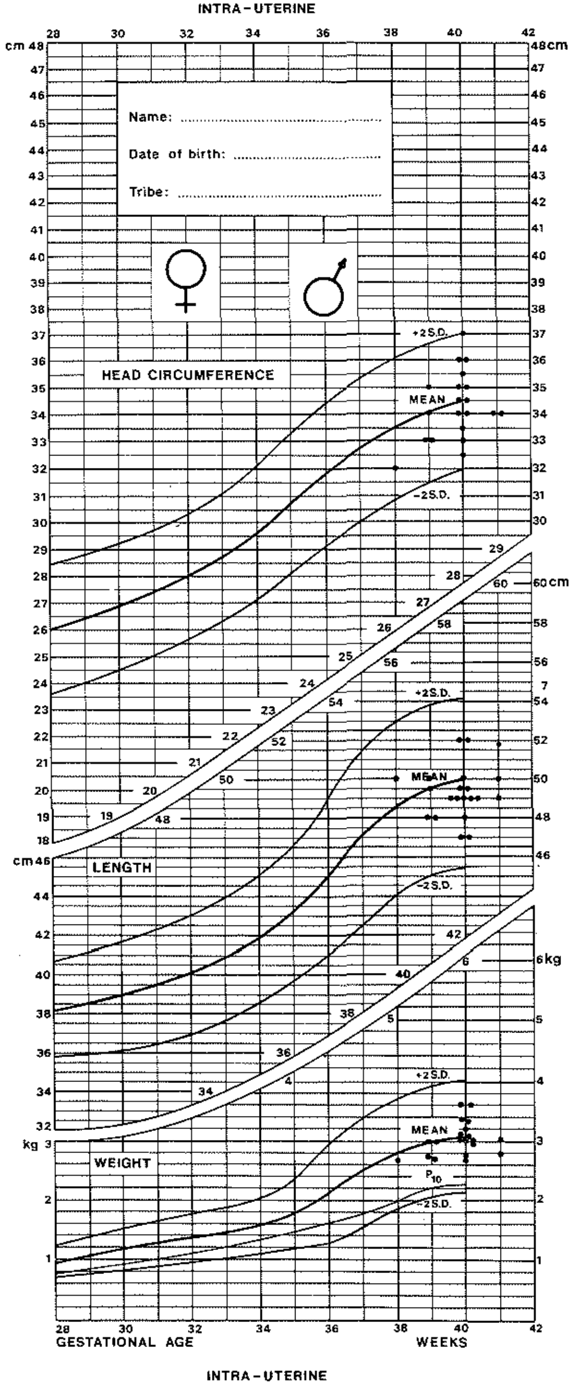

Fig. 1. Weight, length and head circumference at birth of the infants studied plotted on the local intra-uterine growth chart for both sexes (Boersma and Mbise, 1979).

RESULTS

The mean ± S.D. for the individual amino acids in maternal serum of Tanzanian mothers at delivery is compared with plasma values from Swedish mothers (Lindblad and Baldesten, 1967) in *Table II*.

Table II. Free amino acid concentrations (µmol/l) in maternal serum, immediately after delivery are compared to those of maternal plasma for Sweden (Lindblad and Baldesten, 1967).

	Tanzania			*Sweden*		
	*n**	*mean*	*SD*	*n**	*mean*	*SD*
Essential amino acids						
Lysine	20	219	47	10	99	12
Threonine	20	166	32	3	124	29
Valine	20	170	27	10	121	18
Leucine	20	188	40	10	64	17
Isoleucine	20	83	13	10	34	8
Methionine	19	trace	-	9	8	3
Phenylalanine	20	123	22	10	36	7
Non-essential amino acids						
Taurine	20	66	32	10	43	11
Histidine	20	108	30	4	79	8
Arginine	17	169	62	4	23	8
Alanine	20	510	96	10	339	67
Proline	20	215	80	10	115	32
Glycine	20	307	69	10	94	35
Serine	20	242	42	3	73	24
Ornithine	18	178	59	10	29	11
Tyrosine	20	68	13	10	26	5

**n* = Number of cases where the amino acid was determined successfully.

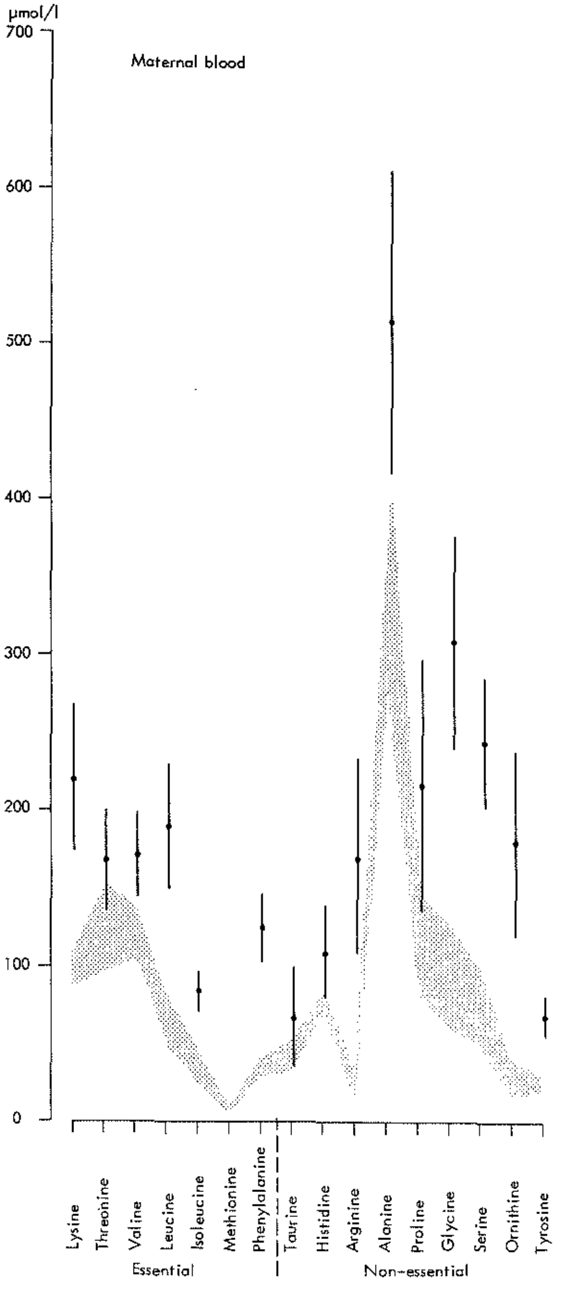

Fig. 2. Mean and ± SD for the individual amino acids of maternal serum immediately after delivery as compared with those of maternal plasma for Sweden (dotted area).

From these data an "aminogram" is composed as shown in *Figure 2.* By addition of all amino acid values which both Lindblad and we had studied, it was possible to determine a mean total concentration, which could be used for comparitive purposes. This total concentration was 1307 μmol/l in Swedish mothers and 2822 μmol/l in Tanzanian mothers at delivery. All amino acid levels measured were higher in Tanzanian mothers.

Individual amino acid levels (mean ± S.D.) in cord blood in Tanzanian term appropriate for gestational age infants are compared with those from Swedish infants (Lindblad and Baldesten, 1967) as shown in *Table III.* The ratio between the cord level and that of maternal venous blood was calculated in each pair and is presented in *Table III*, together with those obtained from Sweden (Lindblad and Baldesten, 1967).

Mean amino acid levels ± S.D. are shown graphically in *Figure 3.* Using the same method of additional total amino acid concentration as was done in the mothers, the total concentrations in cord blood for Tanzanian and Swedish infants were 3260 μmol/l and 2519 μmol/l respectively. A uniform but slight increase of all amino acids was found in Tanzanian infants with the exception of lysine, threonine, valine and histidine, whose mean values fell within the ± 1 S.D. range of Swedish cord blood samples. The mean value of taurine was lower than the - 1 S.D. for Sweden.

The mean feto/maternal ratio was much lower compared with the Swedish survey for the same amino acids (average 1.15 and 2.15 respectively). The wide range of ratios for the different amino acids shown in Sweden (1.3 - 3.4) was not found in Tanzania (0.6 - 1.6).

Table III. Free amino acid concentrations (μmol/l) in whole cord serum in comparison to those of cord vein plasma for Sweden (Lindblad and Baldesten, 1967) together with mean cord/maternal ratios for the individual amino acids in both countries.

	Tanzania				*Sweden*			
	*n**	*mean*	*SD*	*cord/ maternal ratio*	*n**	*mean*	*SD*	*cord/ maternal ratio*
Essential amino acids								
Lysine	20	347	111	1.6	10	318	33	3.3
Threonine	20	221	62	1.3	3	234	26	1.9
Valine	20	211	50	1.2	10	224	28	1.9
Leucine	20	165	42	0.9	10	118	33	1.9
Isoleucine	20	90	21	1.1	10	62	12	1.9
Methionine	19	50	18	-	10	18	6	2.4
Phenylalanine	20	109	28	0.9	10	67	10	1.9
Non-essential amino acids								
Taurine	20	107	81	1.6	10	181	58	1.7
Histidine	20	110	31	1.0	4	112	17	1.5
Arginine	11	98	42	0.6	9	65	30	3.4
Alanine	20	588	171	1.2	10	441	75	1.3
Proline	20	230	53	1.1	10	160	28	1.5
Glycine	20	366	80	1.2	10	239	32	2.5
Serine	20	226	69	0.9	3	130	3	1.9
Ornithine	19	261	69	1.5	9	89	20	3.3
Tyrosine	20	81	20	1.2	10	61	14	2.4

* *n* = Number of cases where the amino acid was determined successfully.

The aminogram of the mean ± S.D. values in whole cord blood serum is compared to that of maternal venous serum for Tanzania in *Figure 4*. A mean cord blood level above

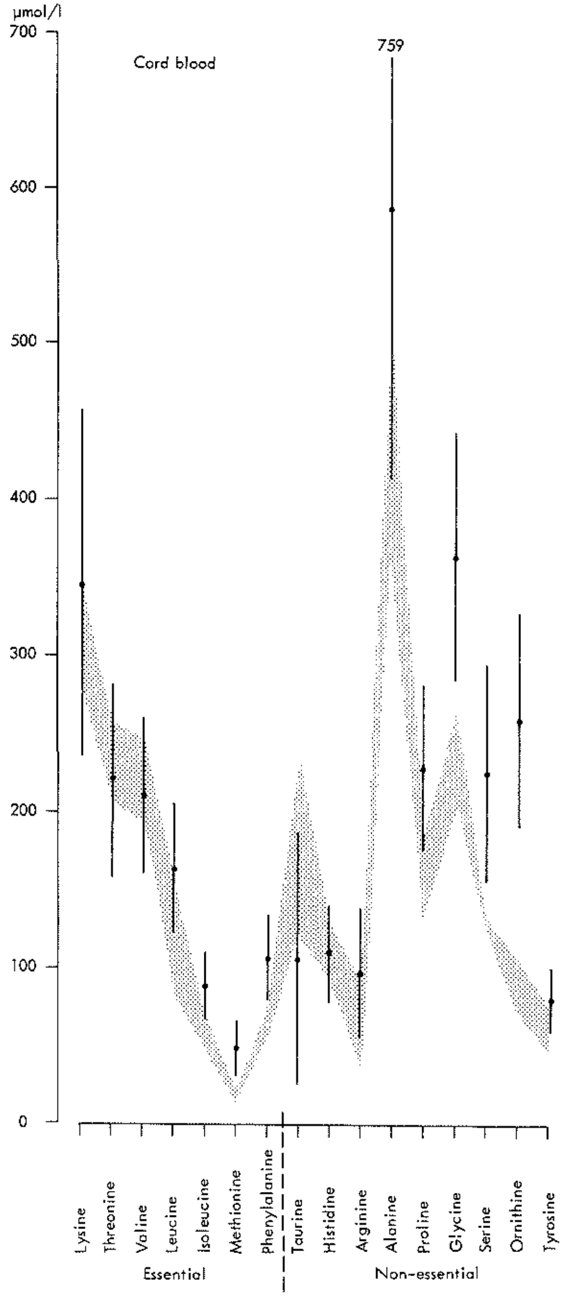

Fig. 3. Mean and $\pm$ SD for the individual amino acids in whole cord serum as compared with those of venous cord plasma for Sweden (dotted area).

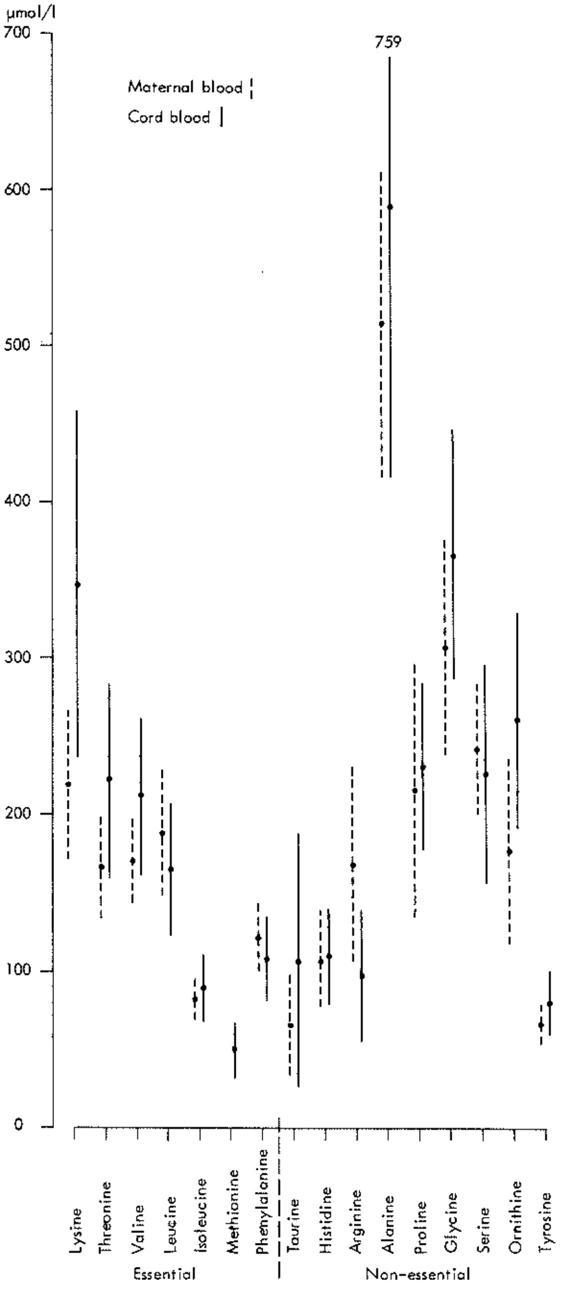

Fig. 4. Mean and ± SD for the individual amino acids of maternal venous serum (dotted lines) as compared with those of whole cord serum (solid lines).

1 S.D. of that in maternal serum was found for lysine, threonine, valine, taurine and ornithine, whereas mean values of leucine, isoleucine, phenylalanine, histidine, alanine, proline, glycine, serine and tyrosine fell within the $\pm$ 1 S.D. of maternal serum level at delivery. A lower mean cord blood level was only found for arginine.

DISCUSSION

Pitfalls in the interpretation of quantitative data on amino acids are well documented by Scriver and Rosenberg (1973), Lindblad (1970) and Perry and Hansen (1969). At the time of amino acid analysis the peaks of glutamic acid and asparagine overlapped in most of the chromatograms. Glutamine was usually decreased due to decomposition during storage of the sera. Cystine was hardly detectable because cystine has a tendency to be bound to serum albumin. Tryptophan was destroyed during the deproteinising procedure at lower pH. Technical difficulties during the process of analysis resulted in a slightly reduced number of determinations of ornithine and arginine levels. Methionine levels in most maternal samples were hardly detectable.

We should like to emphasise that amino acid analysis was performed in serum and not in heparinised plasma samples. But most authors (Scriver and Rosenberg, 1973) consider serum and plasma amino acid values comparable, if no hemolysis has occurred.

Two assumptions were made in an attempt to relate the levels of individual amino acids in the venous blood of the mother and cord blood of the infant with those of other studies. Firstly it was assumed that the methods used would make a comparison with other studies justified. Secondly it was assumed that *mixed* cord blood amino acid levels were comparable with those studies of *venous* cord blood values of other studies. The last assumption is probably valid since the arterio-venous differences are usually less than 6 percent and frequently no differences can be detected with modern methods (Lindblad, 1979). Regarding the first assumption: the measurements of the individual amino acids by Lindblad and Baldesten (1967), Ghadimi and Pecora (1964) and Young and Prenton (1969) in venous cord blood in relation to the individual amino acid levels in normal mothers just after delivery have shown how wide the normal range of variation is. Therefore our values in comparison with other studies have to be interpreted with caution. In this study histidine, cystine, tyrosine and taurine were regarded as non-essential, although some studies have demonstrated that these amino acids may be essential in utero (Snyderman *et al*, 1963; Sturman *et al*, 1970; Jakubovic, 1971; Gaull, 1978).

Various clinical conditions may influence the amino acid pool, so that emphasis was laid on careful standardisation of the population studied. This was done with the help of the local intrauterine growth standards obtained in a previous study (Boersma and Mbise, 1979).

The daily energy intake of a comparable group of pregnant women in Tanzania, gave an estimate of 1845 calories (equivalent to 7.7 M J) and a mean protein intake of 32 gram of reference protein (Maletnlema and Bavu, 1971). These values are to be compared with the recommended basic requirements of 2300 Calories (=9.6 M J) and 38 gram of reference protein per day (FAO/WHO, 1973).

Many studies on free amino acid levels have been done in infants, children and adults from different countries and races on different diets. There is no evidence for any racial difference in amino acid levels in children of the same age (Lindblad, 1970). However, information is limited on amino acid levels in maternal and cord blood at the time of delivery in the developing countries. When compared with Swedish standards Lindblad *et al* (1969) found a general tendency towards increased amino acid levels (especially the non-essential amino acids glycine and ornithine) in 10 mothers of low socio-economic class in West Pakistan who had a low protein intake but who were without clinical deficiency symptoms (except anaemia). He also found a slight but uniform increase in amino acids in cord blood (especially glycine and proline) resulting in reduced feto/maternal gradient. The reduction in the ratio was because of the higher maternal denominator. A similar tendency was observed in our study, although the maternal amino acid levels were generally even higher. Our results were consistent with those found in West Pakistan on cord blood (Lindblad *et al*, 1969). The even higher maternal amino acid concentration in Tanzania resulted in still lower feto/maternal ratios. However, it should be mentioned that the population in the study from West Pakistan had a gestation between 37 and 40 weeks with birth weights between 1700 and 2800 gram, in contrast to those in our study. When we compare our results with those of a middle class group of mothers in West Pakistan who were on a "balanced" diet according to Western standards (Lindblad *et al*, 1969), higher maternal values were found for almost all amino acids except methionine, valine, taurine and histidine. In cord blood, however, most amino acid concentrations fell within the range $\pm$ 1 S.D. from the mean except ornithine, proline and phenylalanine, whose mean values were higher and taurine whose value was lower in Tanzanian samples.

The reduction of the feto/maternal gradient by a relative elevation of the maternal level was also shown in West Pakistan when compared to Swedish standards, however, not to the extent as was observed in Tanzania.

A reduction of the feto/maternal ratio by an elevation of the maternal level was reported in pathological conditions like toxaemia of pregnancy (Crumpler *et al*, 1950), hypertensive women giving birth to underweight infants (Lindblad and Zetterström, 1968) and in conditions when the cord was around the neck of the fetus (Clemetson and Churchman, 1954). We do not know whether under various *"unfavourable" conditions* compensatory mechanisms exist to ensure an adequate supply from the mother to the fetus.

Studies on animals have shown that the passage of amino acids across the placental membrane is influenced by the maternal amino acid concentrations (especially for the branched chain amino acids leucine, isoleucine and valine) but is probably influenced to a greater extent by the maternal blood flow (Hill and Young, 1973). It is not known whether the same mechanisms apply to the human placenta and under conditions of fluctuating uterine and umbilical blood flow.

The controversial results obtained by using free amino acid levels in the early detection of malnutrition has led to the use of the glycine/valine quotient as a way to detect early protein undernutrition in pregnancy and in small-for-dates infants at birth (Lindblad, 1970). This was born from the concept that experimental protein undernutrition and the clinical syndromes of kwashiorkor and marasmus would increase this ratio to more than one. From this it would be expected that glycine/valine ratios would be more than one. This was indeed so: 1.8 and 1.7 respectively in our study. However, it should be noted that in mothers neither clinical nor biochemical studies seem to support evidence of maternal protein undernutrition in the last stage of pregnancy. In fact slightly higher albumin levels were found than those found in more privileged countries. Subsequently, although born with a weight of approximately 500 gram below the Western standards (which can to a certain extent be explained by the difference in height of the mothers) no strong evidence can be brought forward to suggest poor well-being of the fetus in the last stage of pregnancy in Tanzania. On the contrary, as shown in a previous study (Boersma and Mbise, 1979), from 34 to 38 weeks gestation, there is an increased speed of growth with regard to fetal weight, crown-heel length and head circumference when compared to Western standards (Usher and McLean, 1969). At birth higher total protein and albumin values were found in Tanzanian babies than those given for Western babies (Schultze and Heremans, 1966). This suggests that adequate protein synthesis has occurred from sources transferred from the mother to the fetus. Therefore, it seems that the glycine/valine index cannot be used either in pregnancy or in the newborn infant to discriminate early protein undernutrition. Studies have shown that an increased glycine/valine ratio also exists in conditions of prolonged fasting (Ghisolfi *et al*, 1978).

It is unlikely that the markedly elevated maternal amino acid concentrations in our study can be explained by the lesser increase in vascular and extracellular volume as can be estimated from the poor weight gain of the mothers during pregnancy when compared to those in more privileged societies (to be published). Unfortunately we do not have information about the urinary excretion of amino acids in our population.

We do not know whether, under "basal" nutritional conditions, the increased maternal amino acid levels, leading to a reduced placental gradient, could be one of the compensatory mechanisms to maintain an adequate supply to the fetus. The most important regulatory mechanisms for adequate fetal growth in man under unfavourable nutritional conditions are still unknown.

On the other hand there is some evidence that the advantage of a greater birth weight as found in the more prosperous countries, has been overemphasised.

SUMMARY

The pattern of the free serum amino acids was analysed in 20 healthy mothers immediately after delivery and in cord blood from their term, appropriate for gestational age, infants.

Amino acid concentrations were higher in Tanzanian women when compared with Swedish standards, whereas slightly higher or similar values were found in cord blood. Thus there is a marked reduction of the feto/maternal ratio for the individual amino acids in Tanzania.

It might be that under basal nutritional conditions the reduced feto/maternal gradient could be one of the compensatory mechanism to ensure an adequate supply of amino acids to the human fetus.

The validity of the glycine/valine index in recognizing early protein malnutrition in pregnant women and their offspring or in small-for-dates infants is disputed.

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B. *Serum immunoglobulins IgG, IgM and IgA in maternal/cord blood pairs from infants of normal and low birth weight in Dar es Salaam, Tanzania**

The incidence of low birth weight (<2500 g) in Tanzania has been shown to be high (15%) when compared with Western countries (6-7%) (Mbise and Boersma, 1979). The high incidence of infections in the underdeveloped countries has been correlated with unfavourable conditions for intrauterine growth of the fetus (Chandra, 1975), though in an industrialised country such a correlationship could not be demonstrated (Sever, 1975).

Although some authors (Peel and van Hoof, 1948; Garnham, 1949; Bruce-Chwatt, 1952; Kortman, 1972) were unable to demonstrate a significant correlation between malaria during pregnancy and neonatal mortality, the importance of malaria prophylaxis for the prevention of severe maternal anaemia and fetal loss (as reviewed by Kortman, 1972) has led to its wide spread use during pregnancy in endemic areas. Why in the majority of cases a healthy child is born in spite of severe placental malaria infection (Kortman, 1972) remains unsolved.

The aim of this study was to obtain more information on the development of humoral immune status (IgG, IgM and IgA) during fetal life in relation to that of the maternal status in an environment with completely different socio-economic and nutritional conditions than in Western countries.

IgM and IgA, unlike IgG, are synthesised by the fetus, which make them relevant for the assessment of development of the humoral immune status of the newborn infant.

In the Tanzanian population which we studied, the IgG, IgM and IgA levels were determined in maternal and cord blood of term and preterm appropriate for gestational age

* These studies have been accepted for publication in Archives of Disease in Childhood.

and small-for-dates infants immediately after delivery. These data were compared with results from similar studies in Western countries.

Definitions and abbreviations

Term appropriate for gestational age infant (term A.G.A.) - one who is born within 38-42 weeks of gestation and whose birth weight is within ± 1 S.D. from the mean for that particular gestational age using the local standards (Boersma and Mbise, 1979), as shown in *Figure 1.*

Preterm appropriate for gestational age infant (preterm A.G.A.) - one who is born before 37 completed weeks of gestation and whose birth weight is within the mean ± 1 S.D. for the gestational age, using the same local standards.

Small-for-dates infants (S.F.D.) - one whose birth weight is below the 10th percentile for gestational age according to the local standards.

SUBJECTS AND METHODS

This survey forms part of a study on the interaction between malaria and pregnancy carried out between September 1976 and September 1977 at the University Hospital Muhimbili Medical Centre and the Government Maternity Ocean Road Hospital. For details of local health facilities, population, socio-economic and geographical circumstances see previous studies (Boersma and Mbise, 1979; Mbise and Boersma, 1979).

Maternal venous blood and cord blood was collected from the following groups of mothers and their offspring immediately after delivery:

Group 1: the control group was composed of 54 randomly selected mothers and their term appropriate for gestational age infants. The gestation ranged from 38 to 41 weeks.

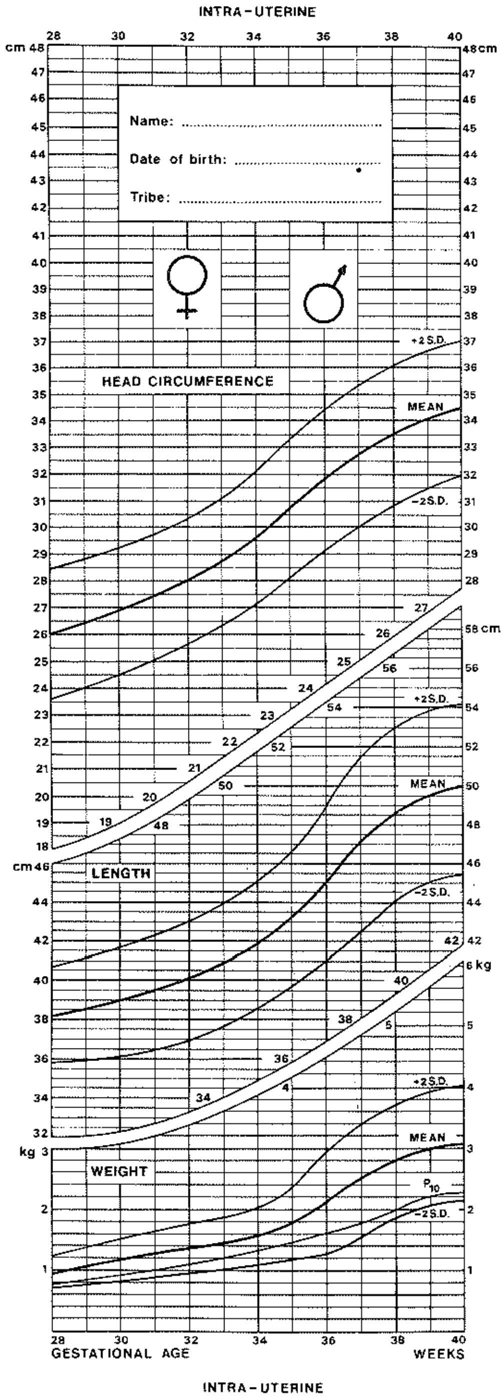


Fig. 1. Intrauterine growth curves for weight, length and head circumference for Dar es Salaam, Tanzania from Boersma and Mbise (1979).

Group 2: consisted of 14 mothers and their preterm appropriate for gestational age infant. The gestational age of these infants ranged from 31 to 37 weeks.
Group 3: comprised 21 mothers and their small-for-dates infants with a gestation ranging from 37 to 40 weeks.

Mothers with hypertension with or without proteinuria and conditions complicating pregnancy such as diabetes, urinary tract infections, multiple pregnancies and antepartum hemorrhage were excluded. All infants were born by normal vaginal delivery and their one-minute Apgar score was 9 or 10. No external malformations or other obvious abnormalities were found on inspection of the infants. Even in the absence of clinical suspicion of intrauterine infection, however, such an infection cannot be definitely excluded, although none of the low birth weight infants had malaria parasites in the thick smear of their peripheral blood. Gestational age of the newborn infants was assessed within 8 hours of delivery using the neonatal physical and neurological scales of maturation suggested by Dubowitz *et al* (1970).

In *Table I*, mean ($\pm$ S.D.) of various anthropometric and clinical data of the 3 different groups of mothers and their infants are summarised. At delivery the umbilical cord was carefully cleaned before collection of approximately 10 ml of whole cord blood. Immediately after delivery 5 ml of venous blood was taken from the cubital vein from the mother. Consent was obtained from each mother. After sampling, serum was separated by centrifugation and stored and transported at -20° C until analysed. Analysis of the samples was done within 3 months of collection of the samples. Serum protein was analysed by the Biuret reaction. IgA, IgG and IgM were measured by single radial immuno-diffusion (Mancini *et al*, 1964), using commercial rabbit antisera to human IgG, IgM and IgA and their specific standards (Behringwerke). Because of the low concentrations to be expected for IgA and IgM in cord blood, low concentration radial immuno-diffusion techniques were used for these determinations. Electrophoresis of serum proteins was performed on cellulose acetate strips using the Beckman microzone electrophoresis equipment and the Beckman densitometer (R - 110).

All laboratory investigations were checked by the laboratories of

Table I. Anthropometric and clinical data (mean ± SD) of 54 term A.G.A., 14 preterm A.G.A. and 21 small-for-dates infants and their mothers. Number of determinations in parenthesis.

Data	*Term A.G.A.*	*Preterm A.G.A.*	*Small-for-dates*
Mothers			
Age, years	24.2 ± 4.5 (52)	21.8 ± 4.8 (13)	21.3 ± 4.7 (19)
Parity	3.5 ± 1.9 (51)	1.8 ± 1.1 (14)	2.5 ± 2.2 (21)
Height, cm	153.5 ± 7.1 (50)	153.0 ± 3.0 (14)	152.5 ± 4.9 (19)
Arm circumference, cm	25.0 ± 2.6 (51)	25.2 ± 2.3 (12)	24.3 ± 1.9 (16)
Infants			
Ratio males/females	26/28	6/8	10/11
Birthweight, g	3036 ± 262 (54)	2035 ± 500 (14)	1553 ± 476 (21)
Length, cm	48.5 ± 1.7 (54)	44.2 ± 3.0 (14)	42.8 ± 4.0 (21)
Head circumference, cm	34.4 ± 1.0 (54)	31.3 ± 2.1 (14)	30.4 ± 1.6 (21)
Gestational age, weeks	40.1 ± 0.6 (54)	35.0 ± 1.9 (14)	37.7 ± 2.1 (21)

Sophia Children's Hospital, Rotterdam, The Netherlands by the same methods. The correlation coefficient (r) of the investigations performed in Dar es Salaam and those in Rotterdam was 0.9 or better. Where applicable statistically significant differences between means were measured by Student's t-test.

RESULTS

Maternal blood tests

Mean serum concentration (± S.D.) of total protein, immunoglobulins (IgG, IgM and IgA) among mothers of term A.G.A., preterm A.G.A. and small-for-dates infants are shown in *Table II*. Total protein, IgG, IgM and IgA showed a nearly symmetrical distribution in the three different groups of mothers, except for IgM in mothers of small-for-dates infants. Significantly higher levels of total protein were found in mothers of preterm A.G.A. and small-for-dates infants when compared with mothers of term A.G.A. infants ($p < 0.001$ and $p < 0.05$ respectively). In mothers of term A.G.A. 42% of the total protein concentration (6.8 g/100 ml) was albumin (2.9 g/100 ml) and 20% was γ-globulin (1.4 g/100 ml). IgG levels were slightly higher in mothers of preterm A.G.A. than in mothers of term A.G.A. and small-for-dates infants, but this was not significant. In mothers of small-for-dates infants higher values of IgA ($p < 0.01$) and IgM were found when compared with mothers delivering term A.G.A. infants. No notable changes in maternal IgG were observed during the last eight weeks of pregnancy as calculated by multiple regression analysis ($r = 0.246$).

Cord blood tests

Total proteins and IgG levels showed a nearly symmetrical distribution in the three different groups of infants, whereas for IgM and IgA a nearly normal distribution among these groups of infants could only be obtained after logarithmic transformation of the values measured. Mean serum concentration (± S.D.) of total protein, immunoglobulins (IgG, IgM and IgA) among term A.G.A., preterm A.G.A. and small-for-dates infants in cord blood are shown in *Table II*. In term A.G.A. infants the mean serum

Table II. Total protein, IgG, IgM and IgA of maternal/cord serum pairs in 54 term A.G.A., 14 preterm A.G.A. and 21 small-for-dates infants and their mothers (mean ± SD). Number of determinations in parenthesis.

Data	*Mothers*			*Babies*		
	Term A.G.A.	*Preterm A.G.A.*	*Small-for-dates*	*Term A.G.A.*	*Preterm A.G.A.*	*Small-for-dates*
Total protein, g/100 ml	$6.8 \pm 0.8^{a*, b***}$ (49)	7.8 ± 0.6 (14)	7.5 ± 0.9 (18)	$6.9 \pm 0.5^{c***, d***}$ (49)	6.3 ± 0.7 (12)	6.2 ± 1.0 (15)
IgG, mg/100 ml	1840 ± 419 (49)	2059 ± 530 (14)	1918 ± 539 (19)	1471 ± 304 (49)	1398 ± 442 (14)	1505 ± 361 (16)
IgM, mg/100 ml	155 ± 51 (49)	180 ± 57 (14)	254 ± 227 (18)	15.3 ± 9 (49)	28.8 ± 24.6 (14)	20.4 ± 17.3 (16)
IgA, mg/100 ml	$152 \pm 78^{b**}$ (49)	177 ± 79 (14)	216 ± 95 (19)	5.5 ± 5.8 (49)	2.8 ± 6 (14)	5.6 ± 4.9 (16)

*Difference between means $p < 0.001$

**Difference between means $p < 0.01$

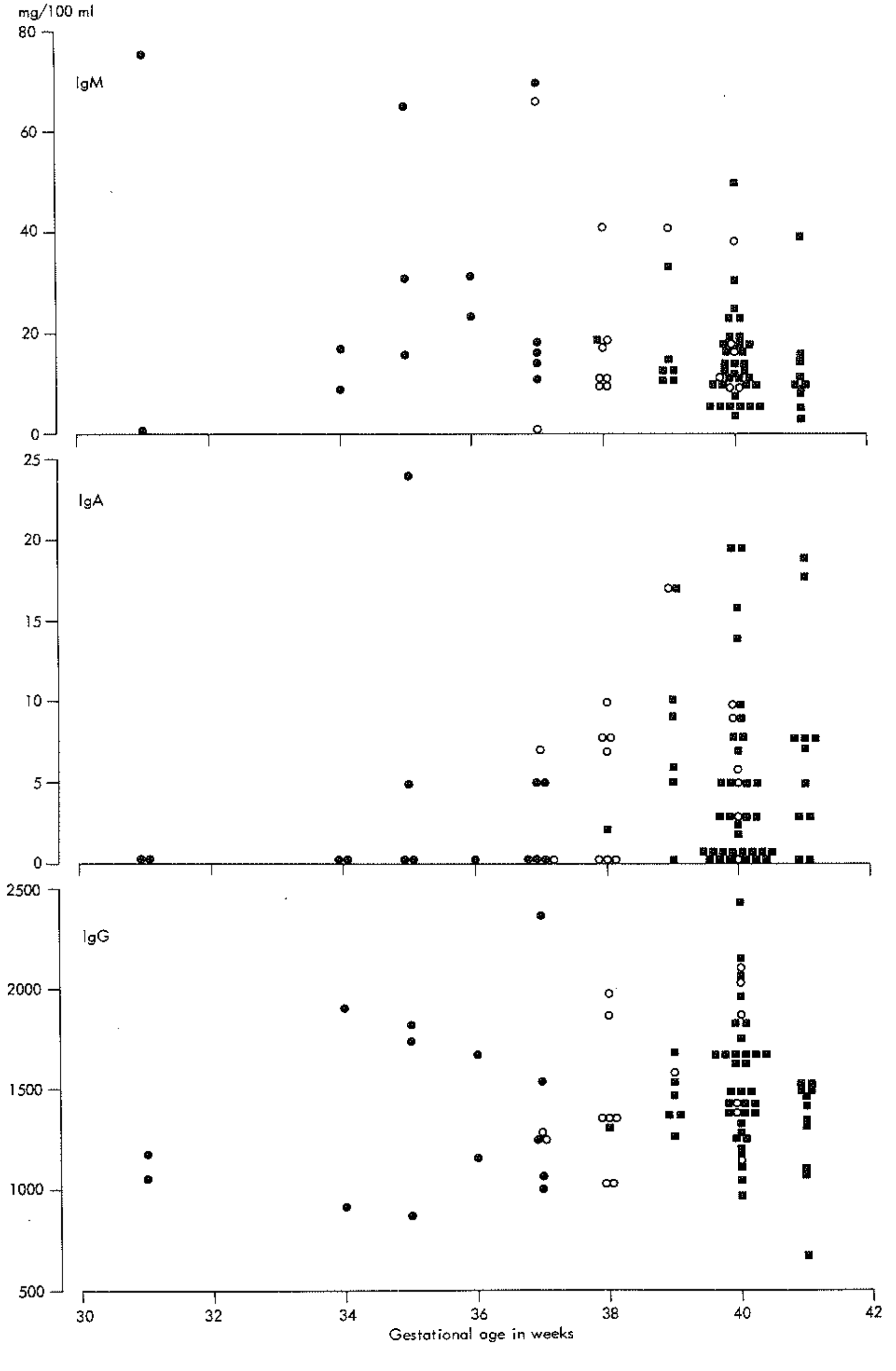
***Difference between means $p < 0.05$

a = Comparison of values between mothers of term and preterm infants

b = Comparison of values between mothers of term and small-for-dates infants

c = Comparison of values between term and preterm infants

d = Comparison of values between term and small-for-dates infants


mg/100 ml
IgM
80
60
40
20
0
IgA
25
20
15
10
5
0
IgG
2500
2000
1500
1000
500
30
32
34
36
38
40
42
Gestational age in weeks

total protein was 6.9 $\pm$ 0.5 g/100 ml. This was slightly higher than that in preterm A.G.A. and small-for-dates infants ($p < 0.05$). In this group of infants albumin accounted for 60% and γ-globulins 20% of the total protein values (4.1 $\pm$ 0.2 and 1.4 $\pm$ 0.2 g/100 ml respectively). No differences were found in the mean levels of immunoglobulins IgG, IgM and IgA in the 3 subgroups of newborn babies. The IgM was above 20 mg% at birth in 40% of the small-for-dates, 25% of the preterm A.G.A. and 14% of the term A.G.A. infants. Individual values of serum IgG, IgM and IgA from cord blood of term A.G.A., preterm A.G.A. and small-for-dates babies are plotted against gestational age in *Figure 2*. IgM was detectable at the 31st week of gestation, whereas IgA levels were detected from the 35th week of gestation.

In normal term infants mean IgG in cord serum was higher in children of primiparous than of multiparous mothers (1723 versus 1327 mg/100 ml respectively). This difference was not observed for IgA and IgM. In this group of infants IgM was detectable in all the cord sera. In 13 (27%) of the term A.G.A. children IgM values were 20 mg/100 ml or higher. Among this group of infants mean birth weight was sligthly higher when compared with mean birth weight of the whole group, but this difference was not significant. The mean IgA level in the term A.G.A. infants was 5.5 mg/100 ml. In 17 (35%) of these infants IgA could not be detected in cord serum.

Fig. 2. Individual values for serum IgM, IgA and IgG in cord blood of preterm A.G.A. (●), small-for-dates (o) and term A.G.A. infants (■) plotted against gestational age.

Maternal/fetal blood ratios

The mean concentration of IgG in the mother was 1.25 times greater than her child in the term A.G.A. group; 1.47 times greater in the mothers of preterm A.G.A. and 1.27 times greater in the mothers of small-for-dates babies. In general higher values of IgG in the mother corresponded with higher values in the fetus.

DISCUSSION

Two assumptions were made in an attempt to relate the levels of IgG, IgM and IgA in maternal and cord blood in Tanzania with those of other studies in Western countries. Firstly it was assumed that the immunoglobulin levels in "preterm appropriate for gestational age" infants and their mothers reflect in some way the normal events during pregnancy. Secondly it was assumed that the methods used would make a comparison with other studies justified. Regarding the first assumption it should be remembered that the term "preterm appropriate for gestational age" is in some way paradoxical, as events leading to or accompanying preterm birth are in principle "abnormal" and may well affect the relative proportions of some components in the mother and/or her fetus. However the same criteria were used by studies in Western countries. The last assumption is probably valid since the low concentration radial immuno-diffusion techniques were used for the IgA and IgM determinations in cord blood, with a detection limit of 1 mg/100 ml for IgM.

In this study among mothers delivering a term appropriate for gestational age infant mean value for total protein (6.8 g/100 ml) and albumin (2.9 g/100 ml) was higher than found in Caucasian women (de Alvarez *et al*, 1961; Robertson, 1970; Hytten and Leitch, 1971; Morse *et al*, 1975 and Reboud, 1976): range of means 5.9 to 6.4 g/100 ml for total protein and 2.4 - 2.75 for albumin. Somewhat higher values for total protein (7.2 - 8.0 g/100 ml) were found in well-nourished African, Hindu and Bantu women towards the end of pregnancy (Sénécal and Berton, 1957 and Plagnol, 1958). Mean IgG values at the end of normal pregnancy (1840 mg/100 ml) were higher when compared with the observed range for Caucasian women (1000-1400 mg as reviewed by de Muralt, 1978), whereas IgA and IgM levels were quite similar to observations in Western countries. This was also found in another study in Africa (McFarlane and Udeozo, 1968). The reason for the higher IgM and IgA levels among mothers of small-for-dates infants remains unclear. Though it might be explained by a higher incidence of (subclinical) infections among these mothers. More extensive studies are needed to prove this.

In the group of Tanzanian term A.G.A. infants we studied, mean total protein level was higher than that reported in infants from Western countries (average 5.8 g/100 ml, Schultze and Heremans, 1966), which may be partly explained by the higher albumin levels: 4.1 versus 3.5 - 4.0 g/100 ml in Western term infants (de Muralt, 1978).

When the individual values in the three groups of Tanzanian infants in relation to their gestational age (*Fig. 1*) were compared with studies in the U.S.A. (Stiehm, 1975) the *de novo* synthesis of IgM and IgA by the fetus seems to be activated at an earlier gestational age. This assumption is further substantiated by the higher incidence of detectable IgM (100%) and especially IgA levels (65%) in the term A.G.A. infant at birth when compared to the infant in Western countries (75% for IgM and 0-30% for IgA as reviewed by de Muralt, 1978).

Since the fetus synthesises most of its proteins, with the exception of IgG, from amino acids which have been transferred across the placenta (Gitlin and Gitlin, 1975) it can be assumed that the rate of synthesis of albumin, IgM and IgA by the Tanzanian fetus is greater than that found in Western countries during the last stage of pregnancy. The high endogenous synthesis of IgM and IgA in the fetus might be explained by increased induction from antigenic stimuli in the maternal environment, although a genetic origin cannot be excluded. It was beyond the scope of this study to evaluate the incidence of intrauterine infection among the infants studied, although it can be said that none of the infants in the low birth weight groups and only one infant in the term A.G.A. group had malarial parasites in the *cord blood* smear at birth. In this particular infant IgM level was 20 mg/100 ml; the child was clinically well and went home without any treatment. On the postnatal follow-up no abnormalities could be detected. Among the preterm A.G.A. infants all were discharged home in good condition except one with a gestational age of 31 weeks. This infant died at the age of 3 weeks due to severe dehydration. In the small-for-dates group all were discharged home in good condition.

No attempts were made to evaluate the cellular immunity in this community of mothers and infants.

In conclusion, in paired Tanzanian maternal/fetal blood generally higher values were detected for total protein, albumin and IgG in maternal blood at the end of pregnancy compared to Western standards. The concentration of total protein, albumin and IgG in the fetal circulation was also increased compared to the same standards, with a higher detection rate for IgM and IgA, which could be explained by an increased induction of the fetal humoral antibody synthesis from antigenic stimuli in the maternal environment. Contrary to findings in Western countries IgG in the maternal sera tended to be higher than in the corresponding fetal circulation.

SUMMARY

Serum total protein, albumin, IgG, IgM and IgA were determined in cord blood of 54 term appropriate for gestational age, 14 preterm appropriate for gestational age and 21 small-for-dates infants and in their mothers immediately after delivery in Dar es Salaam, Tanzania. The mean serum level of total protein, albumin and IgG in mothers who delivered a term appropriate for gestational age infant were 6.8 g/100 ml, 2.9 g/100 ml and 1840 mg/100 ml respectively, whereas those from their corresponding infants were 6.9 g/100 ml, 4.1 g/100 ml and 1471 mg/100 ml respectively.

The *de novo* synthesis of IgM and IgA during fetal life seems to be activated at an earlier gestational age when compared with observations in Westerns countries, which subsequently resulted in a higher detection rate for IgM and IgA in cord blood of term appropriate for gestational age infants. IgG in Tanzanian mothers was generally higher than in corresponding cord blood sera, which is contrary to finding in Europe.

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Chapter three

STUDIES ON LIPID METABOLISM

A. *Serum lipids in maternal/cord blood pairs from normal and low birth weight infants in Dar es Salaam, Tanzania**

The metabolism of lipids seems to be important to the development of the embryo and fetus. In man total body fat increases from about 1 to 12-16% by weight between the 26th and 40th week of gestation (Widdowson, 1964; Mettau, 1978). Prenatally, lipid synthesis predominates over lipid breakdown. After birth the stored fat serves as an important source of energy when the limited glycogen stores tend to become exhausted. The most rapid change in serum lipids occurs in the first year of life. For example in Western countries, between birth and 1 year of age total cholesterol has increased by 130 to 240% (Darmady *et al*, 1972 and Frerichs *et al*, 1978) and triglycerides by 68% (Frerichs *et al*, 1978).

The incidence of arteriosclerosis in Tanzania is low. Cholesterol values in adulthood have also been found to be low in other developing countries (Mendez *et al*, 1962; Truswell, 1968; Sinnett *et al*, 1973, Connor, 1978), which would be regarded by many to be a factor in the low incidence of arteriosclerosis, the precursor of coronary heart disease (Truswell, 1978). In order to gain further understanding of the role of serum lipids during intra-uterine life in a community living in completely different socio-economic and nutritional conditions than those in Western countries the serum total cholesterol and tri-

*These studies have been submitted for publication to Acta Paediatrica Scandinavica.

glycerides levels were measured in Tanzanian mothers and their infants immediately after delivery. These maternal/ cord serum lipids for preterm appropriate for gestational age, small-for-dates and term appropriate for gestational age infants were compared with data from similar studies from Western countries.

Definitions and abbreviations

Term appropriate for gestational age infant (term A.G.A.) - one who is born within 38-42 weeks of gestation and whose birth weight is within ± 1 S.D. from the mean for that particular gestational age using the local standards (Boersma and Mbise, 1979) shown in *Figure 1*.

Preterm appropriate for gestational age infant (preterm A.G.A.) - one who is born before 37 completed weeks of gestation and whose birth weight is within the mean ± 1 S.D. for the gestational age, using the same local standards.

Small-for-dates infants (S.F.D.) - one whose birth weight is below the 10th percentile for gestational age according to the local standards.

PATIENTS AND METHODS

This survey forms part of a study of the interaction between malaria and pregnancy carried out between September 1976 and September 1977 at the University Hospital Muhimbili Medical Centre and the Government Maternity Ocean Road Hospital. For details regarding local health facilities, population, geographical and socio-economic circumstances see previous study (Boersma and Mbise, 1979; Mbise and Boersma, 1979).

Maternal venous blood and cord blood was collected from the following groups of fasting mothers and their offspring immediately after delivery:

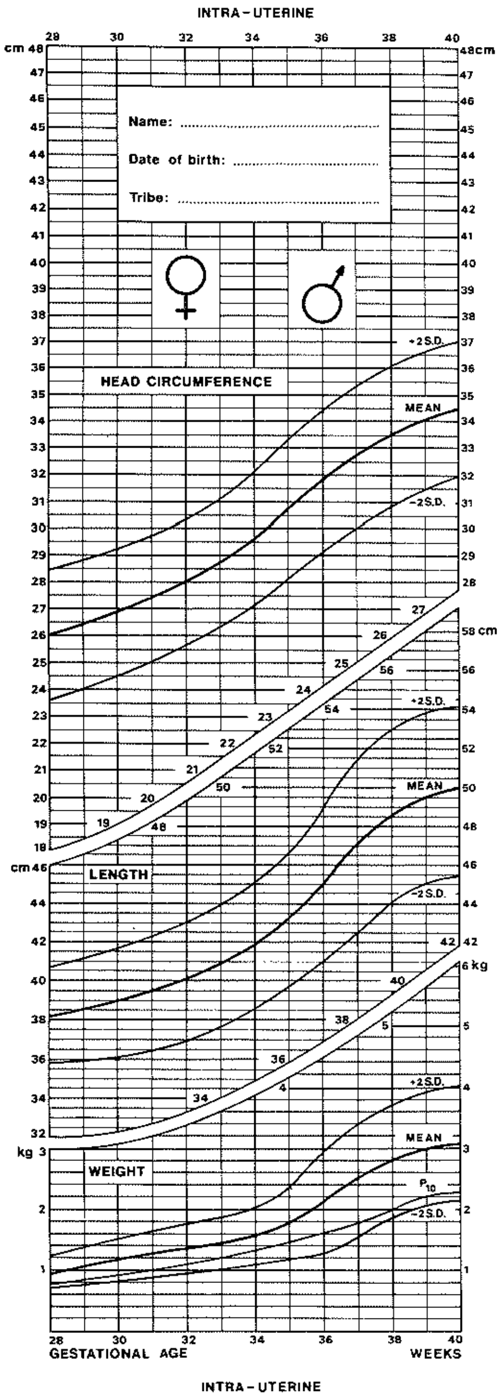

Fig. 1. Intrauterine growth curves for weight, length and head circumference for Dar es Salaam, Tanzania from Boersma and Mbise (1979).

Group 1: 54 randomly selected mothers and their term appropriate for gestational age infants. The gestation ranged from 38 to 41 weeks.
Group 2: 14 mothers and their preterm appropriate for gestational age infant. The gestational age of these infants ranged from 34 to 37 weeks.
Group 3: 17 mothers and their small-for-dates infants with a gestation ranging from 37 to 40 weeks.

Mothers excluded were those with hypertension with or without proteinuria and conditions complicating pregnancy such as diabetes, multiple pregnancies and antepartum hemorrhage or fetal malformations. All infants included were born by normal vaginal delivery and their one-minute Apgar score was 9 or 10. Standing height of mothers was recorded in centimeters. The left midupper arm circumference was taken by a non stretchable tape measure to the nearest 0.5 cm. Anthropometric measurements were taken from the newborn infant immediately after delivery. Gestational age of the newborn infant was assessed using the neonatal physical and neurological scales of maturation as described by Dubowitz *et al* (1970). In *Table I* the mean ($\pm$ S.D.) of various anthropometric and clinical data of the 3 different groups of mothers and their infants are summarised.

At delivery the umbilical cord was carefully cleaned before collection of approximately 10 ml of mixed cord blood. Immediately after birth 5 ml of venous blood was taken from the cubital vein from the mother. Consent was obtained from each mother. Serum was separated by centrifugation and stored and transported at $-20^{o}C$ until analysed. Serum total cholesterol was analysed in duplicate by the Liebermann Burchard reaction (Huang *et al*, 1961). Serum triglycerides were analysed in duplicate by the Fletcher method (1968). All laboratory investigations were checked by the laboratories of Sophia Children's Hospital, Rotterdam, The Netherlands. Unfortunately reliable determinations could not be performed in all samples. The correlation coefficient (r) of the investigation performed in Dar es Salaam and in Rotterdam was 0.9 or greater. Where applicable statistically significant differences between means were

Table I. Anthropometric and clinical data (mean ± SD) of 54 term A.G.A., 14 preterm A.G.A. and 17 small-for-dates infants and their mothers. Number of determinations in parenthesis.

Data	*Term A.G.A.*	*Preterm A.G.A.*	*Small-for-dates*
Mothers			
Age, years	24.2 ± 4.5 (52)	21.7 ± 5.0 (13)	21.4 ± 4.6 (17)
Parity	3.5 ± 1.9 (51)	2.0 ± 2.0 (14)	2.6 ± 2.1 (17)
Height, cm	153.5 ± 7.1 (50)	152.7 ± 3.1 (14)	152.6 ± 4.7 (17)
Arm circum-ference, cm	25.0 ± 2.6 (51)	24.8 ± 2.0 (14)	24.4 ± 1.9 (17)
Infants			
Ratio $\frac{\text{males}}{\text{females}}$	$\frac{26}{28}$	$\frac{7}{7}$	$\frac{8}{9}$
Birthweight, g	3036 ± 262 (54)	2096 ± 464 (13)	1610 ± 470 (17)
Length, cm	48.5 ± 1.7 (54)	44.5 ± 2.9 (13)	43.4 ± 3.6 (17)
Head circum-ference, cm	34.4 ± 1.0 (54)	31.4 ± 2.2 (13)	30.5 ± 1.5 (17)

measured by Student's t-test, a p-value <0.05 was considered as significant.

RESULTS

Table II shows the fetal and maternal concentrations of total cholesterol and triglycerides in the 3 groups immediately after delivery. Total cholesterol and triglyceride showed a virtually normal distribution in the three different groups of maternal/cord serum pairs, except

Table II. Serum concentration of total cholesterol and triglyceride in maternal and cord blood of the three different subgroups. Mean ± SD. Total number of determinations in parenthesis.

	Mothers			*Babies*		
	Term A.G.A.	*Preterm A.G.A.*	*Small-for-dates*	*Term A.G.A.*	*Preterm A.G.A.*	*Small-for-dates*
Gestation, range in weeks	38 - 41	34 - 37	37 - 40	38 - 41	34 - 37	37 - 40
			Serum concentrations			
Total cholesterol, mmol/l	6.3 ± 1.3 (46)	5.5* ± 1.5 (12)	5.1** ± 0.9 (14)	1.9 ± 0.4 (51)	2.2 ± 0.6 (10)	2.4* ± 0.8 (14)
Triglycerides, mg/100 ml	169 ± 62 (46)	172.5 ± 53 (13)	122.4** ± 44 (12)	25.8 ± 17.0 (46)	18.2 ± 9.3 (10)	67.8 ± 24 (14)

Using Student's t-test mean significantly different from that in term group: ** $p < 0.01$ * $p < 0.05$

for triglyceride in cord serum of the three different groups of infants, where a skewed distribution toward high concentrations was found.

Maternal serum lipids

Mean total cholesterol level in maternal sera in mothers of term A.G.A. infants was 245 mg/100 ml (range 159 - 359 mg/100 ml) equivalent to 6.3 mmol/l (range 4.1 - 9.2 mmol/l). Mean maternal cholesterol level in mothers of term A.G.A. infants was significantly higher than that found in mothers of preterm A.G.A. and small-for-dates infants ($p < 0.05$ and $p < 0.01$ respectively). Inspection of the individual values of total cholesterol in the 3 groups studied, as plotted against gestational age in *Figure 2* (upper part), suggest a slight increase from 34 to 40 weeks gestation. Mean triglyceride values were higher in the 2 groups of mothers giving birth to appropriate for gestational age infants (preterm or term), compared to the mothers of small-for-dates infants ($p < 0.01$).

Cord serum lipids

In the corresponding cord sera of term A.G.A. infants total cholesterol value was 74 mg/100 ml (range 47 - 108 mg/100 ml) equivalent to 1.9 mmol/l (range 1.2 - 2.8 mmol/l). Mean cord level of term A.G.A. infants was quite similar to that of preterm A.G.A., but slightly lower than that of small-for-dates infants ($p < 0.05$). Individual values in cord sera of total cholesterol for the 3 different groups are plotted against gestational age in *Figure 2* (lower part). In the appropriate for gestational age babies, the individual cholesterol concentrations varied little from 34 to 41 weeks gestation, whereas the concentrations in the small-for-dates infants were generally higher than in the appropriate for gestational age babies. Among the three groups of infants mean triglyceride concentration at birth was higher in the term than in the preterm A.G.A. infants (25.8 and 18.2 mg/100 ml respectively), but was highest in the small-for-dates babies (67.8 mg/100 ml).

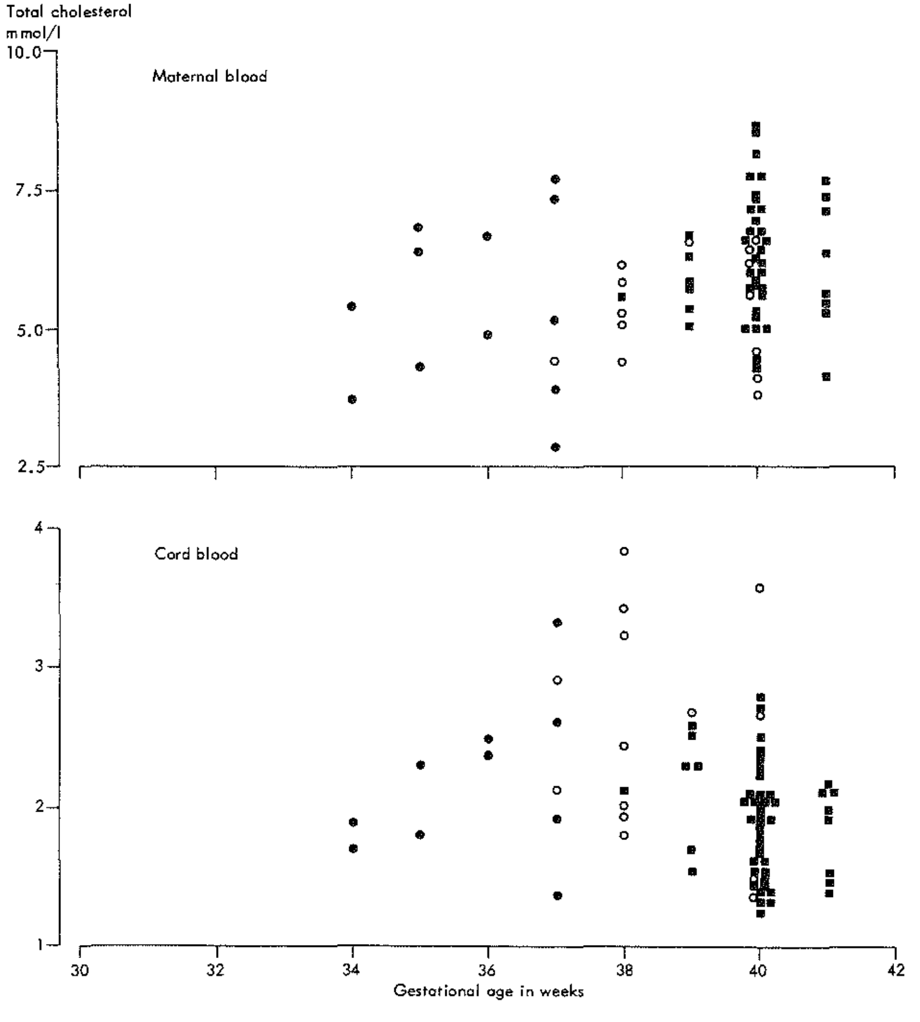

Fig. 2. Individual values for serum total cholesterol in mothers (upper part) of preterm A.G.A. (●), small-for-dates (○) and term A.G.A. (■) and those of their offspring plotted against gestational age (lower part).

DISCUSSION

Anthropometric measurements of mothers of term A.G.A., preterm A.G.A. and small-for-dates infants and their offsprings were in general quite similar to those of our previous studies (Boersma and Mbise, 1979; Mbise and Boersma, 1979). The average height of Dutch mothers (van Wieringen *et al*, 1965) is greater than that seen in this study (166 cm against 153 cm). An important part of the difference of average birth weight between the Western countries and Tanzania can be accounted for by the difference in height of the mother, as maternal height affects birth weight more than the duration of gestation (Butler and Alberman, 1969; Mbise and Boersma, 1979).

Arm circumference was lower in mothers giving birth to low birth weight babies when compared to mothers of term or preterm appropriate for gestational age infants. However when matched for age no significant difference was observed. Human pregnancy is accompanied by maternal hypercholesterolaemia (Hytten and Leitch, 1971; Ross, 1973). Isotope studies suggest that the increased maternal steroid production during pregnancy is derived from increased circulating cholesterol (Hellig *et al*, 1969). Although in underdeveloped countries lower cholesterol values have been found in non-pregnant women (Connor *et al*, 1978), in this study at the end of normal pregnancy total cholesterol values (6.3 $\pm$ 1.3 in mmol/l equivalent to 245 $\pm$ 50 mg/100 ml) did not differ notably from the range of means reported in Western countries: 5.66 to 6.48 mmol/l equivalent to 221 to 253 mg/100 ml (Kleeberg and Polishuk, 1963; Spellacy *et al*, 1974; Kesteloot *et al*, 1975). There is some evidence (Hytten and Leitch, 1971; Friedman *et al*, 1978) that the level of cholesterol declines or at least stops rising during the last stage of pregnancy in Caucasian mothers, whereas in this study it seems to rise up to term and remained nearly constant after term (*Figure 2*). It remains uncertain whether this relatively greater increase in Tanzanian women during the last stage of pregnancy could indicate a different pattern of steroid production.

Mean total cholesterol levels in cord blood from term appropriate for gestational age infants in this study (1.9 ± 0.4 mmol/l equivalent to 74 ± 16 mg/100 ml) were comparable to the range of means reported from Western countries: 1.58 to 2.49 mmol/l equivalent to 62 to 97 mg/100 ml (Kleeberg and Polishuk, 1963; Darmady *et al*, 1972; Fosbrooke and Wharton, 1973; Dyerberg *et al*, 1974; Kesteloot *et al*, 1975; Cress *et al*, 1977; Frerichs *et al*, 1978). No notable differences were observed between males and females (75 and 73 mg/100 ml respectively). Our observations show that in appropriate for gestational age babies delivered beyond 34 weeks gestation, serum total cholesterol concentrations remained virtually constant, similar to findings in Great Britain (Fosbrook and Wharton, 1973) and the U.S.A. (Friedman *et al*, 1978).

Apparently the factors influencing the serum cholesterol value during *postnatal* life in the different societies were not already operating at birth. During the first year of life we were able to confirm a marked rise in cholesterol level during breast-feeding. But at one year of age mean total cholesterol concentration was lower in Tanzanian than in British children (Darmady *et al*, 1972): 3.7 and 4.9 mmol/l (144 and 191 mg/100 ml) respectively, however, quite similar to values in the U.S.A. (Tsang *et al*, 1974) of 3.4 mmol/l (equivalent to 131 mg/100 ml). Cholesterol concentrations in the Tanzanian community we studied, remained virtually constant at 4.0 mmol/l (156 mg/100 ml) up to the age of 6 years, lower than data from Andersen *et al* (1979) in Denmark, who found a mean concentration of 4.7 mmol/l (equivalent to 183 mg/100 ml) but from children at the age of 3 to 4.

Maternal triglyceride concentration remained virtually constant during the last stage of pregnancy in mothers delivering an appropriate for gestational age infant. This is in agreement with observations in the U.S.A. (Friedman *et al*, 1978). The lower triglyceride values in mothers giving birth to a small-for-dates infant when compared to those who delivered an appropriate for gestational age infant, remains unexplained.

In cord blood triglyceride values increased with gestation but were highest in small-for-dates infants, which could be explained by an increased mobilisation of the fetal adipose tissue stores in response to intrauterine stress (Cress *et al*, 1977). Postnatally (to be published) triglycerides increased remarkably during the stage of breast-feeding to values up to 130 mg/100 ml at the age of one year, but thereafter decreased gradually to values of approximately 50 mg/100 ml at the age of 5 to 6 years.

The overall significance of our observations in relation to maternal/cord blood lipids at delivery remains uncertain. It seems that the concentration of these lipids were in general similar in this study and in Western countries during late pregnancy in the mother and her offspring. However, different levels were observed beyond this stage. A similar tendency was observed between Tanzanian and West-European infants as regards the fatty-acid composition of their body fat before and after birth (Boersma, 1979). In that study the differences in the fatty-acid composition were also subtle during the last stage of pregnancy but appeared to be most pronounced during infancy and early childhood.

SUMMARY AND CONCLUSIONS

Serum total cholesterol and triglyceride were determined in the cord blood of 54 term appropriate for gestational age, 14 preterm appropriate for gestational age and 17 small-for-dates infants and their mothers immediately after delivery in Dar es Salaam, Tanzania. The mean serum level of total cholesterol in cord blood of term appropriate for gestational age infants was 74 mg/100 ml (1.9 mmol/l), whereas that from their mothers 245 mg/100 ml (6.3 mmol/l). Both, maternal and cord blood values, corresponded with studies from Western countries. The mean serum level of triglyceride in cord blood of term appropriate for gestational age infants and those from their mothers were 25.8 and 169 mg/100 ml respectively, both in agreement with values obtained in Western countries. Results of maternal cord serum lipids in the low birth weight groups were also similar to those of Western countries. It appears that in man, factors influencing the serum lipid values during adult life and childhood had no effect on these levels during pregnancy on the mother and fetus.

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B. *Changes in fatty-acid composition of body fat before and after birth in Tanzania: an international comparitive study**

Changes in the fatty-acid composition of human adipose tissue before birth and during infancy and childhood were studied in Tanzania and compared with data for British and Dutch infants in relation to their diet. From the 32nd to the 37th week of gestation in Tanzania the proportion in the body fat of the unsaturated fatty acid linoleic acid tended to rise, suggesting an adequate supply of this essential fatty acid from the mother to the fetus. At term 2.5% of the total fatty acids of the body fat was linoleic acid, which corresponded with values in Dutch newborn infants but was significantly higher than those in British infants. For details regarding the complete mean fatty-acid composition of body fat of Tanzanian, British and Dutch infants at term see *Table I*.

During infancy in Tanzania the composition of the fat showed a dramatic increase in the proportions of the saturated fatty acids lauric and myristic acid, which did not occur in Dutch and British infants (see *Table II*). The proportion of linoleic acid increased to 8%. These changes were a reflection of the fatty-acid composition of the fat in the human milk that the infants received. During weaning (1-2 years of age) the fatty-acid composition changed only slightly.

* These studies have been published in the British Medical Journal, 1: 850-853, 1979.

Table I. Mean fatty-acid composition (± SD) of body fat of Tanzanian, British and Dutch infants *at term* (Widdowson *et al*, 1975) (g/100 g total fatty acids).

Fatty acid	*Tanzania* n = 9	*Gr. Britain** n = 14	*The Netherlands** n = 12
Saturated acids			
C12:0 (Lauric acid)	0.2 ± 0.2		
C14:0 (Myristic acid)	4.3 ± 1.0	3.8 ± 0.6	3.3 ± 0.4
C16:0 (Palmitic acid)	48.2 ± 2.2	48.9 ± 3.6	45.8 ± 1.6
C18:0 (Stearic acid)	4.9 ± 0.7	4.1 ± 0.6	3.8 ± 0.4
Unsaturated acids			
C16:1 (Palmitoleic acid)	12.7 ± 1.4	12.6 ± 1.6	15.2 ± 1.2
C18:1 (Oleic acid)	27.8 ± 2.9	29.6 ± 3.0	29.0 ± 1.8
C18:2 (Linoleic acid)	2.3 ± 0.6	1.0 ± 0.8	2.9 ± 0.7

* Reference: Widdowson *et al*, 1975.

Table II. Mean fatty-acid composition (± SD) of body fat of British, Dutch infants aged 6-12 months and Tanzanian children aged 1-2 years, receiving a *mixed diet* (g/100 g total fatty acids).

Fatty acid	*Tanzania* n = 6	*Gr. Britain** n = 7	*The Netherlands** n = 4
Saturated acids			
C12:0 (Lauric acid)	5.4 ± 1.5		
C14:0 (Myristic acid)	13.8 ± 5.0	8.5 ± 1.1	4.8 ± 1.2
C16:0 (Palmitic acid)	27.9 ± 2.2	32.0 ± 2.7	29.7 ± 4.6
C18:0 (Stearic acid)	5.8 ± 1.8	5.6 ± 1.0	2.9 ± 0.7
Unsaturated acids			
C16:1 (Palmitoleic acid)	5.0 ± 2.3	7.0 ± 1.9	13.8 ± 2.7
C18:1 (Oleic acid)	33.4 ± 4.6	43.4 ± 2.9	40.8 ± 3.3
C18:2 (Linoleic acid)	8.9 ± 2.1	3.5 ± 0.8	8.0 ± 4.1

* Reference: Widdowson *et al*, 1975.

The specific fatty-acid composition of the fat in Tanzanian breast milk may have a beneficial influence on the extent of intestinal absorption in the newborn child.

The methods, results, detailed discussion and references are given in paper 3 of the addendum.

Chapter four

MATERNAL WEIGHT GAIN DURING PREGNANCY IN RUBYA, TANZANIA*

There is a wide variation in maternal weight gain during pregnancy. No single figure can be regarded as "normal" (Hytten and Leitch, 1971). The German physician Prochownick, scientist from the beginning of this century, has been credited for being the first person who tried to reduce maternal weight gain by a restricted diet to control the size of her baby, so that birth would be easier (quoted by Hytten and Leitch, 1971).

In primitive societies medical workers believe that many taboos concerning nutrition during pregnancy may effect that women put on little weight during this time which may reduce some of the complications for both mother and child during delivery.

The diminished maternal weight gain during pregnancy, when compared to more affluent societies, has by some authors been interpreted as an important contributory factor to the high incidence of low birth weight so commonly seen in the developing countries and which has been related to the limited nutritional intake of the mother (Gebre-Medhin, 1977).

This study was designed to obtain information regarding the "normal" weight gain of Tanzanian women during pregnancy to form a basis for studying the many physiological changes during this period.

* These studies were done in collaboration with E.M.H. Zuidgeest and have been submitted for publication to Tropical Pediatrics.

METHODS

After selection the antenatal cards of 100 apparently normal pregnant women from Rubya hospital were analysed retrospectively. The weight at the first antenatal visit and the weight of the mother at term (38-42 weeks of gestation) were recorded. Those mothers attending the antenatal clinic for the first time within the last four weeks prior to delivery were excluded. The antenatal cards were selected so that the expected dates of delivery were spread over the whole year to avoid possible seasonal influences. The mothers chosen were all normotensive and physically healthy, with no apparent abnormalities of pregnancy. Only 8 of the 100 were primigravida. Length of gestation was calculated to the nearest week from the first day of the last menstrual period. The accuracy of the estimate was checked against such clinical features as height of the uterine fundus and the time at which the first fetal movements were noticed.

Total weight gain was calculated from the difference between the weight of the pregnant women on the days just before delivery (before rupture of the membranes) and the weight recorded at the first antenatal visit. Weight change as a function of gestation was calculated in the following manner. The mothers were divided into 3 groups according to when they first attended the booking clinic.

Group I: from 10 to 19 weeks of gestation

Group II: from 20 to 29 weeks of gestation

Group III: from 30 to 36 weeks of gestation

The duration of pregnancy was averaged for each group and the weight gain which had occurred was extrapolated working backwards from the average weight increment for Group III, II and I in relation to total weight gain during pregnancy of Group I. Presence in one group excluded presence in another group. Since no information was available on the prepregnancy weight, the weight gain up to 16.5 weeks of pregnancy (the mean gestation of Group I) was estimated to be 1.8 kg, an approximation obtained from the literature on

Western European women (Thomson and Billewicz, 1957).

Rubya Hosptial is a designated district hospital serving a population of approximately 120,000 of the Haya tribe. They live on fertile ridges at approximately 1300 m above sea level in the West Lake district of Tanzania, where they grow coffee and bananas.

RESULTS

The weight gain of each group of pregnant women is shown in *Table I*.

Table I. Weight gain during pregnancy of Tanzanian women measured after different periods of gestation.

Group	*Number*	*Mean gestational age at first visit, weeks*	*Mean weight gain between first visit and term, kg*
I	11	16.5 (12 to 19)	4.2 (-1.0 to +8.4)
II	62	24.5 (20 to 29)	2.6 (-3.0 to +7.3)
III	27	32.1 (30 to 36)	1.4 (-1.8 to +6.3)

In Group I (n=11) the mean observation period was 23.5 weeks (range 21 to 28 weeks).

In Group II (n=62) the mean observation period was 15.5 weeks (range 11 to 20 weeks).

In Group III (n=27) the mean observation period was 7.9 weeks (range 4 to 10 weeks).

As previously described the weight change up to the 16.5 weeks of gestation was estimated to be plus 1.8 kg. An estimate of the total weight increase during the whole gestation can then be calculated: 4.2 kg + 1.8 kg = 6.0 kg.

A curve of the mean weight gain plotted against gestational age for Tanzanian pregnant women can be drawn as shown in *Figure 1.* A curve of the weight gain for Caucasian (British) women is included for comparison (Thomson and Billewicz, 1957). Since no adequate data were available on weight gain before 13 weeks of gestation in Thomson and Billewicz' study and before 16.5 weeks of gestation in our survey, a provisional estimate is dotted into the graph for both studies. The absolute figures for weight gained during pregnancy in successive 10 week periods are given for Rubya in parallel with those from the literature for Caucasian women (Thomson and Billewicz, 1957) in *Table II.*

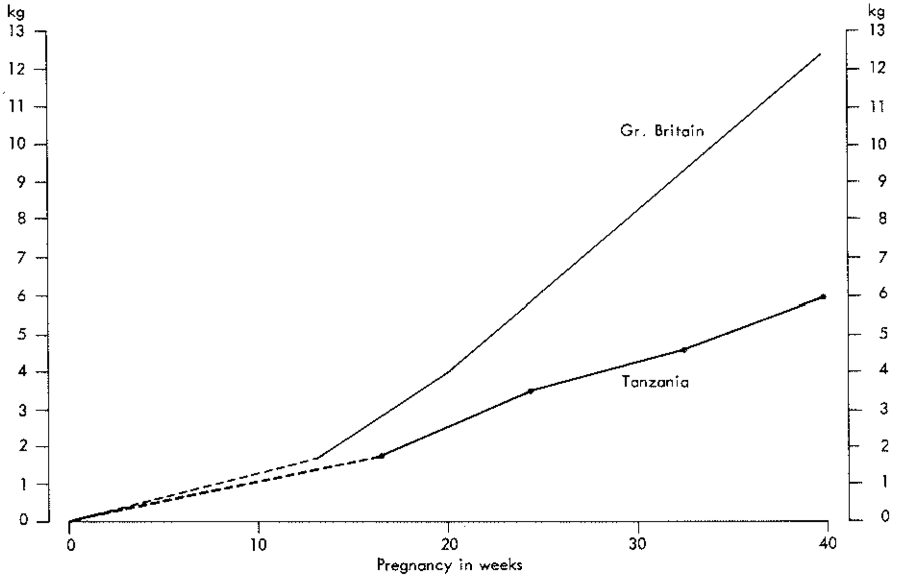

Fig. 1. Mean weight gain in pregnancy for Caucasian (Thomson and Billewicz, 1957) and Tanzanian women.

Table II. Mean weight gain per 10 week pregnancy period for Caucasian and Tanzanian women in kg.

Population	*Period of pregnancy*			
	0-10 week	*10-20 week*	*20-30 week*	*30-40 week*
Rubya, Tanzania	1.1*	1.5	1.7	1.7
Caucasian (Thomson and Billewicz, 1957)	0.65*	3.35	4.5	4.0

* by approximation

The mean birth weight of the infants born from these Tanzanian mothers was 3,118 g (S.D. $\pm$ 440 g). Mean weight at term of the Tanzanian mothers studied was 59.4 kg, whereas mean height of these women was 155 cm.

DISCUSSION

Although these figures of weight gain during pregnancy in Tanzania were obtained retrospectively they are probably representative of the Haya population. However, the mothers who comprised the study group were probably the most motivated ones living in a restricted area within reach of the hospital. Mean total weight gain during pregnancy of these Tanzanian women was much lower than that of Caucasian women (Hytten and Leitch, 1971) i.e. 6 and 12.5 kg respectively. It appears that the difference in weight gain is most pronounced in the second half of pregnancy. From our data the effect of weekly maternal weight gain upon the incidence of low birth weight could not be demonstrated due to the few numbers involved (3% of the total population). The mean birth weight in this study (3118 g) was slightly but not significantly higher when compared with the birth weight in Dar es Salaam (2990 g; Boersma and Mbise, 1979) which may be partly explained by the low number of primiparae in this study (8% versus 40% in Dar es Salaam). Instances were encountered of mothers losing weight during the second half of pregnancy and yet producing infants with a mean birth weight of 2836 g. It was surprising to note that the average weight of these mothers at term was somewhat higher than that of the whole population (60.o kg versus 59.4 kg). The Pearson correlation coefficient between the individual pregnancy weight gain per week of gestation and the birth weight was 0.3742. This correlation (with $p < 0.05$) needs to be interpreted with caution since no attempts were made to separate the effects of age, parity, prepregnancy weight and height of the mother, determinants which probably will influence the pregnancy weight gain.

Other studies in similar socio-economic societies have shown figures comparable to those found in our survey. Gebre-Medhin (1977) found a mean increase of approximately 7 kg in Ethiopians, and Venkatachalam *et al* (1960) found an increase of approximately 6.5 kg in Indians.

In this study no attempts were made to evaluate the dietary intake of the pregnant women. The diet is based on cassave, plantains, sweet potatoes, beans, cabbage, dried fish and fruits such as sweet bananas, mango's and passion fruit. The daily calorie and protein intake was unknown in these mothers but was probably lower than the daily intake of approximately 2,500 calories and 38 g of reference protein recommended by FAO/WHO (1973).

In this study we were specially concerned about the processes of physiological adaptation to these assumed marginal nutritional circumstances in Tanzanian pregnant women. The observation reported in this communication suggests a difference in weight gain during pregnancy between Tanzanian and Caucasian women which can neither be explained by the difference in weight of her offspring nor probably by the difference in weight of the placenta, uterus, amniotic fluid or breast tissue. *Table III* presents a rough estimate of the components to which the weight gain during pregnancy might be attributed for Tanzanian women together with those from the literature (Hytten and Leitch, 1971) for Caucasian women.

Table III. Analysis of estimated weight gain during pregnancy for Caucasian and Tanzanian women.

Data	*Caucasian** *(kg)*		*Tanzanian* *(kg)*
Fetal factors			
fetus	3.4		3.0
placenta	0.65		0.5
amniotic fluid	0.8		0.8
Maternal factors			
uterus	0.97		0.9
breasts	0.4		0.4
blood volume	1.25	6.28	0.4
extracellular fluid	1.7		
fat	3.33		
Total	12.5		6.0

*Reference: Hytten and Leitch, 1971.

Our estimates for the weight gain due to growth of the fetus, placenta, amniotic fluid, uterus and breasts are likely similar to those for Caucasian women. Thus, reduced weight gain in Tanzanian mothers may be caused by a much smaller increase of the remaining components: *blood volume, extracellular fluid* and *fat*.

In conclusion we might state that the difference of weight gained between Caucasian and Tanzanian pregnant women is to a great extent attributable to the storage of water in the intra and extra vascular compartments and/or storage of fat and not to the formation of fetal and maternal non-fat tissue. It seems unlikely to believe that the difference in total caloric intake between pregnant women living in Western countries and those in Tanzania can be explained by the formation of lean body tissue.

SUMMARY

The total weight gain during pregnancy in Rubya, Tanzania is approximately 6 kg, whereas that of Caucasian pregnant women is 11 to 12.5 kg. The difference in weight gain is most pronounced during the second half of pregnancy.

It seems unlikely that the differences of weight gained between the Tanzanian and Caucasian women are wholly due to the differences in the amount of new fetal tissue laid down, since much of the weight gained is attributable to the storage of water and/or fat.

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Chapter five

PERINATAL GROWTH IN DAR ES SALAAM, TANZANIA. AN EVALUATION OF PERINATAL CIRCUMSTANCES IN A DEVELOPING COUNTRY*

Essence of science lies not in discovering facts,
but in discovering new ways to think about them.
W.L. Bragg.

Normal fetal growth depends upon an adequate supply of nutrients from the mother to the fetus. Nutritional deficiencies in pregnant animals produce retarded fetal growth (1-3). In humans the evidence is much less clear. It seems that rather severe forms of maternal deprivation, as seen in war and famine, only reduce the average birth weight by 100 to 200 grams in man (4-6).

Maternal overnutrition prevails in the Westernised societies and thus it is generally only in developing countries that the opportunity arises to study the effects of a limited dietary intake during pregnancy and early infancy on the mother and her offspring, which could also give us some information about the recommended daily dietary allowances under these circumstances.

The incidence of low birth weight in Tanzania has been shown to be high (15%) when compared with so called afflu-

* These studies have been submitted for publication to the American Journal of Clinical Nutrition.

ent populations (6-7%) (7). However, the greater growth velocity between 34 and 38 weeks gestation of the Tanzanian fetuses (7) when compared to fetuses in the developed countries (8) may indicate well being in Tanzanian fetuses in the last months of pregnancy -a period which seems to be critical for the normal development of brain (3, 9, 10). This is also the stage when the fetus builds up most of its energy stores, like glycogen and especially fat, needed for metabolism at and immediately after birth when the food intake is still insufficient. Postnatally, an adequate supply of nutrients is of importance for the further development of the brain (3).

In this study emphasis was placed on the follow up of 90 almost exclusively breast-fed children, during the first six months to collect anthropometric data relating to cross-sectional growth standards and growth velocity. These data and those from a previous study on intrauterine growth (8) were combined to draw a perinatal growth chart for the population of Dar es Salaam, Tanzania.

In addition some biochemical, immunological and haematological characteristics of maternal/cord serum pairs of these term singleton births and their mothers immediately after delivery are presented. Perinatal circumstances are discussed in comparison with those of Western countries.

MATERIAL AND METHODS

This survey forms part of a comprehensive study of the interaction between malaria and pregnancy carried out between September 1976 and September 1977 at the university hospital: Muhimbili Medical Centre and Ocean Road Hospital. The latter is a government maternity hospital run by the Department of Obstetrics of the University of Dar es Salaam. This unit only admits normal pregnancies. The university hospital only admits at risk pregnancies. Approximately 90% of all deliveries in Dar es Salaam (700,000 people) are performed in these hospitals.

Age, marital status and past obstetric history were recorded from 300 pregnant Tanzanian women who lived within a 10-mile radius of Dar es Salaam. For details regarding local health facilities, population, geographical and socio-economic circumstances see previous studies (7, 11).

Standing height of mothers was recorded in centimeters. The left mid-upper arm circumference was measured with a non-stretchable tape measure to the nearest 0.5 cm. Just after delivery anthropometric measurements were made on the newborn infant. Gestational age of the newborn infant was assessed using the neonatal physical and neurological scales of maturation described by Dubowitz *et al* (12).

At delivery the umbilical cord was carefully cleaned before collection of approximately 10 ml of whole cord blood. Immediately after birth 5 ml of venous blood was taken from the anterior cubital vein of the mother. The haematocrit was measured directly in both samples and the rest was left to clot at room temperature ($\pm$ 23^{o} C) for approximately half an hour. Serum was than separated by centrifugation and stored at -20^{o} C until analysed.

Serum protein was analysed by the Biuret reaction. Electrophoresis of serum proteins was performed on cellulose acetate strips using the Beckmann Microzone electrophoresis equipment and the Beckmann densitometer Model R-110. Immunoglobulin A, G and M were measured by single radial immuno-diffusion (13). Because of the low concentrations to be expected for IgA and IgM in cord blood, low concentration radial immuno-diffusion techniques were used for those determinations. Serum cholesterol was analysed by the Liebermann Burchard reaction (14). Serum triglycerides were analysed according to Fletcher (15).

All laboratory investigations were checked by the laboratories of Sophia Children's Hospital, Rotterdam, The Netherlands. The correlation coefficient (r) of the investigations performed in Dar es Salaam and those in Rotterdam was greater than 0.9.

From the whole population, 90 typical term singleton births (48 males and 42 females) of whom 24 were first born babies were examined according the following protocol: at birth + 2 Hrs, at 1 month ± 4 days, 2 months ± 1 week, 3 months ± 1 week, 4 months ± 1 week, 5 months ± 1 week and at 6 months ± 1 week of age. Measurements outside these intervals were not included. Infants with congenital malformations or with an one-minute Apgar score of less than 8 were excluded. All infants in the follow up study were born after an uneventful pregnancy by normal vaginal delivery.

All examinations were performed by trained examiners under supervision of the author using standardised techniques previously described (7). Capillary haematocrit was taken from the infants routinely at 3 and 6 month of age. In *Table I* and *II* the mean (± S.D.) of various anthropometric and clinical data of the infants followed at birth and

Table I. Clinical data on Tanzanian women at term on the day of delivery (mean ± SD). Number of determinations in parenthesis.

Number	90
Age, years	23.6 ± 4.8 (88)
Parity	2.9 ± 1.8 (89)
Height, cm	154.4 ± 6.4 (83)
Arm circumference, cm	25.5 ± 2.6 (84)

Table II. Anthropometric and clinical data (mean ± SD) of 90 term infants at birth.

Number	90
Weight, g	3027 ± 465
Length, cm	49 ± 1.9
Head circumference, cm	34.3 ± 1.3
Ratio males : females	48 : 42
Gestational age, weeks	39.5 ± 1.1

of their mothers are summarised. The mean and standard deviation were determined for each anthropometric measurement for each group of infants. The groups were separated by the age at which they visited the postnatal clinic according the protocol. Resulting figures were plotted at monthly intervals and smoothed arithmetically to construct the cross-sectional type of standards as shown in the postnatal growth curves. Increments of growth (growth velocity) were obtained by subtracting the values of the anthropometric measurements at the earlier age from the values at the later age. If a child missed an appointment within the protocol period an increment for that span of time was not included. This explains the differences in sample sizes for incremental growth (growth velocity) and the cross-sectional studies. No attempts were made to chart the sexes separately. Of the 90 term infants followed 55 (61%) returned at 1 month, 68 (76%) at 2 months, 58 (64%) at 3 months, 44 (49%) at 4 months, 39 (43%) at 5 months and 37 (41%) at 6 months of age. Failure to attend for examination at the different time intervals were mostly geographic moves, transport problems and heavy rains during the rainy season.

The statistical significance between means was measured by Student's t-test.

RESULTS

Maternal versus cord blood tests

Fetal and maternal concentrations (mean ± S.D.) of total protein, albumin, γ-globulin, immunoglobulins (IgG, IgM and IgA), total cholesterol, triglycerides and haematocrit value at delivery are summarised in *Table III*. Each variable showed a nearly normal distribution, except for IgA in maternal serum and for triglycerides, IgM and IgA in cord blood. These showed a bimodal distribution, with a second peak in the higher concentration.

Mean total protein concentration was slightly, but not significantly higher in cord than in maternal sera (7.0 ± 0.6 versus 6.7 ± 0.8). The mean albumin value in cord sera was higher than in the corresponding maternal sera ($p < 0.001$). In the majority of cases (88%) a higher concentration of IgG was found in maternal than in cord sera. No difference was found between mean concentration of IgG from maternal sera of primipara and that of multipara mothers (2018 ± 689 versus 2025 ± 370 mg/100 ml respectively). In general higher values in the mother corresponded with higher values in the infant at birth. No notable differences in mean concentration of IgG, IgM and IgA were detected between male and female children. Mean IgG in cord serum was higher in children of primipara than those of multipara mothers (1723 ± 454 versus 1327 ± 292 mg/100 ml respectively). This difference was not found for IgA and IgM. IgM was detectable in all the cord sera. In 23 (29%) of the children, IgM values were 20mg/100 ml or greater. Among this group of infants mean birth weight was 3125 g, whereas in the group as a whole mean birth weight was 3027 g (even when matched for parity and height

Table III. Total protein, albumin, γ-globulin, IgG, IgM and IgA, total cholesterol, triglycerides and haematocrit of 90 maternal/cord serum pairs (mean ± SD). n = Number of serum pairs examined.

Data	*n*	*Maternal serum*	*Cord serum*
Total protein, g/100 ml	80	6.7 ± 0.8	7.0 ± 0.6
Albumin, g/100 ml	80	2.8 ± 0.4	4.2 ± 0.3
γ -globulin, g/100 ml	80	1.5 ± 0.26	1.4 ± 0.26
IgG, mg/100 ml	82	2022 ± 477	1414 ± 377
IgM, mg/100 ml	82	173 ± 41	20.0 ± 12.6
IgA, mg/100 ml	82	129 ± 79	5.2 ± 5.3
Total cholesterol, mg/100 ml	81	248 ± 49	80.5 ± 18.1
Triglycerides, mg/100 ml	80	167 ± 62	30.4 ± 21.3
Haematocrit, %	80	38.5 ± 3.8	58.0 ± 8.1

of the mother no notable differences were found). The mean IgA level in the term infants was 5.2 mg/100 ml (range 0-19 mg/100 ml). IgA could not be detected in 30% of the infants.

Mean cholesterol level in maternal sera was 248 ± 49 mg/100 ml (range 153 - 335 mg/100 ml) equivalent to 6.35 ± 1.25 mmol/l (range of 3.9 - 8.6 mmol/l). In the corresponding cord sera mean value was 80.5 ± 18.1 mg/100 ml (range 46 - 115 mg/100 ml) equivalent to 2.1 ± 0.5 in mmol/l (range 1.18 - 2.9 mmol/l).

Postnatal growth of term infants

90 Singleton term infants (from whom the anthropometric measurements at birth were given in *Table II*) were followed monthly from birth to the age of 6 months. Histograms were

drawn for the frequency distribution of weight for each month between 0 and 6 months (*Figure 1*). A nearly normal distribution was found in all age groups. Data relating the mean anthropometric data (± S.D.) for each month are recorded for both sexes in *Table IV*. Smoothed growth curves were plotted from these cross-sectional data in which the mean ± 2 S.D. for weight, crown-heel length and head circumference are shown against postnatal age for both sexes. These growth curves are shown together with the intrauterine growth curves for both sexes obtained in a previous study (7) as the perinatal growth chart for Dar es Salaam, Tanzania (*Figure 2*).

Data relating to mean postnatal growth velocity (± S.D.)

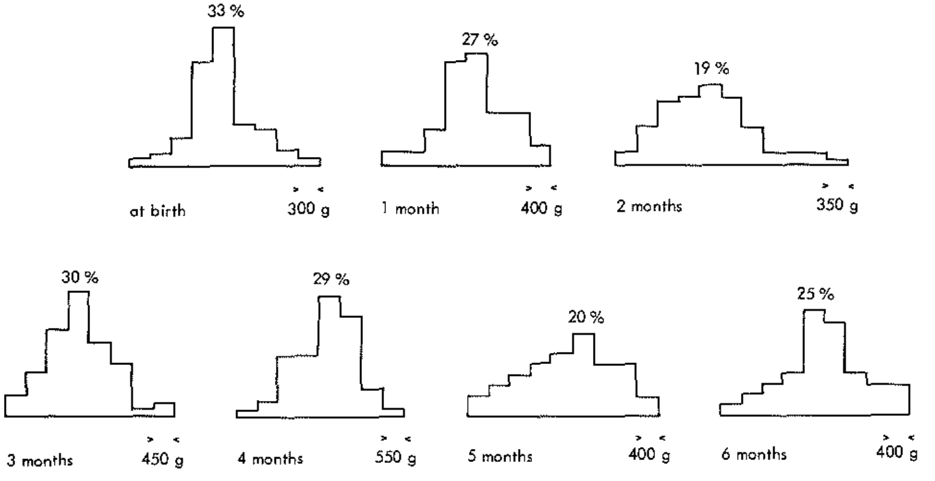

Fig. 1. Histograms showing frequency distributions of weight at various ages after birth. The peak distribution for each histogram is given in percent.

Table IV. Anthropometric measurements of 90 term infants (males 48, females 42) followed during the first 6 months postnatally. Mean ± SD of the cross-sectional growth measurements.

Age (months)	*Number of infants*	*Weight(g)*		*Length (cm)*		*Head circumference (cm)*	
		Mean	*S.D.*	*Mean*	*S.D.*	*Mean*	*S.D.*
at birth	90	3027	465	49.0	1.9	34.3	1.3
1	55	4153	646	54.2	2.2	37.5	1.4
2	68	4943	754	56.3	2.2	38.9	1.6
3	58	5825	736	59.0	2.0	40.5	1.5
4	44	6307	824	61.1	2.1	41.5	1.5
5	39	6579	822	63.0	1.9	42.1	1.4
6	37	6901	1276	64.4	1.8	42.9	1.4

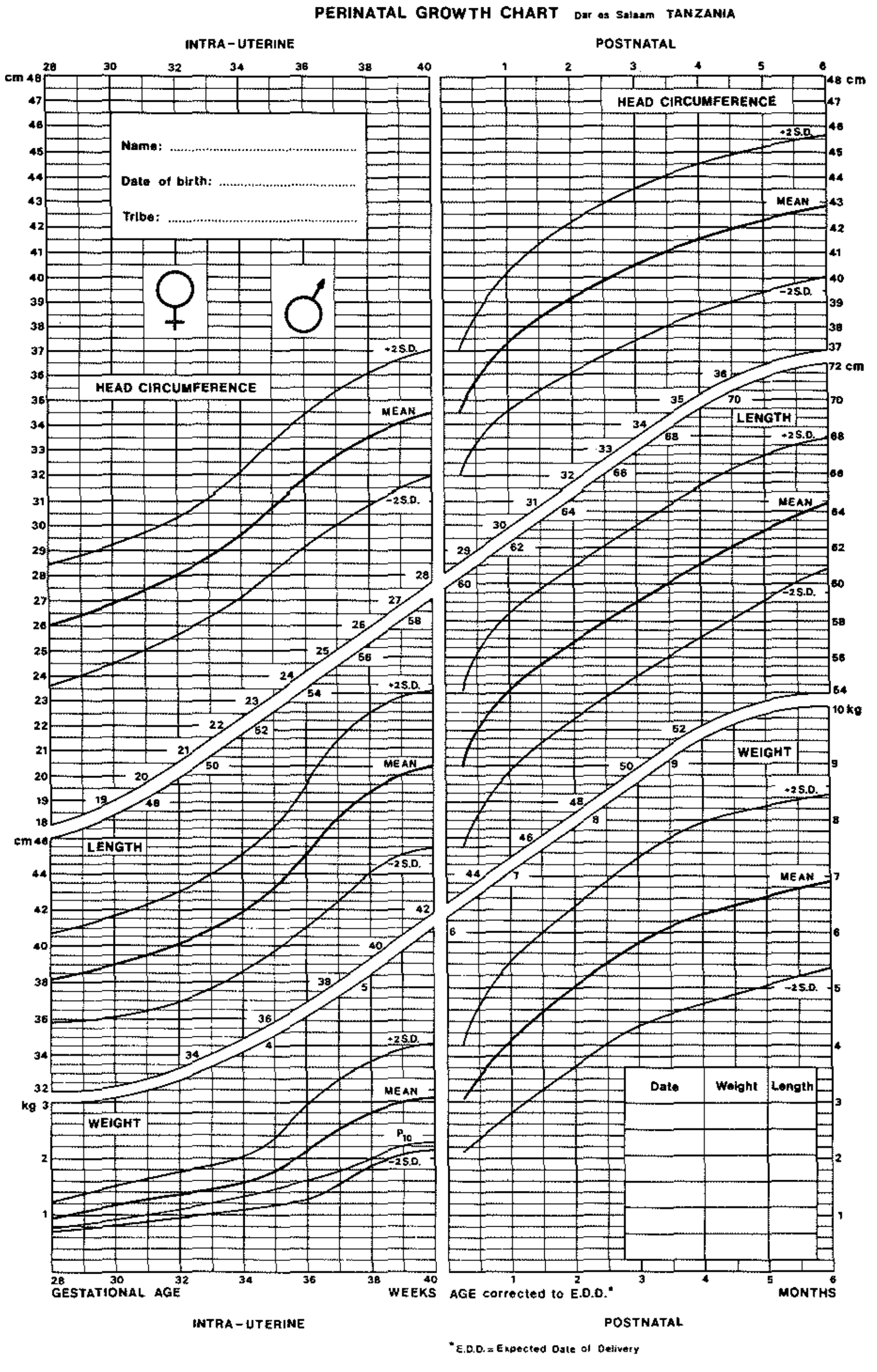
PERINATAL GROWTH CHART Dar es Salaam TANZANIA
INTRA-UTERINE
POSTNATAL
Name: ....
Date of birth: ....
Tribe: ....
HEAD CIRCUMFERENCE
LENGTH
WEIGHT
+2 S.D.
MEAN
−2 S.D.
P_{10}
Date
Weight
Length
GESTATIONAL AGE
WEEKS
AGE corrected to E.D.D.*
MONTHS
INTRA-UTERINE
POSTNATAL
*E.D.D. = Expected Date of Delivery

Fig. 2. Perinatal growth chart for both sexes. The left part of the chart shows the intra-uterine growth curves (7), on the right the growth curves postnatally after term are shown. For infants born before term correction of postnatal age should be made according to the expected date of delivery (E.D.D.).

Table V. Postnatal growth velocity of term Tanzanian infants of both sexes at designated intervals.

Mean increments ± S.D.	*Postnatal age intervals in months*					
	Birth - 1	*1 - 2*	*2 - 3*	*3 - 4*	*4 - 5*	*5 - 6*
Weight, g	1233 ± 472	825 ± 387	872 ± 401	519 ± 340	348 ± 297	432 ± 237
Length, cm	5.5 ± 1.4	2.4 ± 0.9	2.4 ± 1.1	2.0 ± 1.0	1.9 ± 1.2	1.4 ± 0.8
Head circumference, cm	3.2 ± 0.9	1.7 ± 0.8	1.5 ± 0.7	0.9 ± 0.6	0.8 ± 0.5	0.8 ± 0.5
Number of infants	55	41	46	44	35	33

are recorded at monthly intervals in *Table V*. The most rapid growth in all parameters occurred during the first month of life. The mean rate of gain in weight was 1223 g during the first month of life, equivalent to 41 g per day. During the same interval the mean rate of gain in crown-heel length was 5.5 cm and in head circumference 3.2 cm. During the second and third month of life increments in weight were approximately 840 g per month (equivalent to 28 g per day). This growth velocity for weight was not maintained in the 4th, 5th and 6th month of life and slowed to approximately 14 g per day. The same pattern of growth velocity was found for crown-heel length and for head circumference.

Haematocrit values (± S.D.) of these infants were 58 ± 8% at birth, 34 ± 4.4% at 3 months and 33 ± 3% at 6 months of age.

DISCUSSION

Environmental and dietary circumstances

On average Bantu adults in the urban surroundings of Dar es Salaam consume a limited amount of nutrients. The only documented survey of family consumption in rural Kisarawe, a district immediately south of Dar es Salaam showed an intake of approximately 1970 Cal. per person per day (16). The daily intake of pregnant women, all mainly of Bantu descent living in the same district has been calculated by Maletnlema and Bavu (17) to be approximately 1900 Cal., with a mean protein intake of 52 g (S.D. ± 19) per day. If converted to reference protein the mean intake was 32.4 g (S.D. ± 10.4) per woman per day. The diet of pregnant women in Maletnlema and Bavu's survey

(17) was based on cassava and a stiff maize porridge which contributed about 40% and 15% of the total energy intake respectively, whereas rice, coconut and pulses contributed 10% each. White sugar amounted to about 5% of the total energy intake. 30% of the protein was derived from fish, 10% from pulses, 10% from maize and 5% each from rice, meat and cassava. The main source of fat eaten by the subjects in this study was from fresh coconuts. Apart from iron, the intake of all other nutrients was below F.A.O./ W.H.O. recommendations (18). Vitamin A and calcium were relatively more deficient in the diet than calories and proteins.

In Dar es Salaam the average pregnant women takes one heavy meal per day and in addition 2 to 3 light meals consisting either of sugared tea with bread or a soft maize porridge (uji) with sugar. Green vegetables such as amaranth (mchicha) and leaves of the cassava plants are eaten regularly. No exact information is available regarding her energy expenditure. It is likely that the reduced energy intake of the pregnant women will be compensated for by cutting down on daily activity. After delivery the mother is given help by relatives for a few weeks. Immediately the child is born it is placed on the breast and induced to suck. This is an important attachment for the mother to know that she has a normal child who is able to suck. During the first few days when the colostrum is not enough most mothers give their children plain water, water with cane sugar and some add a little bit of salt to the water. All mothers sleep in the same bed with their newborns from the time of birth. This provides warmth and breast-feeding can be done on demand even during the night. During the first 40 days mothers are kept indoors and are fed on the same diet as that of other adults sometimes with extra milk. The food is made a little softer for it is believed "hard" food stops milk production. Exclusively breast-feeding is practised for the first 5 to 8 months after which gradually supplementary feeding is introduced as a thin porridge of maize flour or cassava (uji). The duration of breast-feeding varies but most mothers keep on breast-feeding until she becomes pregnant again, when the child is 1 to 2 years old.

This study

In general, mean anthropometric measurements of the mothers and their corresponding term infants were comperable with those of our previous studies on a population of 16,532 pairs of mothers and their infants (7, 11). On average, height of mothers living in Europe and U.S.A. (19, 20) is greater than that seen in this study. An important part of the difference of average birth weight between the "Westernised" countries and Tanzania can be accounted for by the difference in height of the mother, as maternal height affects birth weight more than gestational age (11, 21). In this study the mid-upper arm circumference, as suggested by Lechtig (22), was not a reliable tool in giving evidence of undernutrition in mothers who gave birth to low birth weight infants. In fact, as shown by multiple regression analysis, arm circumference, like the incidence of low birth weight, was related to the age of the mother ($r = 0.4536$), so that a direct relationship could not be expected.

During normal pregnancy in *Caucasian women* the following biochemical and immunological changes have been documented (23-30): haematocrit values fall in relation to gestation with a slight rise toward term to approximately 35%; total serum protein falls within the first trimester and reaches a plateau of 5.9 to 6.4 g/100 ml at about mid-pregnancy; albumin concentrations tend to fall in early pregnancy to values of 2.4 - 2.75 g/100 ml, γ-globulin values tend to fall to levels of approximately 1.0 g/100 ml, whereas IgG appears to be lower in pregnant than in non-pregnant women. However the IgA and IgM fractions showed no systematic changes during pregnancy. Cholesterol values rise considerably but the level of cholesterol declines somewhat in the last trimester of pregnancy. The exact mechanisms responsible for these changes are still uncertain. When we compare the "normal" biochemical and immunological values at the end of pregnancy for Caucasian women, as just described, with those obtained in this study, generally higher values were found in *Tanzanian women* for venous haematocrit, total proteins, albumin, γ-globulins and immunoglobulins (IgG, IgM and IgA). Somewhat higher values for total protein (7.2 - 8.0 g/100 ml) were found in well nourished African, Hindu and Bantu women towards the end of pregnancy by Sénécal (31, 32). The mean IgG and IgA levels in maternal sera of Nigerian women at the end of pregnancy (33) were even higher (2700 mg/100 ml and 244 mg/100 ml respectively) than those found in this study (2022 mg/100 ml and 129 mg/100 ml), whereas mean maternal IgM level was higher in this survey (173 mg/100 ml versus 92 mg/100 ml in Nigeria). It was interesting to note that the IgG value in maternal sera was generally higher than that found in the corresponding fetal circulation. This was contrary to findings for Caucasian materno/fetal sera but agreed with findings from Nigeria (33). Although in underdeveloped countries lower cholesterol values have been found in non-pregnant women, at the end of pregnancy total cholesterol values in Tanzania (6.35 ± 1.25 mmol/l) did not differ notably from those in countries in the West: 6.05 - 6.48 mmol/l (25, 34). A wide range of maternal triglycerides was found in this study (72 - 352 mg/100 ml). Mean values (167 ± 62 mg/100 ml) were slightly lower than that found by Friedman (35) in the U.S.A. (193 ± 56 mg/100 ml). The small numbers involved in the study by Friedman (35) made a comparison difficult.

In the term *Caucasian infant* born by vaginal delivery after a normal pregnancy the following biochemical and immunological data have been documented (30, 36-39): total protein values range from 5.5 to 6.3 g/100 ml; albumin concentrations vary between 2.8 and 4.2 g/100 ml, but are usually below 3 g/100 ml; mean γ-globulin fraction reaches a mean value of 1.2 g/100 ml (range 0.9 - 1.3 g/100 ml); mean IgG values range between 800 and 1500 mg/100 ml, whereas mean IgM values vary from 6 to 17 mg, but are undetectable in approximately 25% of the Caucasian infants; whereas IgA is usually undetectable in 70 - 100% of the infants at birth.

When these "normal" data, just summarised for Caucasian term infants at birth, are compared with those for the *Tanzanian infant* (see *Table III*) higher values were found for total protein, albumin, γ-globulin and all immunoglobulins investigated (IgG, IgM and IgA). Since the fetus synthesises most of its own proteins, with the exception of IgG, from amino acids which have been transferred across the placenta (40) it can be assumed that the rate of synthesis of these proteins by the Tanzanian fetus is greater than that found for the Caucasian fetus during the last stage of pregnancy. In this respect the greater skeletal maturity discovered in bush-negro infants at birth (41), when compared to British newborns, is an intriguing finding. It is uncertain whether the increased maternal amino acid levels in Tanzanian women (42), leading to a reduced placental gradient, could be one of the mechanisms to maintain an adequate supply of amino acids to the fetus in the last stage of pregnancy. Like the observation in Nigeria (33), the high endogenous synthesis of IgM and IgA in the fetus can be probably explained by increased induction from antigenic stimuli in the maternal environment. It was beyond the scope of this study to evaluate the incidence of intrauterine infections among the group of infants studied, although it can be mentioned that in 2 infants malaria parasites were found in their cord blood in whom one had an IgM level of 41 mg/100 ml and the other of 13 mg/100 ml. The mean birth weight of infants with IgM levels more than 20 mg/100 ml (30% of the infants) was not significantly different from that of the whole population.

Cord blood cholesterol levels in Europe and the U.S.A. fall in the 60 - 80 mg/100 ml range (25, 34, 35, 43-48). In this study mean cord blood value was 80.5 mg/100 ml, without notable differences between males and females (81 and 80 mg/100 ml respectively). In 12 infants (15%) total cholesterol levels were ≥100 mg/100 ml. Values for cord blood triglycerides in Europe and U.S.A. range from 32 - 44 mg/100 ml (35, 44, 47, 48). In our study these values for males were 25 mg and for females 35 mg/100 ml. Mean value of triglycerides among infants born with a birth weight below 2.5 kg (n = 8) was 45 mg/100 ml, notably higher than that of the whole population. The mean cholesterol level of these L.B.W. infants was not different from the whole population. This hypertriglyceridemia among the infants with low birth weight might be associated with fetal stress (47). In a study on serum lipids in Tanzanian children (unpublished observation) mean total cholesterol levels at the age of one year increased to 144 mg/100 ml (3.7 mmol/l) but were lower than in British infants (191 mg /100 ml or 4.9 mmol/l) (43). Up to the age of 6 years cholesterol values remained virtually constant at 156 mg/ 100 ml (4 mmol/l), so lower than in Western countries (49, 50).

Limitations of longitudinal and cross-sectional studies are well documented by Eveleth and Tanner (20). One limitation of a longitudinal study on growth is the inevitable missing of follow up appointments during the course of the study period. Although data were insufficient to chart the sexes separately, males were on average approximately

100 g heavier than females at birth, 300 g heavier at 3 months, and 400 g heavier at 6 months of age. Like Gairdner and Pearson (51) and Tanner and Whitehouse (52) for Western countries, a perinatal growth chart has been designed by us for the population of Dar es Salaam, Tanzania for use in Infant Welfare Clinics (*Figure 2*). This chart makes it possible to plot the weight, length and head circumference of preterm and other infants of both sexes during the period of 28 weeks of fetal life to 6 months of postnatal age, if a correction is made by taking the expected date of delivery (E.D.D.) as the effective date of birth. So an infant born 6 weeks before term, correction of postnatal age is made by subtracting 6 weeks from the postnatal age. No analogous correction of postnatal age need to be made for an infant born post term, since growth in utero after term is negligable (7). Our perinatal growth chart also includes the growth in head circumference, which might be an aid in detecting hydrocephalus.

When postnatal growth and growth velocity for the Tanzanian almost exclusively breast-fed infants are compared with those from European infants, mainly on formula feeding (as compiled by Eveleth and Tanner) (20) the most striking difference found was the increased rate of growth for weight, crown-heel length and head circumference for the Tanzanian infant in the first month of life. Although at birth, on average, the Tanzanian infants lag approximately 500 g behind in weight, 2 cm in length and 1 cm in head circumference, at the age of one month all measurements were greater or equal to those for European infants. During the 2nd and 3rd month the growth velocity for all parameters fell within the European range but after the 3rd month a reduction in growth velocity for weight and length was observed, whereas the rate of growth for head circumference diminished after the 5th month of life when compared to Western standards. In most growth studies of infants of African origin (reviewed by Eveleth and Tanner)(20), in which measurements were taken every three or, more usually six months, growth velocity tended to remain within the European standards until the age of six months.

At present it cannot be stated with certainty whether the increased rate of growth of the Tanzanian infant during the first month can be explained by an increased energy intake or a reduced energy expenditure e.g. at night when the infant shares the bed with the mother (reduced heat loss, night feedings), or a combinations of both. The specific fatty-acid composition of Tanzanian human milk fat (53) could indeed have a benificial influence on the extent of intestinal absorption of fat in the newborn infant. Another factor to explain the difference in growth rate between Caucasian and Tanzanian infants postnatally could be that the Tanzanian fetus retained less body water per kg body weight during pregnancy, which resulted subsequently in a reduced excretion of the excess of water in the first days postnatally. The assumption is supported by clinical observations of a less marked weight loss postnatally and a more rapid regain of weight subsequently (the Tanzanian infant has regained his birth weight approximately 7 days after birth, whereas the Caucasian infant (54) on average after 10 days). Other factors to be considered are the ease with which abundant lactation is established after delivery, although studies in Kenya (55) showed a comparable daily intake of breast milk during the first month of lactation to that of well nourished mothers in Western countries (56).

In conclusion we might state that, although the usual diet of Tanzanian mothers hardly meets recommended allowances as suggested by F.A.O./W.H.O. (18), an adequate rate of growth was observed in the last stage of pregnancy

(7) and during early infancy, which suggests a sufficient supply of nutrients from the mother to her offspring. The present biochemical and immunological data further substantiate the finding of adequate protein synthesis.

The process of birth seems to interfere for a shorter span of time the high rate of growth when compared to Western countries. It is likely that the difference in birth weight between countries like Tanzania and the Western countries is to a certain degree *not* due to a real difference in lean body mass but merely to a difference in total body water. Body composition studies are needed to prove this.

SUMMARY

Although the usual diet of Tanzanian mothers hardly meets recommended allowances, no deleterious effects could be demonstrated on the fetus or young infant. A perinatal growth chart is drawn, which covers a period from 28 weeks of fetal life to 6 months of postnatal age, and allows weight, crown-heel length and head circumference to be charted for use in infant welfare clinics. Prenatally (34-38 weeks gestation) and postnatally (first month), growth velocity was relatively rapid. It seems that the process of birth did not interrupt to the same extent the high rate of growth as observed in Western countries.

At delivery serum values for total protein, albumin, γ-globulin and immunoglobulins in mothers and their term offsprings were higher than those found in studies on Caucasians in Europe and the U.S.A. Total cholesterol and triglycerides values in maternal/fetal sera were almost equal to those of Western standards.

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SUMMARY

In this thesis our own and collaborative work on some physiological aspects is reported for the Tanzanian pregnant woman and her offspring during the last stage of pregnancy and during early infancy and related to data from the literature.

The *introduction* stresses the uncertainties on the effect of restricted maternal nutrition in man on fetal and subsequent growth and development. Although in animals a substantial influence has been documented, it seems reasonable to state that the results of these studies in man are far less conclusive, due to the absence of adequate physiological knowledge under these circumstances. The problem in man is still to find a suitable experimental situation for detailed investigations. Since maternal undernutrition prevails in Tanzania according the criteria laid down by the FAO/WHO(1973), we took the opportunity to study some aspects of the feto/maternal relationship under these circumstances, in an attempt to clarify some of the physiological and metabolic uncertainties.

In *Chapter one (Section A)* the anthropometric standards for fetal weight, crown-heel length and head circumference are given for the last stage of pregnancy. This study was required in order to quantitate normal and abnormal fetal growth patterns in Dar es Salaam, Tanzania. Details regarding local health facilities, population, geographical and socio-economic circumstances are given. From a popula-

tion of 16,532 live births the mean weight for both sexes at 28 weeks of gestation was 960 g, the crown-heel length 38.2 cm and the head circumference 26.0 cm. At 40 weeks gestation the mean weight was 3070 g, crown-heel length 49.8 cm and head circumference 34.5 cm. When the intra-uterine growth curves for Dar es Salaam were related to similar measurements obtained from Caucasian infants (Usher and McLean, 1969), a reduced growth velocity in all three variables was observed between the 30th and 34th week of gestation, whereas an increased growth velocity was found between 34 and 38 weeks of intrauterine life. Although their mean weight was approximately 500 g less at term, the more rapid speed of growth during the last stage of pregnancy may suggest a relative well being of the Tanzanian fetus during this period. The lower mean birth weight observed in Tanzania compared with Western standards, resulted in a higher incidence of low birth weight infants (15% against 6-7% respectively). A birth weight of 2500 g or less has been defined more or less arbitrarely to indicate a high risk group. In *Chapter one (Section B)* some environmental, fetal and maternal factors associated with the birth of low birth weight infants were studied. The incidence of low birth weight was higher among infants of parents of a low socio-economic group and among female infants. Primiparity, short stature of the mother, multiple pregnancy were some of the factors influencing the growth velocity of the fetus, leading to an increased incidence of small-for-dates infants (defined by an infant with a birth weight below the 10th percentile for gestational age). Low maternal age and antepartum hemorrhage mainly affected the duration of gestation, which led to a preponderance of infants born preterm (born before 37th completed week of gestation). In 66% of the mothers with low birth weight infants no associated maternal complication of the pregnancy could be detected. These results were not appreciably different from studies in Western countries. It seems reasonable to reduce the level of 2500 g by 500 g to define a low birth weight infant for those populations with a mean birth weight of approximately 3000 g.

Chapter two describes two studies on protein metabolism in mother and infant immediately after delivery. *Section A* reports on the pattern of free serum amino acids in 20 apparently healthy mothers immediately after delivery and in cord blood from their term appropriately grown infants, as defined by local standards (presented in Chapter one, section A). These studies show that the individual amino acid concentrations were generally higher in Tanzanian women when compared with Swedish standards, whereas slightly higher or similar values were found in cord blood. This resulted in a marked reduction of the feto/maternal ratio for the individual amino acids in Tanzania. It is uncertain whether the specific amino acid pattern found in Tanzania could be one of the mechanisms to maintain an adequate supply of amino acids to the fetus during the last stage of pregnancy. The validity of the glycine/valine index in recognising early protein malnutrition in pregnant women and their offspring, as observed in kwashiorkor, is not supported by these studies. *Section B* reports on serum total protein, albumin and immunoglobulins (IgG, IgM and IgA) in maternal/cord blood pairs of normal term, preterm and small-for-dates infants. Generally higher values were detected for total protein, albumin and IgG in maternal blood towards the end of pregnancy compared to Western standards. In cord blood the concentration of total protein, albumin and IgG were also generally higher compared with values found in Western countries. In addition, a higher detection rate was found for IgM and IgA, which might be explained by an increased induction of fetal humoral antigenic stimuli in the maternal environment. Contrary to findings in Western countries, IgG in the maternal sera was generally higher than in the corresponding fetal circulation. It appears that the net rate of synthesis of serum proteins we studied -with the exception of IgG (which is mainly of maternal origin)- is greater than that found for the Caucasian fetus during the last stage of pregnancy.

In *Chapter three* two studies on lipid metabolism in mothers and their infants before and after birth are presented. Previous studies have shown differences in serum lipid levels between the developing and the developed countries during childhood and adult life. This prompted us to evaluate whether this was so during pregnancy in the mother and her offspring and during infancy and early childhood. In *Section A* serum total cholesterol and triglycerides were determined in cord blood of 54 term appropriate for gestational age, 14 preterm appropriate for gestational age and 17 small-for-dates infants (as defined by local standards) and in venous blood of their mothers immediately after delivery. Results show that values of mean total cholesterol and triglyceride concentrations of the mothers and their infants of the term appropriate for gestational age group correspond with studies from Western countries. Results of the maternal and cord serum lipids in the two low birth weight groups are also similar to those of Western countries. It seems that the nutritional and environmental factors, which are regarded by many to influence the serum lipid values after birth and in adult life, had no detectable influence on these levels in the mother and fetus during pregnancy. In *Section B* the changes in fatty-acid composition of body fat before and after birth in Tanzania are presented. Results are compared with data for British and Dutch infants and a comparison of diets is made. It appears that the differences in the fatty-acid composition of the body fat between the three countries were subtle during the last stage of pregnancy but were most pronounced during infancy and early childhood, which was apparently attributable to the nature of the dietary fat consumed respectively in Tanzania, Great Britain and The Netherlands. The specific fatty-acid composition of the fat in Tanzanian breast milk, with a high percentage of the medium chain fatty acids, could contribute to even better intestinal absorption of the fats in this milk than the fats in human milk from Western countries. An adequate supply of the essential fatty acid, linoleic acid, from the Tanzanian mother to her offspring, before and after birth was found.

Chapter four describes the studies on total maternal weight gain during pregnancy in Rubya, Tanzania. Total maternal weight gain was approximately 6 kg, which is 5 to 6.5 kg less than observations in Western countries. It is thought that the difference of weight gained between the Tanzanian and Caucasian women is to a great extent attributable to the storage of water in the intra and extravascular compartments and/or storage of fat and not to the formation of new maternal or fetal lean body mass.

In *Chapter five* the anthropometric data of 90 almost exclusively breast-fed Tanzanian infants who were followed postnatally for the first 6 months are given. These postnatal standards and those obtained "antenatally" (Chapter one, Section A) were combined to construct a perinatal growth chart, which covers a period from 28 weeks of fetal life to 6 months of postnatal age and allows weight, crown-heel length and head circumference to be charted for use in infant welfare clinics. It appears that the growth velocity was relatively rapid prenatally (34-38 weeks gestation) and postnatally, particularly during the first month, when compared to Western standards. There is some evidence to suggest that the term Tanzanian infant has a reduced amount of total body water compared to the Caucasian infant at birth, which results in a reduced excretion of the excess of water in the first days postnatally and in a more rapid regain of birth weight. Body composition studies are needed to prove this hypothesis.

We may summarise the perinatal circumstances in Tanzania as follows. Our studies in this thesis failed to support the view that the common diet consumed by the Tanzanian women would have any undesirable influence on the mother or the offspring during the last stage of pregnancy and during early infancy. It seems that the advantage of a greater birth weight, as found in the Western countries, has been overemphasised. Obviously under a wide range of dietary habits, the search for more facts on perinatal physiology in man is required to arrive at more conclusive recommendations regarding the nutritional requirements during pregnancy.

SAMENVATTING

Dit proefschrift beschrijft een onderzoek over enkele physiologische aspecten van de zwangere Tanzaniaanse vrouw en haar vrucht gedurende het laatste trimester van de zwangerschap en van het pasgeboren kind tijdens de eerste 6 levensmaanden. De resultaten werden vergeleken met de gegevens uit de literatuur.

De *Inleiding* belicht de controversen die er op het ogenblik bestaan over de invloed die een beperkte voeding van de moeder zou hebben op de foetale groei en ontwikkeling en op die van de zuigeling. Ofschoon bij dierproeven een duidelijke invloed werd waargenomen, lijkt het redelijk om de resultaten van soortgelijke studies bij de mens controversieel te noemen, hetgeen waarschijnlijk vooral moet worden toegeschreven aan de beperkte physiologische kennis die we op dit terrein wat de mens betreft bezitten. Het probleem bij dergelijke studies bij de mens is een geschikt experimenteel model te vinden dat een directe samenhang (in dit verband) mogelijk maakt. Aangezien in Tanzania, naar de maatstaven van de FAO/WHO (1973), ondervoeding van de zwangere vrouw in grote getale voorkomt, was ik tijdens een vierjarig verblijf in Dar es Salaam in de gelegenheid enkele aspecten van de relatie foetus/moeder onder de daar bestaande omstandigheden nader te bestuderen.

In *Hoofdstuk één (Sectie A)* worden de anthropometrische waarden van het foetus voor lengte, gewicht en schedelomtrek beschreven in het laatste trimester van de zwangerschap. Deze studie was in de eerste plaats nodig om normale en abnormale groeipatronen voor de desbetreffende populatie te kunnen kwalificeren. De bijzonderheden betreffende de locale gezondheidsfaciliteiten, de populatie, de geografische en sociaal-economische omstandigheden worden beschreven. Voor jongens en meisjes was bij een zwangerschapsduur van 28 weken het gemiddelde gewicht 960 gram, de lengte 38.2 cm en de fronto-occipitale schedelomtrek 26.0 cm. Bij een zwangerschapsduur van 40 weken bedroeg het gemiddelde gewicht, waarbij geen onderscheid werd gemaakt tussen jongens en meisjes, 3070 gram, de lengte 49.8 cm en de fronto-occipitale schedelomtrek 34.5 cm. Als men de intra-uterine groeicurves voor Dar es Salaam vergelijkt met die van Usher en McLean (1969) voor Westerse kinderen, dan blijkt er een vertraagde groeisnelheid te bestaan voor zowel gewicht, lengte als schedelomtrek tussen de 30ste en 34ste zwangerschapsweek, terwijl daarentegen een grotere groeisnelheid voor deze drie lichaamsmaten wordt waargenomen tussen de 34ste en 38ste week van de zwangerschap. Alhoewel het gemiddelde geboortegewicht van de voldragen Tanzaniaanse pasgeborene ongeveer 500 gram lager ligt dan dat van pasgeborenen in de Westerse landen, wijst de relatief snelle groei van de Tanzaniaanse vrucht gedurende de laatste fase van de zwangerschap op een relatief goede algemene toestand. Men spreekt min of meer arbitrair van kinderen met een laag geboortegewicht wanneer het geboortegewicht 2500 gram of minder bedraagt, dit om aan te geven dat deze kinderen een vergroot risico kunnen lopen. Het lagere gemiddelde geboortegewicht in Tanzania in vergelijking tot dat van de Westerse landen brengt dan ook met zich mee dat volgens dit criterium meer kinderen met een laag geboortegewicht worden geboren (15% van alle Tanzaniaanse pasgeborenen tegenover 6 tot 7% in Westerse landen). Het onderzoek naar de factoren die in verband gebracht zouden kunnen worden met de geboorte van een kind met een laag geboortegewicht wordt vermeld in *Hoofdstuk één (Sectie B)*. Bij kinderen van ouders behorende tot de lagere sociaal-economische milieus bleek een laag geboortegewicht frequenter voor te komen. Onder pasgeboren meisjes kwam een laag geboortegewicht vaker voor dan onder pasgeboren jongens. Enkele factoren die bleken samen te gaan met vertraging van de intrauterine groei waren primipariteit, kleine moeders en meerlingenzwangerschappen, hetgeen tot gevolg had dat vaker een dysmatuur of "small-for-dates" kind geboren werd. Een dysmature of "small-for-dates" baby wordt gedefineerd als een pasgeborene bij wie het geboortegewicht onder de 10 percentiellijn van de locale intrauterine groeicurve ligt. Een premature baby kwam vaker voor bij jeugdige moeders en zwangeren die bloedingen hadden in het laatste trimester van de zwangerschap. Onder een prematuur wordt verstaan een pasgeborene die vóór de 38ste zwangerschapsweek ter wereld komt. Echter bij 66% van de gevallen kon bij de moeders *geen* duidelijke zwangerschapscomplicatie gevonden worden die met het baren van een kind met een laag geboortegewicht in verband gebracht kon worden. Deze bevindingen stemmen in grote lijnen overeen met de resultaten van onderzoekingen in Westerse landen. Het lijkt redelijk de arbitraire grens van een laag geboortegewicht te verlagen van 2500 gram tot 2000 gram voor die populaties waar het gemiddelde geboortegewicht rond de 3000 gram ligt.

In *Hoofdstuk twee* worden de resultaten beschreven van twee studies die trachten een beter inzicht te geven in het eiwit metabolisme van de moeder en haar vrucht in de laatste fase van de zwangerschap. *Sectie A* beschrijft het patroon van de vrije aminozuren direct na de partus in het serum van 20 klinisch gezonde moeders en dat in navelstrengbloed van hun à terme kinderen, die aan de hand van de locale groeicurves (zoals beschreven in Hoofdstuk een, Sectie A) een adequaat geboortegewicht hadden. De resultaten werden vergeleken met een onderzoek in Zweden. De afzonderlijke concentraties van de aminozuren bleken in de sera van Tanzaniaanse vrouwen in het algemeen duidelijk hoger te liggen, doch de concentraties gevonden in navelstrengbloed stemden overeen of waren slechts weinig hoger dan de overeenkomstige aminozuren-concentraties die in Zweden gevonden werden. Hierdoor werd in onze studie een lagere foetus/moeder ratio voor de afzonderlijke aminozuren gevonden. Het zou mogelijk kunnen zijn dat mede door dit specifieke aminozuren-patroon een adequate toevoer van aminozuren van de moeder naar de vrucht in de laatste fase van de zwangerschap plaats vindt. De waarde van de glycine/valine ratio, als maat voor het herkennen van een eiwitondervoeding in een vroeg stadium bij de zwangere en haar vrucht, bleek, in tegenstelling tot studies elders, niet door onze resultaten ondersteund te kunnen worden. In *Sectie B* worden de resultaten vermeld van het onderzoek naar het serumgehalte van totaal eiwit, albumine en de immunoglobulinen (IgG, IgM en IgA), gemeten in het navelstrengbloed van premature, dysmature ("small-for-dates") en normaal à terme pasgeborenen, alsmede in het serum van hun respectievelijke moeders. Vergeleken met normaalwaarden in Westerse landen werden bij de à terme moeders in het algemeen hogere concentraties gevonden voor totaal eiwit, albumine and IgG. In het navelstrengbloed werd hetzelfde gevonden. Tevens kon in een groter aantal van de bepalingen zowel IgM als IgA in het navelstrengbloed worden aangetoond. Dit laatste zou verklaard kunnen worden door een versterkte activatie van de foetale immunoglobuline synthese door antigene stimulatie via de moeder. In tegenstelling tot bevindingen in Westerse landen, was in het algemeen het IgG-gehalte in het bloed van de moeders hoger dan dat van de vrucht. Afgezien van het IgG dat passief verkregen werd van de moeder via passage door de placenta, laten onze studies een adequate foetale synthese van serum-eiwitten in de laatste fase van de zwangerschap zien.

In *Hoofdstuk drie* worden enkele facetten van de vetstofwisseling van moeder en kind pré- en postnataal beschreven. In *Sectie A* worden de resultaten vermeld van studies waarbij in het serum van het navelstrengbloed het totaal cholesterol- en het triglyceride-gehalte werd bepaald bij 14 premature, 17 dysmature ("small-for-dates") en 54 à terme babies met een adequaat geboortegewicht (aan de hand van de locale intrauterine gewichtscurve). Tevens werd dit bepaald in het serum van het veneuze bloed van hun respectievelijke moeders direct na de partus. De resultaten laten zien dat, aan het eind van een normale zwangerschap, zowel in het navelstrengbloed als in het bloed van de moeder de gemiddelde totaal cholesterol- en de triglyceride-concentraties nagenoeg overeenkomen met die van de Westerse geïndustrialiseerde landen. Hetzelfde geldt voor de groepen premature en dysmature kinderen en hun moeders. Het schijnt dat voedings- en milieufactoren, die volgens velen de concentraties van serum-vetten beïnvloeden, slechts van ondergeschikte betekenis zijn tijdens de zwangerschap voor zowel de moeder als voor haar ongeboren kind. De veranderingen in de vetzuursamenstelling van het subcutane vet van het Tanzaniaanse kind voor en na de geboorte worden besproken in *Sectie B*. De resultaten van deze studies werden vergeleken met die van Britse en Nederlandse kinderen in relatie tot de voeding die de kinderen in de drie respectievelijke landen kregen. De verschillen in de vetzuursamenstelling van het subcutane vet tussen deze landen zijn slechts gering tijdens de laatste fase van de zwangerschap, terwijl deze zeer duidelijk worden tijdens de eerste levensjaren. Dit laatste kan worden toegeschreven aan het type vet dat aanwezig is in de voeding van kinderen in Tanzania, Engeland en Nederland. De specifieke vetzuursamenstelling van het vet in de Tanzaniaanse moedermelk —met een hoog percentage aan middelketen-vetzuren— in vergelijking tot het vet in moedermelk in de Westerse landen, zou bij de pasgeborene kunnen bijdragen tot een verbeterde intestinale vetresorptie. De toevoer van het essentiële vetzuur linolzuur van de moeder naar het kind blijkt voldoende te zijn, zowel in utero als na de geboorte via de borstvoeding.

De totale gewichtstoename van de vrouw tijdens de zwangerschap wordt besproken in *Hoofdstuk vier*. Onze studie vond plaats in Rubya, Tanzania. De gemiddelde gewichtstoename van de moeder bedroeg 6 kg, hetgeen 5 tot 6.5 kg minder is dan die welke werd waargenomen bij studies van vrouwen in de Westerse landen. Het is waarschijnlijk dat het verschil in gewichtstoename voor een groot gedeelte moet worden toegeschreven aan de retentie van water in het intra- en extravasculaire lichaamscompartiment, alsmede aan het toenemen van vetweefsel bij de Westerse vrouwen.

In *Hoofdstuk vijf* worden de anthropometrische waarnemingen voor lengte, gewicht en schedelomtrek beschreven van 90 bijna uitsluitend met moedermelk gevoede, voldragen, Tanzaniaanse kinderen, die tijdens de eerste zes levensmaanden werden vervolgd. De groeidiagrammen van vóór en nà de geboorte werden gecombineerd, zodat het mogelijk werd gewicht, lengte en schedelomtrek bij pasgeborenen te vervolgen vanaf de 28ste zwangerschapsweek tot 6 maanden postnataal. In vergelijking met overeenkomstige groeidiagrammen uit Westerse landen is de groei relatief sneller van de 34ste tot de 38ste zwangerschapsweek en postnataal vooral tijdens de eerste levensmaand. Er zijn aanwijzingen dat de totale hoeveelheid lichaamswater bij Tanzaniaanse à terme pasgeborenen geringer is dan bij pasgeborenen in de Westerse landen, hetgeen zou kunnen samengaan met een verminderde excretie van water in de eerste levensdagen. Hierdoor valt het Tanzaniaanse kind post partum minder in gewicht af en zal sneller zijn geboortegewicht weer bereiken. Alleen onderzoek naar de lichaamssamenstelling zal deze hypothese kunnen staven.

Ter evaluatie van de perinatale omstandigheden in Tanzania mogen we stellen dat onze bevindingen geen aanwijzingen geven dat het voedingspatroon in Tanzania een nadelige invloed zou hebben op de zwangere vrouw of op het kind gedurende de laatste fase van de zwangerschap, alsmede in de eerste levensmaanden, mits het borstvoeding krijgt. Vermoedelijk heeft men de voordelen van een groter geboortegewicht, zoals in de Westerse landen worden gevonden, te sterk benadrukt. Het is duidelijk dat er behoefte is aan meer inzicht en kennis van de perinatale physiologie bij de mens met uiteenlopende voedingsgewoonten. Dan ook zal het mogelijk zijn tot meer gerichte aanbevelingen te komen omtrent de voedingsbehoefte tijdens de zwangerschap en lactatie-periode.

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Almost six years of work in the tropics, two years in Curaçao and four years at Muhimbili Medical Centre in Dar es Salaam, have acquainted me with the basic problems in tropical pediatrics. I am grateful to all who contributed to my education in those years: Professor Dr. M. Hamza, a great teacher with a warm heart, Professor Dr. C.A. Winkel, Professor Dr. V.P. Kimati and many others.

Further, I should like to express my gratitude to all collaborators: Dr. Roger L. Mbise, Ir. Wim Blom, Dr. August W. Massawe and Dr. Ems P.W. Zuidgeest for their part in the study and for their suggestions and criticism; to the co-referees Professor Dr. M. Frenkel and Dr. H.C.S. Wallenburg for their constructive criticism of this manuscript; to Dr. Richard G. Pearse and Dr. Richard P.G. Aisbitt, not only for their many improvements of the linguistic standard of this thesis but especially for their typically English way of giving most valuable constructive suggestions during the elaboration of this work. The stimulating help of Dr. Herman J. Degenhart was indespensable for the statistical evaluations.

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Ruud Boersma.

CURRICULUM VITAE

Na het beëindigen van de middelbare school studeerde de schrijver van dit proefschrift medicijnen aan de Rijksuniversiteit van Groningen. Tijdens deze studie was hij 2 jaar student-assistent bij Prof.Dr. J.W. van den Berg (Medische Fysica) en 3 jaar vakantie-assistent bij Prof. Dr. J.H.P. Jonxis (Kindergeneeskunde). Tijdens deze vakantie-assistentschappen bij Prof.Dr. J.H.P. Jonxis onstond speciale belangstelling voor de physiologie van de pasgeborene. Na het behalen van het artsexamen specialiseerde hij zich in de kindergeneeskunde te Groningen onder leiding van Prof.Dr. J.H.P. Jonxis van 1969 tot 1973. Tijdens deze periode was hij één jaar werkzaam op de kinderafdeling van het St. Elisabeth Hospitaal te Curaçao (Prof.Dr. C.A. Winkel) en 8 maanden als gouvernementsarts op dit eiland.

In 1974 vertrok hij met zijn gezin voor bijna 4 jaar naar Dar es Salaam, Tanzania, alwaar hij de eerste 2 jaar werkzaam was als "Lecturer" en vervolgens 2 jaar als "Senior Lecturer in Child Health" aan de Universiteit van Dar es Salaam (Prof.Dr. M. Hamza, Prof.Dr. V.P. Kimati).

Sinds zijn terugkomst in Nederland in 1977 heeft hij een aanstelling als kinderarts aan het van Dam ziekenhuis en een deelaanstelling als kinderarts-consulent aan de Rijkskweekschool voor Vroedvrouwen te Rotterdam. Tevens is hij als honorair wetenschappelijk hoofdmedewerker aan het Sophia Kinderziekenhuis te Rotterdam werkzaam op de afdeling Pasgeborenen Pathologie van de afdeling Kindergeneeskunde (Prof.Dr. H.K.A. Visser).

ADDENDUM

Paper 1. Reprinted from Tropical and Geographical Medicine

COMMUNICATIONS

INTRAUTERINE GROWTH OF LIVE-BORN TANZANIAN INFANTS

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Summary. The incidence of low birthweight infants, the effect of intrauterine growth retardation on anthropometric measurements, and local standards of intrauterine growth curves for weight, crown-heel length and head circumference together with curves of body measurement ratios of weight/length, weight/head circumference and weight/length x head circumference are presented for the population of Dar es Salaam (Tanzania).

A comparison is made with a standard composed for a Caucasian community with a completely different socio-economic and nutritional status.

From 28 to 34 weeks of gestation weight gain in Dar es Salaam foetuses was reduced, while length and head circumference were relatively less affected. However, an increased intrauterine growth velocity was recorded from 34 to 38 weeks of gestation.

INTRODUCTION

Foetal growth in utero is a function of seed and soil. It is dependent upon the height of the mother, the growth potential of the foetus itself and upon the availability to a healthy intrauterine environment to fulfil this potential. The results of interaction between these factors is a wide distribution of birthweights for any given gestational age and a wide variation of the nutritional status at birth. Extra-uterine survival on the other hand seems to be related more to the duration of the pregnancy than to the birthweight (Lubchenco, 1972). For this reason the degree of maturity at birth is a most useful criterion for the clinician as a guide to the management of a particular infant. This is especially so in the low birthweight infant in whom most of the complications occur. The determination of standards for a neonatal population in a certain area is necessary in order to quantitate normal foetal growth and to enable the assessment of abnormal foetal growth or maturation for that particular society.

Since the growth of foetuses in utero cannot be measured, standards for intrauterine growth can only be based on infants born alive at various gestational ages. It is recognised that premature birth itself is an abnormal feature and will give an indeterminable bias in the data presented. Therefore, the pattern of growth as presented in this communication can only be an approximation of the normal pattern of foetal growth with gestational age (Lubchenco *et al.*, 1966; Usher and McLean, 1969).

The intentions of this study were:

–to assess the incidence of low birthweight (L.B.W.)

–to determine the anthropometric measurements of weight, crown-heel length and head circumference for gestational age and to use these data to construct intrauterine growth curves for the population of Dar es Salaam (Tanzania).

–to determine the effect of impaired intrauterine growth retardation on birthweight, crown-heel length and body measurement ratios for the same population.

MATERIALS AND METHODS.

This study is based on a prospective study carried out at Muhimbili and Ocean Road Hospital between September 1st 1975 and March 31st 1976. These hospitals, the only public hospitals in Dar es Salaam cover approximately 90% of all deliveries in the city. Nearly all are Bantu negroes. A few patients of Asian origin or admixture may occur but their number is so small that it did not influence our results. Most pregnant women of Asian descent are delivered in small private clinics or in the Aga Khan Hospital. The total number of deliveries in these two hospitals together is approximately 26,000 per year. One of these, Muhimbili Hospital, serves as a referral as well as a teaching hospital for doctors, nurses and medical auxiliaries.

The city of Dar es Salaam has a population of 700,000 people, mainly of Bantu descent with a slight preponderance of the following tribes: Wazaramo, Ndengerego, Tumbi, Kwere and Pogoro (Nat. Demographic Survey of Tanzania, 1973). The city is at an average altitude of 50 m above sea level. The average relative humidity is 63-81% and the mean minimum and maximum temperatures are 21.1 and 30.1 °C, respectively, with slight seasonal changes (East. Afr. Meteorological Department, 1968).

The study includes 16,532 consecutive live born infants born during the period under review. The mean birthweight *at term* was calculated from 200 babies drawn randomly from the group of infants selected as suitable for inclusion using the criteria given below. Standards for the construction of intrauterine growth curves of weight, crown-heel length and head circumference were obtained using a method described by Usher and McLean (1969). They measured single live born Caucasian infants at Montreal from 28 to 42 weeks until a sufficient number of cases was obtained at each gestational week for statistical analysis. Standard values were determined at two-week intervals. Based on these data they constructed an *intrauterine growth curve* for the foetal population concerned.

In the part of the study in which we constructed the standards for our population a total of 459 live born infants *of all gestational ages* (206 males and 253 females) selected at random were included. Numbers of infants as separate sexes for the short gestational ages were too small for valid statistical conclusions to be made. For a comparison with *low birthweight infants* (L.B.W.) corresponding values were calculated using exclusively a second group of 458 (204 males, 254 females) infants with a birthweight below the usual cut-off point of 2.500 g.

In the construction of these curves, the following were excluded:

Twins, triplets and quadruplets,

Infants with congenital malformations e.g. hydrocephalus, microcephaly, hydrops foetalis, Down's Syndrome, congenital heart diseases etc.,

Infants with cephalhaematoma and excessive caput succedaneum,

Infants of mothers with E.P.H. gestosis, A.P.H., diabetes mellitus, or any other major illness.

Abbreviations used in this text

A.P.H. – Antepartum haemorrhage; E.P.H. – Edema, proteinuria and hypertension (see also under definitions); H.C. – Head circumference; L.B.W. – Low birthweight; SD – Standard deviation; S.F.D. – Small-for-dates.

Definitions

E.P.H. gestosis – Toxaemia of late pregnancy characterised by hypertension, oedema and proteinuria. This syndrome was commonly known as preeclampsia and eclampsia.

Low birthweight infant – is one whose birthweight is 2,500 g (5 lbs. 8 oz) or less irrespective of the gestational age.

Preterm infant – Born before 37 completed weeks of gestation.

Small-for-dates infant – One whose birthweight is below the 10th percentile for gestational age irrespective of the gestational age.

Term infant – One who is born within 38-42 weeks of gestation.

Socioeconomic Class in Tanzania

Grade	*Annual Income*
I	– More than Tshs. 12,720/– p.a. (about $ 1,590,–)
II	– Tshs. 8,880/– – Tshs. 12,720/– p.a. ($ 1,110,– – $ 1,590,– p.a.)
IV	– Less than Tshs. 8,880/– p.a.

Examination techniques

Measurement of birthweight: The babies were weighed naked to the nearest 5 g, immediately after birth, using a baby weighing machine model No. ZT 10-B (made in China). Equilibration of the equipment was done daily.

Crown-heel length: The baby was held with the head against the top of a vertical board and in a supine position with legs extended. A non-elastic nylon tapemeasure was used and the measurements were taken to the nearest 0.5 cm.

Head circumference: This was measured with a non-elastic nylon tapemeasure. The largest occipito-frontal circumference was taken to the nearest 0.5 cm.

Assessment of gestational age: Information regarding the date of the last menstrual period in women of developing countries is still less reliable according to Stein and Ellis (1974) and Brueton *et al.* (1973). The gestational age was therefore assessed objectively using several characteristics from a scheme, suggested by Lubchenco (1970) and slightly adapted to the dark skin colour of the African newborn (see *Table I*). The method is applicable to both sick and well babies. The assessment was made within 24 hours after birth by one of the authors (R.L.M.).

The criteria used are: oedema, skin colour, skin textures, sole creases, breast size, nipples and earfirmness. The method was checked on 50 infants by another observer using the method suggested

TABLE I
SCHEME USED IN THE ASSESSMENT OF GESTATIONAL AGE

	gestational age							
Sign	*28 weeks*	*30 weeks*	*32 weeks*	*34 weeks*	*36 weeks*	*38 weeks*	*40 weeks*	*42 weeks*
Oedema	present on hands, feet and tibia	no oedema or very slight oedema			n o o e d e m a			
Skin texture and Skin opacity	very thin veins easily visible		thin and smooth large veins visible		veins hardly visible		no vessels visible	desquamation of the skin
Skin colour	dark red	uniformly pink		pale pink; variable	pale skin; pink ears lips, palms and soles		slight pigmentation on scrotum and ears	dark pigmentation on scrotum and ears
Sole creases	n o n e		one anterior transverse crease	two anterior transverse creases	major creases on anterior 1/3 of sole	major creases on anterior 2/3 of sole	major creases present on whole sole	deep creases present on whole sole
Breast size	n o n e			< 2 mm	2–4 mm	5–7 mm	> 7 mm	
Nipples	hardly visible		well defined flat areola			well defined raised areola		
Ear firmness	flat, shapeless no recoil			cartilage soft in places; returns slowly from folding		thin cartilage: instant recoil	firm cartilage; remains erect from head	

by Dubowitz *et al.* (1970). The 95% confidence limit for the estimate of gestational age is 2.3 weeks by this method in our material.

The oedema was checked by observation and testing for pitting of the ankles; the skin colour was estimated by inspection when the baby was quiet, the skin texture was tested by picking a fold of abdominal skin between finger and thumb and by inspection; the breast size was measured by picking up the breast tissue between finger and thumb; the nipple was estimated by inspection; and the ear firmness was tested by palpation and inspection. Only deep creases were taken into account. The gestational age is given to the nearest even week. Statistical significance between means were measured by Student's t-test.

RESULTS

Incidence of L.B.W.

During the study period there were 16,532 live births. Of these, 2,507 (15.2%) were L.B.W. infants made up of 1,111 (44.3%) males and 1,396 (55.7%) females. The male to female ratio was 1 : 1.26.

Anthropometric measurements

(I) Mean birthweight at term. The gestational age was 39.8 weeks (SD 1.4) with a range of 38-42 weeks. The mean birthweight at term for male infants is 3,036 g (SD 518); for female infants it is 2,946 g (SD 458) and overall is 2,991 g (SD 488). The difference between the mean birthweight for male and female infants is not statistically significant.

The mean birthweight of both sexes for first born infants is 2,880 g (SD 457) compared with 3,065 g (SD 497) for subsequent born infants.

First born infants are lighter than their subsequent counterparts. The difference is significant ($p < 0.05$). The difference is even more significant when first born female infants only are compared with their subsequent counterparts. The mean birthweight for first born female infants is 2,790 g (SD 431) whilst that of subsequent born female infants is 3,050 g (SD 424) ($p < 0.005$).

First born female infants are lighter than their male counterparts ($p < 0.05$). There was, however, no statistically significant difference between either subsequent born male infants and their female counterparts, or between first born male infants and their subsequent counterparts. The mean birthweight for first born male infants is 2,970 g (SD 463) while that of subsequent male infants is 3,080 g (SD 582).

(II) Actual body measurements for gestational age. Nearly normal distribution of all body measurements for each gestational age-group were found. *Table II* presents data for the anthropometric measurements of weight, crown-heel lenght, and head circumference for each gestational age proposed for an intrauterine growth chart of the general population. The measurements presented are for both sexes. The 10th percentile for weight for each gestational age-group is also

TABLE II
ACTUAL BODY MEASUREMENTS AGAINST GESTATIONAL AGE FOR ALL BABIES
PROPOSED FOR AN INTRAUTERINE GROWTH CHART
(mean ± 2 S.D., including the 10th percentile for weight (P_{10}))

Gestational Age (weeks)	*Number of babies*	*Weight*				*Length (cm)*			*Head circumference (cm)*		
		− 2 S.D.	MEAN	+ 2 S.D.	P_{10}	− 2 S.D.	MEAN	+ 2 S.D.	− 2 S.D.	MEAN	+ 2 S.D.
28	30	674	960	1246	780	35.8	38.2	40.6	23.6	26.0	28.4
30	40	802	1160	1518	910	36.0	39.0	42.0	24.7	27.0	29.0
32	55	998	1370	1742	1110	36.8	40.0	43.2	25.7	28.0	30.3
34	57	1104	1590	2076	1300	38.6	41.8	45.0	27.1	29.6	32.1
36	65	1284	2120	2956	1600	40.8	44.8	48.8	29.2	31.8	34.4
38	75	1890	2790	3690	2000	44.2	48.6	53.0	30.9	33.5	36.1
40	105	2120	3070	4020	2270	45.4	49.8	54.2	32.0	34.5	37.0
42	32	2140	3100	4060	2370	45.1	49.7	54.3	31.9	34.6	37.4

TABLE III
ACTUAL BODY MEASUREMENTS, MEAN ± 2 S.D. AGAINST GESTATIONAL AGE FOR LOW BIRTHWEIGHT BABIES

Gestational Age (weeks)	*Number of Babies*	*Weight (g)*			*Length (cm)*			*Head circumference (cm)*		
		− 2 S.D.	MEAN	+ 2 S.D.	− 2 S.D.	MEAN	+ 2 S.D.	− 2 S.D.	MEAN	+ 2 S.D.
36	65	1284	1690	2080	39.5	42.5	45.5	28.5	30.5	32.5
38	75	1540	1980	2420	40.9	44.7	48.5	29.2	31.9	34.6
40	105	1980	2300	2720	43.1	46.6	50.1	30.7	33.3	35.9
42	31	1780	2260	2740	43.6	47.0	50.4	30.6	33.4	36.2

Measures from 28 to 34 weeks are equal to those of the general population in *Table II* because below 34 weeks a distinction is not yet possible.

TABLE IV
DATA FOR THE MEAN BODY MEASUREMENT RATIOS AGAINST GESTATIONAL AGE
FOR NORMAL DAR ES SALAAM AND MONTREAL* BABIES, AND L.B.W. BABIES IN DAR ES SALAAM

Gestational Age (weeks)	*Weight / Length* ratio			*Weight / Head circumferences* ratio			*Weight / Length x head circumferences* ratio		
	Dar es Salaam Babies	*Montreal Babies*	*Dar es Salaam L.B.W. Babies*	*Dar es Salaam Babies*	*Montreal Babies*	*Dar es Salaam L.B.W. Babies*	*Dar es Salaam Babies*	*Montreal Babies*	*Dar es Salaam L.B.W. Babies*
28	25.1	29.6	25.1	36.9	43.6	36.9	0.97	1.16	0.97
30	29.7	34.4	29.7	43.0	49.7	43.0	1.10	1.25	1.10
32	34.3	40.7	34.3	49.0	58.3	49.0	1.22	1.38	1.22
34	38.0	47.0	38.0	53.7	67.2	53.7	1.29	1.50	1.29
36	47.3	54.6	39.8	66.7	78.5	55.4	1.49	1.65	1.30
38	57.4	62.9	44.3	83.3	91.3	62.1	1.71	1.83	1.39
40	61.6	68.0	49.4	89.0	99.1	69.1	1.88	1.95	1.48
42	62.4	68.2	48.1	89.6	100.1	67.7	1.80	1.94	1.44

* Calculated from data by *Usher and McLean* (1969)

presented. At 28 weeks of gestation, the weight is 960 g (SD 143), the crown-heel length is 38.2 cm (SD 1.2) and the head circumference is 26.0 cm (SD 1.2). At 40 weeks of gestation, the weight is 3,070 g (SD 475), the crown-heel length is 49.8 cm (SD 2.2), while the head circumference is 34.5 cm (SD 1.25).

Similar measurements for L.B.W. infants are presented in *Table III*. As all babies below 34 weeks of gestation weighed less than 2,500 g, measurements from 28-34 weeks have to be equal with those of L.B.W. infants.

After 34 weeks of gestation, all anthropometric measurements for L.B.W. infants progressively deviated from those of the general population of newborns. Thus at 40 weeks, the mean birthweight for L.B.W. infants is 2,300 g (SD 210), whilst the crown-heel length is 46.6 cm (SD 1.8) and the head circumference 33.3 cm (SD 1.3).

Intrauterine growth curves

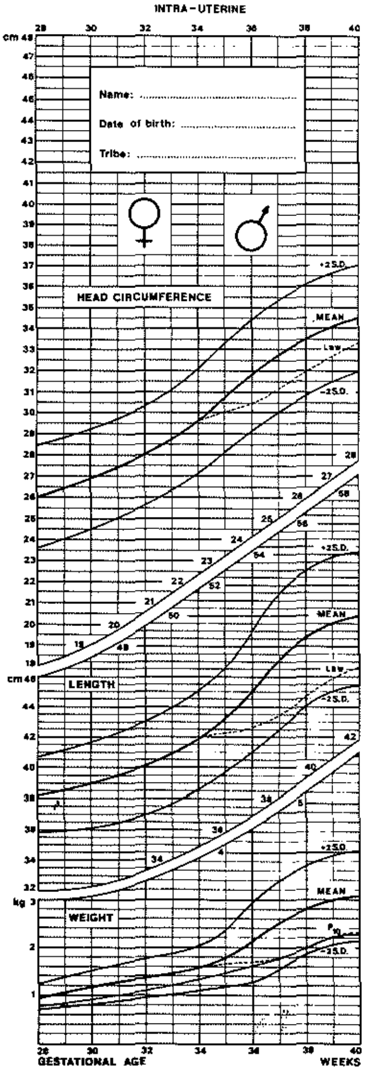
Intrauterine growth curves in which the mean ± 2 SD for birthweight, crown-heel length and head circumference are plotted against gestational age for both sexes of the population are shown on the *Intrauterine Growth Chart (Fig. 1)*. The 10th percentile for weight against gestational age, used to define small-for-dates infants is also shown on this Chart. The values used in the construction of the curves are presented in *Table II*. In all the three measurements considered, there is a spurt of growth between 34-38 weeks of gestation, and then the velocity of growth starts slowing down progressively. After 40 weeks of gestation, increase in these measurements is very slight. The mean ± 2 SD for birthweight crown-heel length and head circumference of the general newborn population are presented on the Intrauterine Growth Chart, alongside the mean values of L.B.W. infants for comparison. The data for the mean values of L.B.W. infants are presented in *Table III*. The curves of the L.B.W. infants do not show the increased speed of growth from the 34th to the 38th week of gestation as observed in the general population of new borns.

The impaired growth of the L.B.W. group affects all three measurements considered. The effect is most marked on birthweight and to a lesser extent on crown-heel length and head circumference.

Body measurement ratios

Curve values of mean body measurement ratios of weight/length, weight/head circumference, and weight/length x head circumference for both, the general population and L.B.W. infants, are plotted against gestational age in *Figure 2*. The values used in the construction of these curves are presented in *Table IV*. Data for Montreal babies as obtained by calculation from figures presented by Usher and McLean (1969), are included for comparison (see under discussion). In general, the indices described show how heavy the baby is for his length and/or head circumference. A low ratio describes an infant who is thin for his length and/or

INTRAUTERINE GROWTH OF LIVE-BORN TANZANIAN INFANTS



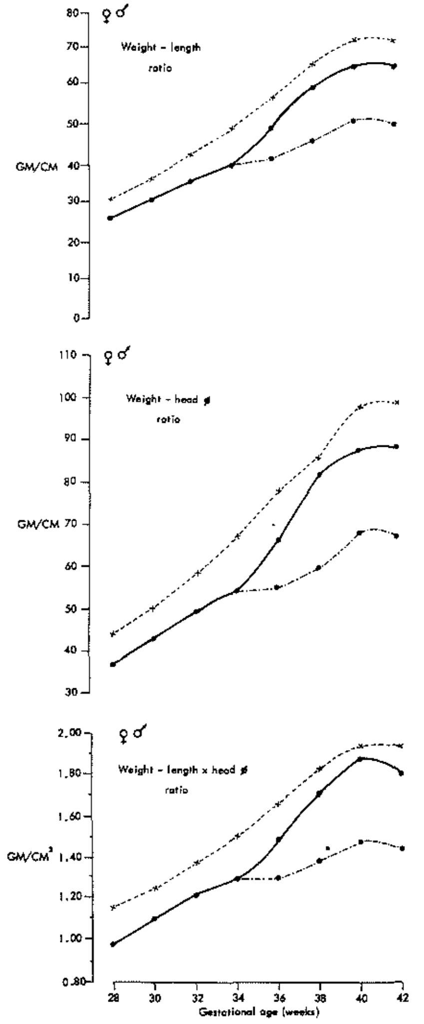


Fig. 1 For explanation see opposite text. *Fig. 2*

head circumferences. The curves show features not apparent in separate curves of weight, crown-heel length and head circumference. Up to 40 weeks of gestation, growth in weight is greater than that of either crown-heel length or head circumference. The foetus gains maximum weight in relation to length and head circumference during the period of growth spurt i.e. 34 – 38 weeks of gestation. A plateau is reached at 40 weeks of gestation. In the L.B.W. group the weight is relatively more affected by the reduced growth support than the crown-heel length and the head circumference.

DISCUSSION

Mean birthweight

The mean birthweight of 3,036 g for males and 2,946 g for females at term is similar to that of 3,000 g for males and 2,800 g for females reported in Mwanza almost 20 years ago (McLaren, 1959). It is however, smaller than that of 3,152 g for males and 3,083 for females reported among infants of the more privileged mothers i.e. Grades I and II in Dar es Salaam (Okeahialam, 1974). When compared with figures found in the literature for other African countries, though all not on the same altitude, the weight of 2,991 g for both sexes at term is lower than that of 3,090 g for Nigeria (Ebrahim, 1969) and much lower than that of 3,115 g for Ethiopia (Young, 1967) and 3,345 g for Kenya (Oduori, 1974).

Mean birthweight of 3,415 g for Britain (Crosse, 1971) and 3,400 g for United States of America (Schaffer and Avery, 1971) are very much higher than that found in this study, and indeed figures from other African countries.

Incidence of L.B.W. infants

The incidence of L.B.W. infants of 15.2% found in this study is very similar to that of 15.6% reported in Mwanza (McLaren, 1959). It is, however, slightly higher than that of 13.6% reported in Moshi (Holmes, 1973). Compared with evidence from other African countries, the incidence in this study is slightly higher than that of 13.6% reported for Nigeria (Lesi, 1967). It is, however, somewhat lower than that of 16.6% reported among Africans in Rhodesia (Houghton and Fraser-Ross, 1953), 19.5% for Africans in South African (Salber and Bradshaw, 1953) and distincly so from the 28.4% for Indians in Zambia (Leitch, 1967).

The difference in the mean birthweights and consequently in the incidence of L.B.W. infants is, among other factors as discussed later, due to a difference in the height of the mother and also to the difference in the socioeconomic status between the communities considered. When mean birthweights were correlated with socioeconomic status and hence indirectly to the maternal nutritional status (Ebrahim, 1969), it was found that infants from the most privileged groups in developing countries were heavier than those from the less privileged groups in the same area and just as heavy as those from Europe and America.

The incidence of L.B.W. in Dar es Salaam was found to be 15.1% in Grade IV women. This is in contrast with 6.5% in Grade I and II mothers living in the same city (to be published). Figures recorded in supposedly properous environments elsewhere confirms this contrast (6.7% for Great Britain, Butler and Alberman, 1969; 6.1% for U.S.A., Bain *et al.*, 1949; and 4.2% for Caucasians in South Africa, Salber and Bradshaw, 1953). The effect of socioeconomic status on the birthweight of the offspring thus appears to be notable (Butler and Alberman, 1969; Baird, 1952) and greater than on gestational age.

Anthropometric data, growth curves and body parameter ratios

The anthropometric measurements of birthweight, crown-heel length and head circumference at term are slightly less than those reported by Okeahialam (1974) for the most privileged section of the society in Dar es Salaam. He analysed 2,070 newborn infants with a mean gestational age of 39.7 ± 1.5 weeks and a range of 35 – 42 weeks. In contrast to our method, the gestational age was based on the mother's date of the last menstrual period.

Our intrauterine growth data were related to similar measurements of Caucasian infants born at sea-level in Montreal (Usher and McLean, 1969). All three body measurements considered were greater than those of African infants born in Dar es Salaam. When we compare our calculated mean weekly gain in weight, crown-heel length and head circumference in two week intervals during the last trimester with mean values of the Montreal study (Usher and McLean, 1969) *(Table V)*, a reduced growth velocity in all three measurements considered is noticed for the Dar es Salaam foetus during the 30th to 34th week of gestation. However, on the same

TABLE V

COMPARISON OF AVERAGE INTRAUTERINE GAIN IN WEIGHT, CROWN-HEEL LENGTH AND HEAD CIRCUMFERENCES FOR DAR ES SALAAM AND MONTREAL FOR DIFFERENT GESTATIONAL AGE GROUPS

Gestational age-groups	*Average gain in weight per week of gestation gram*		*Average gain in crown-heel length cm*		*Average gain in head circumference per week cm*	
	Montreal	*Dar es Salaam*	*Montreal*	*Dar es Salaam*	*Montreal*	*Dar es Salaam*
30-31 weeks	175	95	1.3	0.5	1.0	0.5
32-33 weeks	195	110	1.3	0.9	0.9	0.8
34-35 weeks	240	265	1.2	1.5	0.8	1.1
36-37 weeks	270	335	1.2	1.9	0.65	0.9
38-39 weeks	175	140	0.7	0.6	0.4	0.5

basis between the 34th to 38th week of gestation a *catch-up-growth* for these measurements is shown.

When weight/length, weight/head circumference and weight/length x head circumference ratios were compared the increased velocity of growth between 34 and 38 weeks of gestation was more pronounced for weight than on either length or head circumference. These ratios also indicate that the weight of the Tanzanian foetus is less for its length and/or head circumference when compared with their Caucasian counterparts throughout the last trimester.

Under circumstances* of intrauterine growth all body measurements are affected. However, the effect on weight is more pronounced than on either length or head circumference. This is in keeping with findings by Usher and McLean (1969).

The implications for the infant in the African-negro environment, which we studied, will be discussed later.

We express our appreciation to Professor J.H.P. Jonxis, Professor H.K.A. Visser and Dr. B.G. Woodcock for their valuable suggestions. We also thank the nursing and medical staff from Muhimbili Medical Centre for their great support. In addition we thank Mr. M. Kassam and Mr. A.A.M. Kempers and their staff for their technical assistance. We are grateful to the Medical Superintendent of MUhimbili and Ocean Road Hospital for allowing us to carry out this study.

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Paper 2. Reprinted from Tropical and Geographical Medicine

FACTORS ASSOCIATED WITH LOW BIRTH WEIGHT IN THE POPULATION OF DAR ES SALAAM, TANZANIA

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Summary. Factors associated with low birthweight in Dar es Salaam have been evaluated. The incidence of low birthweight is higher among female infants and infants belonging to parents of a low socioeconomic status. Primiparity, short stature of the mother, a multiple pregnancy, "toxaemia" of pregnancy are some of the factors influencing the growth velocity of the foetus leading to an increased indidence of small-for-dates infants. Low maternal age and antepartum haemorrhage mainly affect the duration of gestation and lead to a preponderance of preterm appropriate-for-gestational-age infants.

However, in 66% of the mothrs with low birthweight infants no associated maternal complication of the pregnancy could be detected.

INTRODUCTION

The concept of low birthweight (L.B.W.) has evolved over the years and has been expanded on the intuitive notion of a pregnancy which terminates before term. Currently, it has assumend the connotation of a pregnancy which terminates before the foetus has derived the benefit of a satisfactory intrauterine development. It is thus not limited to pregnancies which terminate early: it implies, rather, that the lapse of time in utero or the quality of nurture was judged unsatisfactory. The incidence of L.B.W. infants is high among the least privileged populations of the world (Boersma and Mbise, 1979). Low birthweight may be the result of a short gestation (preterm appropriate-for-gestational-age infant) or an both factors. The exact cause of l.b.w. is not yet known. Many factors have been found to influence the growth of the foetus and to a lesser extent the maturation of the foetus (Donelly *et all.*, 1964; Ambramowicz and Kass, 1966).

In the study we shall discuss some of the factors which affect the duration of the gestation period and the growth of the foetus for the population of Dar es Salaam, Tanzania. These factors will roughly be divided into at least three groups namely: environmental, maternal, foetal and leaving a fourth to be unknown origin.

METHODS AND MATERIALS

This prospective study is based on the same negro population of Dar es Salaam as considered in the paper (Boersma and Mbise, 1979). The methods used, details regarding the population, duration of the study, geographical circumstances, anthropometric measurements, assessment of the gestational age, abbreviations, definitions, socioeconomic grading and statistical analysis are given in the preceding report in this issue.

The study comprises 868 mothers, who delivered a total of 973 low birthweight infants all admitted in the neonatal unit of the maternity ward of Muhimbili Medical Centre, and 184 randomly selected subjectively healthy mothers giving birth to term appropriate for gestational age infants. The criteria for admission in the neonatal unit included one or more of the following;

(1) Infants with a birthweight of less than 2,000 g,
(2) Infants with a 5-minute Apgar-score (a score based on heart and respiration rate, activity, tonus of muscles and colour of the skin) of less than 6,
(3) Infants born by caesarean section, vacuum extraction or breech delivery,
(4) Infants whereby the mother for various reason was unable to breastfeed.

The unit had a capacity of 60 cots. The total admission number was approximately 4,500 per year. Because of the congestion two or three infants were sometimes occupying one cot. The infants were discharged as soon as they were well enough to be breastfed adequately. During the period of admission, the mothers were staying around and helped with feeding and other minor nursing duties. The three rooms for infants weighing less than 2,000 g were maintained at an environmental temperature of 30 °C by radiant heaters. If necessary extra heat was provided by cotside lamps or incubators. The nursing care was limited due to the shortness of staff especially at night. From the 868 mothers, whose low birthweight infants were all admitted the following information was recorded: maternal age, parity, maternal height, socioeconomic status of the husband based on Tanzanian standing orders (Tanzania Government, 1971), past obstetric history and marital status. The same information was abtained from the control mothers (n=184).

Full clinical examination was done on all the 973 L.B.W. infants to determine, among other things, the presence or absense of congenital malformations. Anthropometric measurements were presented in the former paper. Differentiation between the subgroups of L.B.W. infants was made with the help of the *Dar es Salaam Intrauterine Growth Chart* (this issue, page 15).

From the total 868 mothers, 114 mothers of preterm appropriate-for-gestational-age and 130 bearing small-for-dates infants (both randomly selected) were studied in more details on age, height and parity and compared with the 184 mothers giving birth to normal term appropriate for gestational age infants. The following mothers were excluded from this part of the study.

(1) Mothers with multiple births,
(2) Mothers of infants with congenital malformations, e.g. hydrocephalus, microcephaly, hydrops foetalis, Down's Syndrome, congenital heart diseases etc.,
(3) Mothers of infants with cephalhematoma or excessive caput succedaneum.

Infants falling outside the − 1 SD limit but within the 10th percentile were regarded as atypical and so, *unlike other authors*, we have not included them in the appropriate-for-gestational-age groups.

FACTORS ASSOCIATED WIRH LOW BIRTH WEIGHT IN TANZANIA

Definitions and abbreviations

Term appropriate-for-gestational-age infant (Term A.G.A.) – one who is born within 38 - 42 weeks of gestation and whose birthweight is within ± 1 SD from the mean for gestational age according to the local standards (Boersma and Mbise, 1979).

Preterm appropriate-for-gestational-age infant (Preterm A.G.A.) – one who is born before 37 completed weeks of gestation and whose birthweight is within the mean ± 1 SD for the gestational age, using the same standards.

Small-for-dates infant (S.F.D.) – one whose birthweight is below 10th percentile for gestational age according to the local standards.

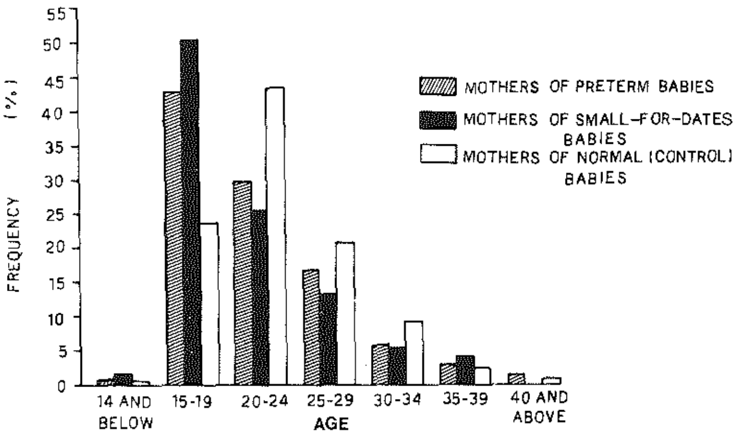

Fig. 1 A comparison of maternal age in mothers of preterm appropriate-for-gestational-age, small-for-dates and normal term appropriate-for-gestational-age infants (controls).

RESULTS

During the seven month period under review a total of 16,532 livebirths were recorded. The total number of L.B.W. infants during this period was 2,507 (15.1%).

Out of 973 low birthweight infants (L.B.W.), all admitted, 528 (54.3%) were born within the 38 to 42 weeks of gestation whereas 445 (45.8%) were born before

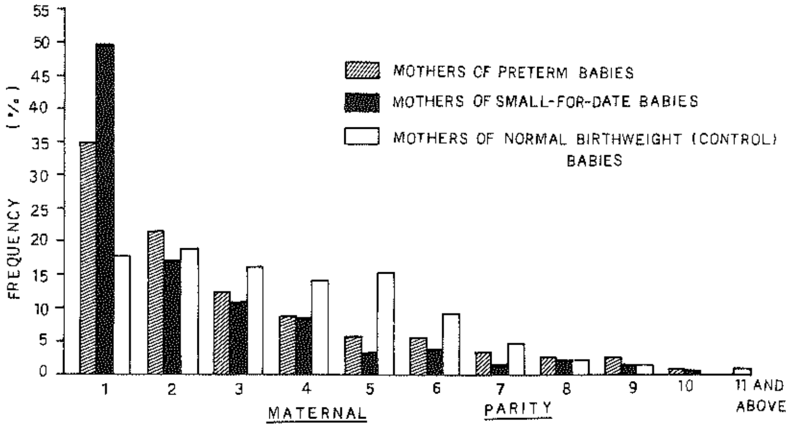

Fig. 2 Comparison between the parity of mothers of preterm appropriate for gestational age, small-for-dates and term appropriate for gestational age infants (controls).

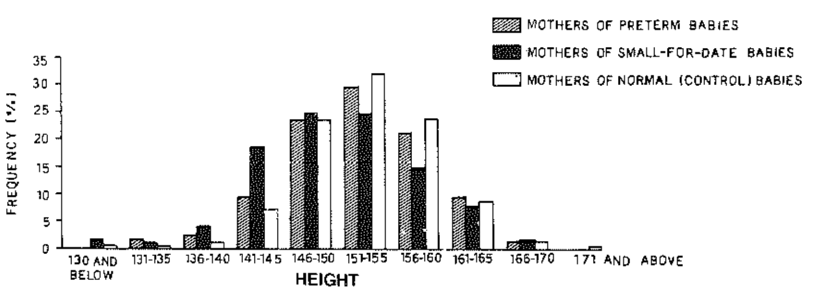

Fig. 3 Comparison of maternal height in mothers of preterm appropriate-for-gestational-age, small-for-date infants and term appropriate-for-gestational-age infants (control).

the 37th completed week of gestation. 401 (41.2%) of the L.B.W. infants were small-for-dates and 298 (30.6%) were preterm A.G.A. Of the remaining 274 (28.2%) L.B.W. infants the weights fell between the − 1 SD and the 10 th percentile for weight.

Environmental causes of low birthweight

Socioeconomic status. Out of the total population of 16,532 livebirths, 430 were born to mothers belonging to the high or middle socioeconomic groups (Grade I and II) while 16,102 to mothers in the low socioeconomic group (Grade IV). The incidence of L.B.W. infants among Grade I and II mothers was 28 (6.5%) and among Grade IV mothers it was 2,497 (15.6%).

Maternal factors

(1) Age of the mother. Fig. 1 shows a comparison of maternal age in mothers of preterm A.G.A., S.F.D. and normal term A.G.A. infants (controls). For data used, see *Table I*. 43.9% of mothers of preterm A.G.A. infants and 52.3% of mothers giving birth to S.F.D. infants were below 20 years of age. This is in marked contrast with 23.4% of mothers of normal term A.G.A. infants. Mothers of preterm A.G.A. infants and mothers of S.F.D. infants are, on the average, younger than mothers of normal full term infants ($p < 0.005$). However, analysis of the mothers below the age of 20 years into two subgroups of 15-17 and 18-19 years *(Table II)* shows that, in contrast to the mothers of preterm A.G.A. infants, the incidence of mothers of S.F.D. infants was not increased in the younger subgroup.

TABLE I

PERCENTAGE DISTRIBUTION IN MATERNAL AGE OF MOTHERS OF PRETERM A.G.A. SMALL-FOR-DATES AND TERM A.G.A. (CONTROL) BABIES.

Maternal age (years)	*Mothers of preterm babies-appropriate for gestation*		*Mothers of small-for-date babies*		*Mothers of normal birthweight (control) babies*	
	Number	*Percent*	*Number*	*Percent*	*Number*	*Percent*
14 and below	1	0.9	1	0.8	1	0.5
15 - 19	49	43.0	67	51.5	43	23.4
20 - 24	34	29.8	33	25.4	80	43.5
25 - 29	19	16.7	17	13.1	38	20.7
30 - 34	7	6.1	7	5.4	17	9.2
35 - 39	3	2.6	5	3.8	4	2.2
40 and above	1	0.9	0	0.0	1	0.5
Total	114	100.0	130	100	184	100.0
Mean ± S.D.	21.7 ± 5.4		21.0 ± 5.3		23.6 ± 4.8	

(2) Parity (Birth order). A. comparison between the parity of mothers of preterm A.G.A., S.F.D. and term A.G.A. infants is shown in *Table III* and *Fig.2*. 35% of mothers of preterm A.G.A. and 50% of mothers of S.F.D. infants were primiparous. This in contrast to 18% of mothers of term A.G.A. infants. On the whole, mothers of preterm A.G.A. infants had a lesser parity than mothers of term A.G.A. ($p<0.005$) but those of S.F.D. infants even less ($p<0.001$). The mean parity ± 1SD among mothers of preterm A.G.A., small-for-dates and those of the control babies were 3.0 ± 2.4, 2.4 ± 2.0 and 3.6 ± 2.0 respectively. However, analysis of all primiparas into the different age groups *(Table IV)* showed no significant difference in age distribution among the three groups considered.

(3) Maternal height. A comparison of maternal height in mothers of preterm A.G.A., S.F.D. infants, and term A.G.A. infants is presented in *Fig. 3*. For data see *Table V*. Mothers of preterm A.G.A. infants do have approximately the same height as mothers of term A.G.A. babies. However, a significantly shorter stature was found in mothers of S.F.D. infants ($p<0.05$).

(4) Maternal complications during pregnancy. Of the total 868 mothers whose L.B.W. infants were admitted in the neonatal unit, 13.1% had E.P.H. gestosis, 12.4% had twins and 0.35% had triplets. The remaining complications were antepartum haemorrhage (A.H.P.) (3.5%), hypertension (0.23%), cervical incompetence (0.23%), pulmonary tuberculosis (0.23%) bronchial asthma (0.23%) and clinical malaria (0.12%). In 66.1% of the mothers no associated maternal complication could be found.

TABLE II

MOTHERS OF PRETERM A.G.A., SMALL-FOR-DATES AND TERM A.G.A. (CONTROL BABIES) AND ANALYSIS OF MOTHERS BETWEEN 15-19 YEARS OLD.

Maternal age (in years)	*Mothers of preterm appropriate for gestational infants*		*Mothers of SFD infants*		*Mothers of full term (control) infants*		*TOTAL*	
	Number	*Percent*	*Number*	*Percent*	*Number*	*Percent*	*Number*	*Percent*
15 - 17	24	34.8	25	36.2	20	29.0	69	100
18 - 19	25	27.8	42	46.6	23	25.6	90	100
Total	49	30.8	67	42.2	43	27.0	159	100

Two mothers had positive serological tests for syphilis (Kahn and P.P.R.) but their babies had no stigmata of congenital syphilis and their serological tests for syphilis were negative.

Pregnancy complicated by E.P.H. gestosis resulted predominantly in infants born at term. However, antepartum haemorrhage and multiple births resulted in more or less the same number of preterm and term infants, though the latter

TABLE III

PERCENTAGE DISTRIBUTION IN MATERNAL PARITY OF MOTHERS OF PRETERM A.G.A., SMALL-FOR-DATES AND TERM A.G.A. (CONTROL) BABIES.

Maternal parity	*Mothers of preterm babies appropriate for gestation*		*Mothers of small-for-date babies*		*Mothers of normal birthweight*	
	Number	*Percent*	*Number*	*Percent*	*Number*	*Percent*
1	40	35.0	65	50.0	33	17.9
2	24	21.1	23	17.0	35	19.0
3	14	12.3	14	10.8	30	16.3
4	10	8.8	11	8.5	26	14.1
5	7	6.1	4	3.0	28	15.2
6	7	6.1	5	3.8	17	9.2
7	4	3.5	2	1.5	9	4.9
8	3	2.6	3	2.3	4	2.2
9	3	2.6	2	1.5	2	1.1
10	1	0.9	1	0.8	0	0.0
11 and above	1	0.9	0	0.0	0	0.0
Total	114	100.0	130	100.0	184	100.0

TABLE IV

AGE DISTRIBUTION OF PRIMIPARAS OF PRETERM A.G.A., SMALL-FOR-DATES AND TERM A.G.A. (CONTROL) BABIES.

Maternal age (in years)	*Mothers of preterm appropriate for gestational age infants*		*Mothers of SFD infants*		*Mothers of normal full term (control) infants*	
	Number	*Percent*	*Number*	*Percent*	*Number*	*Percent*
14 and below	1	2.5	1	1.5	1	2.7
15 - 19	32	80.0	56	86.2	27	82.0
20 - 24	7	17.5	7	10.8	5	15.3
25 and above	0	0.0	1	1.5	0	0.0
Total	40	100.0	67	100.0	33	100.0

showed a slight preponderance. 31.5% of the total 108 mothers with twin pregnancy had preterm A.G.A. infants compared with 68.5% who gave birth to S.F.D. infants; 6.1% of the total 114 mothers with E.P.H. gestosis delivered a preterm A.G.A. infant, compared with 45.6% who had a S.F.D. infant. Of 30 mothers with

A.P.H. recorded, 30% of them delivered a preterm A.G.A. infant, whereas 13.3% gave birth to a S.F.D. infant.

(5) Maternal cigarette smoking during pregnancy. None of the 868 mothers whose L.B.W. infants were admitted gave a history of smoking during pregnancy.

TABLE V
PERCENTAGE DISTRIBUTION IN MATERNAL HEIGHT OF MOTHERS OF PRETERM A.G.A., SMALL-FOR-DATES AND TERM A.G.A. (CONTROL) BABIES.

Maternal height (cm)	*Mothers of preterm babies appropriate for gestation*		*Mothers of small-for-date babies*		*Mothers of normal birthweight (control) babies*	
	Number	*Percent*	*Number*	*Percent*	*Number*	*Percent*
130 and below	0	0.0	2	1.8	1	0.5
131 - 135	2	1.7	1	0.9	1	0.5
136 - 140	3	2.6	5	4.4	2	1.1
141 - 145	11	9.6	21	18.6	13	7.1
146 - 150	27	23.7	28	24.8	44	23.9
151 - 155	34	29.8	28	24.8	59	32.1
156 - 160	24	21.1	17	15.0	44	23.9
161 - 165	11	9.6	9	8.0	16	8.7
166 - 170	2	1.7	2	1.8	3	1.6
171 and above	0	0.0	0	0.0	1	0.5
Total	114	100.0	113	100.0	184	100.0
Mean ± S.D.	153.0 + 7		150.1 + 7.2		153.8 ± 5.9	

(6) Illegitimacy. 2.2% out of the 868 mothers of L.B.W. infants were not married.

(7) Prenatal care. 7.5% of 868 mothers of L.B.W. infants did not receive prenatal care at all. However, most of those who did, reported very late in

pregnancy, having made only 2-3 antenatal visits before delivery. The majority of those who did not get prenatal care came to deliver in hospital because of some complications. Hence the number available for analysis was too small to allow statistical comparison.

Foetal causes of low birthweight

(1) Male to female ratio. During the total 7 months study period 2,507 L.B.W. infants were born of whom 1111 (44.3%) were males and 1396 (55.7%) females. The male to female ratio was 1 : 1.26.

(2) Congenital malformations. Only 18 (1.9%) out 973 L.B.W. infants had major congenital abnormalities. Among these were five infants with congenital cyanotic heart disease, two trisomy 16-18 and one each with Down's Syndrome, Pierre Robin syndrome, microcephaly, oesophageal atresia, spinal meningo-myelocele, occipital meningo-encephalocele, Turner's syndrome, imperforate anus, congenital rubella syndrome, exomphalus and arthrogryphosis multiplex congenita were recorded.

The incidence of congenital malformation among the general population under review was 1.2%, half of that of the L.B.W. infants. The numbers of patients were however too small for any statistical conclusion to be made.

DISCUSSION

Knowledge of the gestational age of newborn infants and subdivision of L.B.W. infants into either preterm A.G.A. or S.F.D. is necessary, for this may alter their further management and improve their short and long-term prognosis (Avery, 1975). Most small-for-dates infants who survive the birth process are active and

TABLE VI

SUMMARY OF THE FACTORS AFFECTING LOW BIRTHWEIGHT.

Maternal factors	*Low Birthweight*	*Preterm A.G.A.*	*Small-for-dates*
Low Socioeconomic Class	+		
Young mothers	+	+	–
Primiparity	+	–	+
Short stature	+	–	+
E.P.H.-gestosis	+	–	+
Multiple births	+	±	+
A.P.H.	+	+	–
Foetal factors			
Females	+		

usually do well in the neonatal period. Hypoglycaemia and hypothermia are two of the most important complications which may occur soon after birth. The management is generally not very complicated. Infants who are delivered prior to term are subject to various disorders which complicate their neonatal course. Optimal management of these children requires expert nursing and medical care: a great problem in the developing countries.

The most important factors studied affecting low birthweight and their subgroups are summarized in *Table VI*.

The *socioeconomic status of a population* has a multifacetted influence on the incidence of L.B.W. (Baird, 1952; Drillien and Richmond, 1956; World Health Organization, 1961; Butler and Alberman, 1969). The difference in incidence of L.B.W. infants among the socioeconomic classes have been considered in a former paper (Boersma and Mbise, 1979). Improved socioeconomic conditions in a population and hence the nutritional status of the mother during childhood has been indirectly related to an increase of the mean height of the mother which may simultaneously lead to an increase of the average weight of the offspring (Baird, 1952; Greulich, 1957).

Regarding the *maternal factors* associated with L.B.W. infants the age of the mother seems not to have any effect on the rate of intrauterine growth velocity, as shown by the lower incidence of S.F.D. infants among mothers in the youngest subgroup of mothers below the age of 20 years *(Table II)*. It does however affect the duration of the gestation leading to a preponderance of preterm appropriate-for-gestational-age infants. In the British Perinatal Mortality Survey of 1958 (Butler and Alberman, 1969) the occurrence of a positive correlation between maternal age and intrauterine foetal growth rate might be explained by the higher proportion of primiparous women among the very young mothers, a factor which by itself has a great influence on the intrauterine foetal growth.

Primiparas formed 35% of mothers of preterm A.G.A. and 50% of mothers giving birth to S.F.D. infants but only 17.9% of mothers of normal term A.G.A. babies. However, when matched for age primiparity affects predominantly the intrauterine growth velocity. This is in agreement with findings by others authors (Millis and Seng, 1954; Butler and Alberman, 1969).

Maternal height predominantly affects intrauterine growth rate rather than duration of gestation, thus leading to an excess of S.F.D. infants. This is in keeping with findings from the British Perinatal Mortality Survey of 1958 (Butler and Alberman, 1969).

Mothers of preterm A.G.A. infants have approximately the same height as mothers of term A.G.A. babies. However, mothers of S.F.D. infants were significantly shorter.

The most important *maternal complications* of pregnancy associated with L.B.W. in this series were: E.P.H. gestosis (13.1%), twins (12.4%), A.P.H.

(3.5%). A small number had a combination of two of these. It is important to note that in *66.1% of the mothers no definite complication was found.* This distribution shows a slight difference from that reported in India by Sainaba (1972). In their series, twins occurred in 24.6%, E.P.H. gestosis on 15.8%, A.P.H. in 14.7% of the mothers. No definite complication could be found in 32% of the mothers in their study.

The incidence of *E.P.H. gestosis* among mothers of L.B.W. infants was 13.1% compared with 6.5% in the general population during the period under review. E.P.H. gestosis has a predominant effect on intrauterine foetal growth thus leading to a preponderance of S.F.D. compared with preterm A.G.A. infants. This is also reported by other authors (Chakravorty, 1967; Butler andAlberman, 1969). It is however, different from the findings of Ounsted (1973) who found no difference between the weight distribition of infants of mothers with E.P.H. gestosis and those of control mothers. Gruenwald (1966) found an excess of both small-for-dates and large-for-dates infants in mothers with E.P.H. gestosis. The basis for the association of E.P.H. gestosis and impaired intrauterine growth rate is not clear. Although placental microinfarcts are quite often seen in patients with E.P.H. gestosis Gruenwald (1963) and Shanklin (1970) could not identify any specific placental pathology as a major aetiological factor in association with L.B.W.

Multiple births predominantly affect intrauterine foetal growth velocity thus resulting in a higher incidence of S.F.D. than preterm A.G.A. infants. This is in keeping with findings reported by other authors (McKeown and Record, 1952; Butler and Alberman, 1969). The normal supply line can only adequately support a total foetal weight of close to 3,000 g. Beyond this limit, a reduced intrauterine growth velocity occurs. Thus twins, triplets and quadruplets are progressively lighter than normal singleborn infants of the same gestational age. This difference is apparent from 33-34 weeks of gestation onwards (Naeye *et al.*, 1966; Battaglia and Lubchenco, 1967).

A.P.H. affects predominantly the duration of gestation thus leading to an increased number of preterm A.G.A. compared with S.F.D. infants.

We have studied the possible interference by malaria which was found to be insignificant. This aspect will be discussed in a later study.

Cigarette smoking, illegitimacy and poor prenatal care of the mother could not be inculpated as important factors associated with low birthweight.

Apparently the most important determinants of foetal growth are unknown. Regulation of growth depends upon the genetic potential of the foetus and of its ability to make use of the nutrients reaching it. An adequate supply of oxygen and blood from the mother to the placenta are some of the factors determining its nutrition and rate of growth. Another factor, the composition of the maternal blood, will be discussed later.

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Changes in fatty-acid composition of body fat before and after birth in Tanzania: an international comparative study

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Summary and conclusions

Changes in the fatty-acid composition of human adipose tissue before birth and during infancy and childhood were studied in Tanzania and compared with data for British and Dutch infants in relation to their diet. From the 32nd to the 37th week of gestation in Tanzania the proportion in the body fat of the unsaturated fatty acid linoleic acid tended to rise, suggesting an adequate supply of this essential fatty acid from the mother to the fetus. At term 2·5% of the total fatty acids of the body fat was linoleic acid, which corresponded with values in Dutch newborn infants but was significantly higher than those in British infants. During infancy in Tanzania the composition of the fat showed a dramatic increase in the proportions of the saturated fatty acids lauric acid and

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myristic acid, which did not occur in Dutch and British infants. The proportion of linoleic acid increased to 8%. These changes were a reflection of the fatty-acid composition of the fat in the human milk that the infants received. During weaning (1-2 years of age) the fatty-acid composition changed only slightly.

The specific fatty-acid composition of the fat in Tanzanian breast milk may have a beneficial influence on the extent of intestinal absorption in the newborn child.

Introduction

In Tanzania and the other developing countries of Africa the incidence of arteriosclerosis is low. Establishing a correlation between the quality and quantity of fat intake during childhood and the genesis of risk factors for arteriosclerosis in adult life is difficult, as is shown by the controversial findings of several studies.[1–5] Dietary fat in young infants not only serves as the most important source of energy but also contains nutrients essential for normal growth and development. The nature of the fat consumed in terms of the proportions of fatty acids and their different chain lengths can have an important influence on the fatty-acid composition of adipose tissue[6] and human milk fat,[7] but probably not on the composition of lipids in cell membranes and nervous tissue. Since diets are subject to custom as well as to socioeconomic circumstances, comparing the fatty-acid composition of adipose tissue in different countries may yield useful information, particularly during intrauterine life and infancy.

I studied changes in the fatty-acid composition of human adipose tissue before birth, during infancy, and during childhood. I compared analyses of subcutaneous fat samples from the thigh of Tanzanian infants with data on British and Dutch infants.[6] I also evaluated the effects of the gestational age and nutritional state on the composition of fatty acids in adipose tissue of Tanzanian fetuses.

Patients and methods

Samples of adipose tissue from the thigh were obtained from 10 preterm infants whose birth weights were appropriate for their gestational age—that is, within the mean ±1SD weight for gestational age according to local standards[8]; from nine infants who were small for dates—that is, whose birth weights were below the 10th percentile for gestational age according to local standards; and from nine infants, born at term with birth weights appropriate for gestational age, within four hours after perinatal death. The gestational ages of the preterm infants varied from 28 to 36 weeks (average 34 weeks); those of the small-for-dates infants varied from 32 to 40 weeks (average 35 weeks). Assessment of the gestational age was based on physical characteristics according to a scheme suggested by Lubchenco[9] adapted for the skin colour of negro children.[8] Subcutaneous fat tissue was also obtained from the thigh in 15 children (aged from 3 weeks to 2 years) who had died; only two of them (1 and 2 years old) showed appreciable evidence of malnutrition (kwashiorkor). All patients studied were admitted to the Muhimbili Medical Centre. Table I shows the different groups of children studied and their sources of dietary fat.

TABLE I—*Groups of infants studied and sources of dietary fat*

Group	Age	No of infants	Diet
1	Newborn: term	9	
2	Newborn: preterm	10	
3	Newborn: small for dates	9	
4	1-7 months	8	Breast milk
5	1-2 years	6	Mixed

The samples of body fat (50-100 mg) were washed with isotonic saline and stored and transported at −20°C until analysed. Milk specimens were collected by manual expression from 12 women living in urban and semi-urban areas within a 10-mile radius of Dar es Salaam; these samples were taken about one month after labour and stored and transported at −20°C until analysed. All samples were analysed in the paediatric laboratory of the University of Groningen by the methods of Metcalfe *et al*[10] and Lipsky *et al.*[11]

The statistical significance between means was measured by Student's *t* test.

Results

Figure 1 shows the different fatty acids as percentages of the triglycerides in the total body fat of term, preterm, and small-for-dates infants plotted against gestational age. Table II shows the mean (±SD) values in these infants at birth. The ratio of unsaturated to saturated fatty acids during the last trimester is shown in table III and indicates a trend for the body fat to become more saturated towards term. The percentage of the essential fatty acid linoleic acid (C18:2) seemed to increase between 32 and 37 weeks' gestation. At term the percentage correlated with values obtained in Dutch newborn infants but was significantly higher ($P < 0.001$) than those in British infants. Palmitic acid (C16:0) was the only fatty acid that correlated with gestational age during the last trimester ($r = 0.530$).

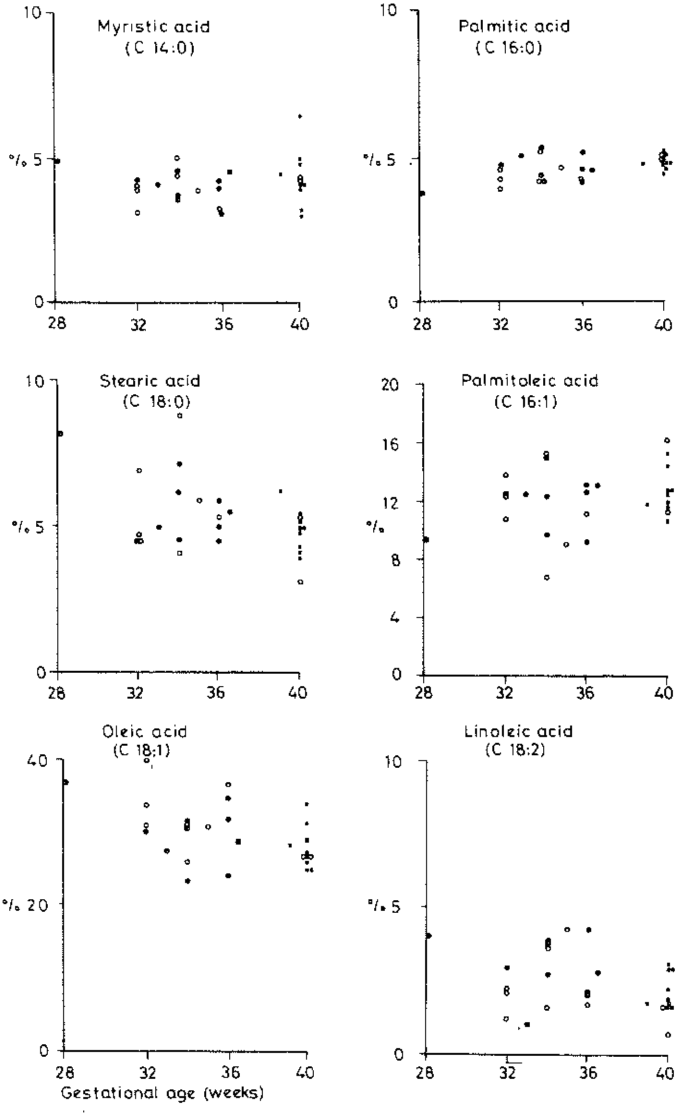

FIG 1—Individual fatty acids as percentages of total fatty acids in body fat of preterm, small-for-dates, and term infants in Tanzania related to gestational age.
● = Preterm infants. ○ = Infants small for dates. ■ = Term infants.

No notable changes were observed during the last months of pregnancy in the other fatty acids studied. At term, however, the percentages of myristic acid (C14:0) and lauric acid (C12:0) were higher in Tanzanian newborn than in Dutch babies ($P<0\cdot005$). Palmitoleic acid (C16:1) was present in the same proportions in Tanzanian and British infants at term, this proportion being lower than that found in Dutch infants ($P<0\cdot001$). No notable differences were observed between the fatty-acid composition of preterm and small-for-dates babies of the same gestational age.

In figure 2 the individual fatty acids as percentages of the total fatty

TABLE II—*Mean fatty-acid composition ($\pm SD$) of body fat in infants born at term and preterm with birth weights appropriate for gestational age and in small-for-dates Tanzanian infants (g/100 g total fatty acids)*

Fatty acid		Term (n = 9)	Preterm (n = 10)	Small for dates (n = 10)
		Saturated acids		
Lauric	(C12:0)	0·2 ± 0·2	0	0
Myristic	(C14:0)	4·3 ± 1·0	4·2 ± 0·4	4·2 ± 0·8
Palmitic	(C16:0)	48·2 ± 2·2	45·7 ± 4·9	45·5 ± 4·3
Stearic	(C18:0)	4·9 ± 0·7	5·7 ± 1·2	5·8 ± 1·9
		Unsaturated acids		
Palmitoleic	(C16:1)	12·7 ± 1·4	12·0 ± 1·9	11·8 ± 2·8
Oleic	(C18:1)	27·8 ± 2·9	29·5 ± 4·1	30·2 ± 5·1
Linoleic	(C18:2)	2·3 ± 0·6	2·9 ± 1·0	2·6 ± 1·7

TABLE III—*Ratios of unsaturated to saturated acids during last trimester in Tanzanian fetuses*

Gestational age in weeks	28-32	33-36	37-40
Unsaturated: saturated acids (No of fetuses) ..	0·93 (5)	0·79 (11)	0·74 (12)

acids in the subcutaneous fat of Tanzanian infants after birth up to the age of 2 years are plotted together with the values obtained in British and Dutch infants.[6] Individual data were available only for linoleic, myristic, palmitic, and stearic (C18:0) acids in British infants up to the age of 5 months and Dutch infants up to the age of 6 months. Between 4 and 8 weeks after birth the fatty-acid composition of the body fat tended towards that of the milk given in each country.

Table IV shows the mean fatty-acid composition of the subcutaneous fat of Tanzanian infants at birth, during breast-feeding (1-7 months of age), and while receiving a mixed diet (1-2 years old). After birth the proportions of lauric and myristic acids increased considerably at the expense of the longer-chain palmitic acid ($P<0\cdot001$). Of the unsaturated fatty acids, the proportion of linoleic acid increased significantly to 8·1% ($P<0\cdot001$) and the percentage of palmitoleic acid de-

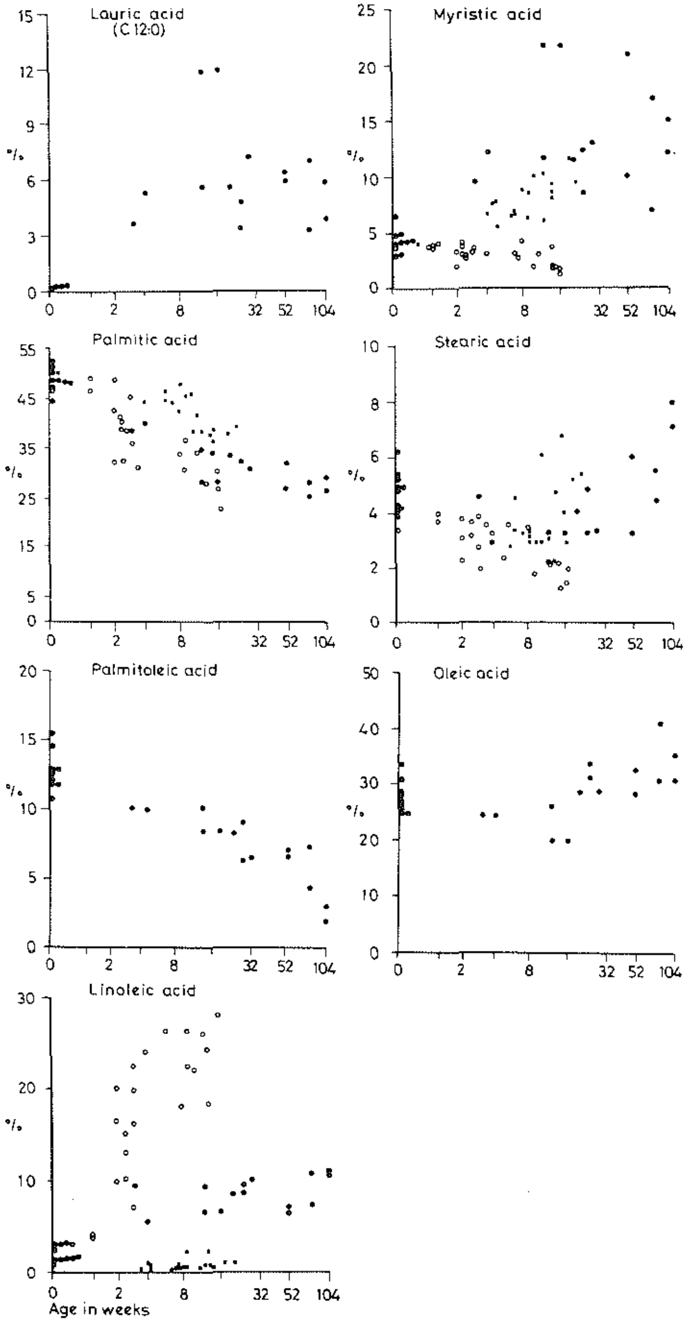

FIG 2—Individual fatty acids as percentages of total fatty acids in subcutaneous fat of Tanzanian, British, and Dutch infants. Data for British and Dutch infants obtained only for linoleic, myristic, palmitic, and stearic acids, from Widdowson *et al.*[6]

● = Tanzanian infants. ■ = British infants. ○ = Dutch infants.

TABLE IV—*Mean fatty-acid composition (±SD) of subcutaneous fat in nine Tanzanian infants at birth, eight breast-fed infants aged 1-7 months, and six children aged 1-2 years receiving a mixed diet (g/100 g total fatty acids)*

Fatty acid	Age		
	At birth (n = 9)	1-7 months (n = 8)	1-2 years (n = 6)
	Saturated acids		
Lauric acid	0·2 ± 0·2*	7·0 ± 3·2	5·4 ± 1·5
Myristic acid	4·3 ± 1·0*	14·1 ± 4·9	13·8 ± 5·0
Palmitic acid	48·2 ± 2·2*	32·2 ± 3·7**	27·9 ± 2·2
Stearic acid	4·9 ± 0·7*	3·4 ± 0·8***	5·8 ± 1·8
	Unsaturated acids		
Palmitoleic acid	12·7 ± 1·4*	8·4 ± 1·4***	5·0 ± 2·3
Oleic acid	27·8 ± 2·9	26·8 ± 5·1***	33·4 ± 4·6
Linoleic acid	2·3 ± 0·6*	8·1 ± 1·7	8·9 ± 2·1

Significance of difference: *P <0·001 compared with values at age 1-7 months. **P <0·05, ***P <0·01 compared with values at age 1-2 years.

creased (P < 0·001). Oleic acid (C18:1) showed no change in percentage while the children were breast-fed. During weaning the fatty-acid pattern of the subcutaneous fat did not show notable changes except in the proportions of oleic, stearic, and palmitoleic acids (P < 0·01).

When the fatty-acid composition of body fat in Tanzanian children during weaning (age 1-2 years) was compared with that in British and Dutch children receiving a mixed diet but of a younger age group (6-12 months), the most important differences were higher proportions of lauric and myristic acids in Tanzanian children (P < 0·001) and simultaneously a smaller proportion of the unsaturated fatty acid oleic acid. The percentage of palmitoleic acid was lower in Tanzanian children when compared with Dutch (P < 0·001) but not with British children. The proportion of linoleic acid differed significantly from that in British infants only (P < 0·001).

The remarkably high proportion of saturated fatty acids in Tanzanian children compared with British and Dutch children is seen from the ratios of unsaturated to saturated acids (table V).

The fatty-acid composition in the two children with kwashiorkor, who received a mixed diet, did not appreciably differ from that of the well-nourished children of the same age group.

TABLE V—*Ratios of unsaturated to saturated acids in Tanzanian, British, and Dutch children receiving a mixed diet*

Nationality	Tanzanian	British	Dutch
Unsaturated: saturated acids	0·89	1·17	1·67

Discussion

I compared children in Tanzania, Great Britain, and the

Netherlands because of the notable differences in the composition of the fat fed to infants and pregnant women in these three countries. Most Tanzanian infants are breast-fed during the first year of life. During weaning, which starts at the age of about 8-14 months, the Tanzanian child living along the coast receives a thin porridge of cassava or maize flour as supplementary food and continues breast-feeding until the age of 2 or even 3 years, which provides an important source of high-quality protein and essential fatty acids. Most British infants who are not breast-fed are given a formula based on cows' milk to which carbohydrate has been added. Most Dutch infants who are not breast-fed are fed on Almiron, a formula in which the fat in cows' milk has been completely replaced by maize oil (with a linoleic acid content of 58%).

In Tanzania the staple food for pregnant and lactating mothers is maize or cassava supplemented with some vegetables. This diet is low in energy, fat, and proteins but relatively rich in carbohydrates. The physical work output of these women is said to be high, although no investigations have been carried out to prove this. Table VI shows the differences in fatty-acid composition between the fat of milk formulas fed to British and Dutch infants[6] and of human milk from Tanzania and Great Britain. The high percentages of lauric and myristic acids found in the samples of breast milk of Tanzanian mothers when

TABLE VI—*Fatty-acid composition of breast-milk fat fed to Tanzanian infants compared with that fed to British infants and formulas fed to British and Dutch infants*[6] *(g/100 g total acids)*

Fatty acid	Formula feeding		Human milk	
	Great Britain*	The Netherlands†	Great Britain	Tanzania
	Saturated acids			
Caprylic acid (C 8:0)	0	0	0	0·1
Capric acid (C10:0)	2·4	0	1·0	1·6
Lauric acid	3·2	0	4·8	13·7
Myristic acid	11·5	Trace	6·2	17·1
Palmitic acid	30·0	10·7	23·7	23·0
Stearic acid	14·3	2·0	6·7	2·3
	Unsaturated acids			
Palmitoleic acid	2·0	Trace	4·6	2·9
Oleic acid	31·1	27·2	37·4	26·9
Linoleic acid	1·8	58·2	9·0	12·4
Linolenic acid (C18:3)	Trace	1·6	3·4	0

*Cow and Gate, Ostermilk, and National Dried Milk.
†Almiron (Nutricia).

compared with British mothers[6] might be due to the high dietary carbohydrate intake.[7 12] The proportion of the essential linoleic acid in Tanzanian human milk was higher than that found by Widdowson *et al*,[6] suggesting an adequate dietary intake of linoleic acid by the Tanzanian women. The percentages of the easily absorbed medium-chain caprylic acid (C8:0) and capric acid (C10:0), though only small, were higher in the milk of Tanzanian than British mothers.[6]

Information regarding the fatty-acid composition of the subcutaneous fat of fetuses born before term is scarce. Pavey,[13] in a cross-sectional study of British and Dutch fetuses from 24 weeks' gestation to term, found that the proportion of linoleic acid decreased towards term in both populations, whereas in our study a tendency for an increase was observed between 32 and 37 weeks, which might indicate a better supply of this essential fatty acid from the Tanzanian mother to the fetus in this period. The increase in the proportion of palmitic acid in British and Dutch fetuses agrees with the findings in our study. Proportions of stearic acid did not change over the last trimester in British and Dutch fetuses, whereas they tended to decrease in this study. The proportions of palmitoleic acid remained constant in all the children studied.

An increased intake of myristic acid raises the total plasma cholesterol concentrations and especially the low-density lipoproteins or β-cholesterol fraction, which is presumed to be one of the factors positively related with coronary heart disease.[5]

In a study on serum lipids in Tanzanian infants (to be published) mean cholesterol concentrations at birth were $1{\cdot}95 \pm$ SD $0{\cdot}38$ mmol/l (76 ± 15 mg/100 ml), equivalent to values in British newborn babies of $2{\cdot}0 \pm 0{\cdot}6$ mmol/l (78 ± 23 mg/100 ml).[14] At one year mean cholesterol concentrations were lower in Tanzanian than British children (3·7 and 4·9 mmol/l (144 and 191 mg/100 ml) respectively). Up to the age of 6 cholesterol concentrations remained virtually constant at 4·0 mmol/l (156 mg/100 ml). If the composition of the subcutaneous fat is assumed to reflect the dietary intake, which was certainly true in our study during breast-feeding, the higher proportions of myristic acid found in Tanzanian children do not correspond with the higher cholesterol concentrations in the first years of life. This contrasts with the Dutch population, in which the diet contains less myristic acid and the serum cholesterol concentration is higher. Although the unsaturated fatty acid linoleic acid may lower serum cholesterol concentrations, a lower percentage of this fatty acid in the breast milk of Tanzanian women (12%) compared with the Dutch formula (58%) did not correspond with higher cholesterol concentrations in Tanzanian breast-fed infants.

The interpretation of these results is still uncertain. To what extent does the composition of the fat consumed in utero and early life affect the tendency to coronary heart disease in adulthood? Certainly it does not seem justifiable to draw any conclusions on the influence of the individual components of dietary fat on lipid metabolism because this is obviously influenced by many factors.

Theoretically,[12] the composition of the saturated fatty acids in human milk in Tanzania (with a higher percentage of the medium-chain caprylic and capric acids and of lauric and myristic acids, a relatively high percentage of palmitic acid, and a low percentage of stearic acid) will contribute to even better intestinal absorption of the fats in this milk than the fats in human milk in developed countries. Since calcium absorption, like that of other essential nutrients—for example, fat-soluble vitamins—is closely related to fat absorption, an increased absorption of these nutrients may also be expected in children in Tanzania, which might contribute to the increased speed of growth during the first month of life (as will be shown in a study to be published).

I conclude that differences obviously exist between Tanzanian, British, and Dutch infants in the fatty-acid composition of their body fat. These differences are subtle during the last stage of pregnancy but appear to be most pronounced during infancy and early childhood and are apparently attributable to the nature of the dietary fat in the three countries.

Breast-feeding is still the most common feeding practice for Tanzanian infants during at least the first year of life, and Tanzanian breast milk showed a different fatty-acid composition when compared with the fat of milk formula based on cows' milk, of formula in which the fat in cows' milk had been entirely replaced by maize oil, and even of human milk from Great Britain. This specific fatty-acid composition of the fat in Tanzanian breast milk might ensure even better intestinal absorption by the newborn infant when compared with the fatty-acid composition of human-milk fat in Great Britain.

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