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Causes of Low Birthweight in Developing Countries

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Low birthweight was originally defined as 2,500 g or below, but more recently it has been revised to less than 2,500 g. It is a simple definition requiring only an accurate measurement of weight. It does not infer that all light babies will require special care but, like all babies whatever their weight, special attention will be necessary to provide adequate warmth, food, and love—and if they come to medical attention—to prevent cross-infection from one baby to another.

It is of course also necessary to characterize the baby's weight in relation to other features as well, particularly his gestational age, and then to compare this with some external reference data (or standard) of weight for gestational age. There are varied and strongly held views on whether local or international reference data should be used and whether they should be based on the total or on only a selected "normal healthy" population; we have discussed this in detail previously (1). Even after these allowances other adjustments must be made: Some intrinsic biological law results in boys being heavier than girls (this is intriguing in its own right, but it would be unreasonable to expect girls on average to be as heavy as boys); first born children are lighter than subsequent births wherever birthweight has been studied; and so on. There is probably no end to the adjustments and allowances one can make. Crude as it is, therefore, "birthweight," lone and unadorned, summarizes an amalgam of biological and pathological factors which have affected the child's growth.

In this chapter I have drawn on published work from many developing countries, and for those who wish to pursue particular points in further detail, I have tried to give at least a passing reference to many of the papers concerned with the causes of low birthweight in developing countries which have been published in English since 1983. Rather than give a mere literature review, however, I have also drawn on our own experience at Sorrento Maternity Hospital in Birmingham, England, which has for many years looked after many mothers and their babies from the Indian subcontinent, particularly from Pakistan. A number of recent papers have also drawn lessons from ethnic differences in birthweight (2–10). Elsewhere in this volume, Canosa describes the problems as actually seen in India and Bangladesh.

THE SORRENTO EXPERIENCE

Immigration from the Indian subcontinent to Britain began during the Second World War and gathered pace thereafter. People came from particular areas such as Gujarat and the Punjab and tended to settle in local communities. Immigration of Asian British subjects from East Africa also occurred and this was enhanced by the expulsion of Asian people from Uganda in 1974. The East African Asians had probably enjoyed a higher standard of living than those from India and Pakistan. Last to arrive were people from Bangladesh who had often been living in conditions of extreme privation.

As immigration declines and the newcomers acclimatize to their new environment the opportunity to study and learn from them will similarly decline and so it is useful to have this opportunity to summarize our experience to date. Table 1 shows the changes which have occurred in the weight of Pakistani babies born at Sorrento and the changes in some of the major factors known to affect birthweight, i.e., gestational age, parity, and the height of the mother. Table 2 shows a multiple regression analysis of these factors as they affect birthweight, first in a single year (1983) (i.e., a static or "one point in time" analysis), and second as an explanation of the change occurring in the decade 1968–1978. Many multivariate analyses of birth-

TABLE 1. *Details of Pakistani babies and their mothers at Sorrento Maternity Hospital, Birmingham, England*

	1968[a]	1978[a]	1983[b]
n	152	228	260
Birthweight (kg)			
Mean	3,022	3,161	3,204
Percent < 2500 g	9	7	—
Gestational age (weeks)			
Mean	38.2	38.5	39.12
Percent < 37 weeks	13	10	5
Previous births			
Mean	2.1	2.5	2.2
Percent none	32	19	22
Percent 1–4	55	61	58
Percent > 4	14	20	20
Maternal height (cm)			
Mean	152.8	153.3	153.7
Percent < 150 cm	37	24	
Mean time elapsed since previous birth (years)	1.9	2.2	
Percent teenage mothers	11	8	

[a]Data from ref. 42.
[b]Data from ref. 17.

TABLE 2. *Influence of various factors on birthweight of Pakistani babies born at Sorrento, Birmingham, England*

	Factor				
	Gestation	Sex (M vs. F)	Parity (subsequent vs. first pregnancy)	Maternal height	Unexplained by the factors considered
Births in 1983[a]	+ 150 g/week	+ 124 g	+ 134 g	+ 12 g/cm	78%
Change 1968–1978[b]	+ 0.3 week		+ 0.4 birth	+ 0.5 cm	
Effect of change on birthweight[b]	+ 23 g		+ 34 g	+ 16 g	47%

[a]Data from ref. 17.
[b]Data from ref. 42.

weight have been published. Recent ones from developing countries include those by Lun et al. (11) and Bantje (12). Perhaps the outstanding conclusion from such analyses, including ours, is that so much of the variance in birthweight remains "unexplained" after taking all of these factors into account. Presumably it is in this unexplained sector where there is progress to be made. It is interesting that in a static analysis, i.e., that for 1983, our mathematical approach cannot account for 78% of the spread in birthweight, but when analyzing change, i.e., from 1968–1978, the unexplained proportion has fallen to 47%. I am wary of over-interpreting this but perhaps a continued analysis of secular change in birthweight is likely to be more fruitful in identifying the crucial factors in the determination of birthweight.

Having discussed the "parameters" of birthweight using an essentially mathematical analysis, this chapter now turns to a developmental approach, following the fetus from before conception to birth.

BEFORE CONCEPTION

Maternal Height

Shorter mothers tend to have lighter babies. In our own studies of Pakistani mothers in Birmingham an extra centimeter of maternal height was associated with an extra 12 g of baby weight (± 2 SEM, range 4–20 g).

Clearly then, the health of the mother during her own girlhood is an important factor in the epidemiology of low birthweight. Anything that improves growth in childhood will make some contribution to improved fetal growth in the next generation, but it is more important that the particular pregnancy is healthy.

In 10 years, although the height of our Pakistani mothers in Birmingham had increased by only 0.5 cm, this had made an estimated 16 g contribution to the observed increased birthweight of 139 g seen during that time. This accounts for 12% of the total increase, hardly dramatic but at least an encouragement for steady endeavor. The effect of maternal stature on birthweight in Thailand has been recently reported (13).

Fertility Behavior

There are various behavioral aspects of fertility which appear to affect intrauterine growth, including age of the mother, birth interval, and parity.

Teenage mothers tend to have lighter babies. In many parts of the world, teenage pregnancy, although accepted with reluctance, is not regarded as ideal. Consequently, mothers are more likely to be unsupported and to live in poorer socioeconomic circumstances. This is true for example in Nairobi, where 14% of babies born to teenage mothers were of low birthweight and 24% were preterm compared with 7% and 7%, respectively, in non-teenage mothers (14). Other recent studies on the development and nutritional aspects of pregnancy in teenagers are those by Frisancho et al. (15,16). However, in some parts of the world early teenage marriage and pregnancy are common and quite accepted. It is not known whether these girls carry on growing throughout their pregnancy, or what effect pregnancies during the growing period have on ultimate adult stature.

Short birth intervals, particularly of less than 12 months, are associated with an increased risk of low birthweight. Effective contraception is therefore part of a strategy of reducing the prevalence of low birthweight; as breast feeding has receded in some countries, so birth intervals have got less. Again the exact mechanisms are not understood. It is tempting to suggest there has been insufficient time to recover from the nutritional stress of pregnancy, but is this true? After all, at birth the mother has some energy stored as fat to help her through lactation. If lactation is very short because another pregnancy occurs, is this nutritionally more demanding for the mother?

In all societies studied, parity has an effect on birthweight; second babies are heavier than first babies but thereafter the difference is small. We found the difference in weight between the first and subsequently born infants to be 120 g (± 2 SE, range 5–240 g). Presumably the policy towards smaller families in China could lead to a reduction in mean birthweight if there were no other concurrent changes.

CONCEPTION AND EARLY PREGNANCY

Genes

Clearly genes affect intrauterine growth. Many of the major chromosome and specific gene disorders are associated with definite reductions in birthweight, but often the deficiency of growth apparent at birth is small compared to that in later life (e.g., Turner's syndrome).

We are not concerned with these major abnormalities here. While sometimes devastating in their effect on the individual, their effect on the mean birthweight of the population is small. Some "genetic" factors might however have a population effect; parental consanguinity is one such factor. Some studies have shown that consanguinity impairs intrauterine growth while others have not. Table 3 summarizes the results of our own and previous studies on this subject. Our own conclusions were that consanguinity does result in an increase in the number of poorly grown babies (17% of the babies of first cousin parents were below the 10th percentile of weight for gestational age) but overall the effect on mean birthweight of the population is quite small—less than 100 g (17). The mechanism whereby consanguinity results in an increased prevalence of poorly grown babies is not clear. Although the evidence is inconclusive, consanguinity seems to be associated with a higher prevalence of congenital malformations and this may mean that whatever causes the congenital malformation in early pregnancy also begins to retard growth at the same time.

Many mothers in the developing world are Moslem and consanguinous marriages, particularly of first cousins, are preferred.

Another genetic factor is the tendency to have multiple ovulation and therefore multiple births. This is particularly common in Nigeria (18,19). More general reviews of the various factors affecting birthweight in Nigeria were summarized in 1985 by Ransome-Kuti (20) and since then there have been several further analyses (21–24).

LATER PREGNANCY

Gestational Age

In all analyses, gestational age is the most important factor affecting birthweight. In our study of Pakistani mothers, an extra week of gestation was associated with an increase in birthweight of 150 g (± 2 SEM, range 110–190). This was 20 g more than the difference due to parity and 30 g more than that due to sex. It was the equivalent of an extra 12.5 cm in maternal height.

Although the prevalence of low birthweight in different environments has received considerable attention, the prevalence of preterm birth has received much less, perhaps because the determination of gestational age is more difficult.

Gestational age is less easily assessed in developing societies, and so many of the lessons which may be relevant to the developing world have to be drawn from developed industrial societies. In Birmingham we found part of the secular increase in the weight of Pakistani babies was due to a slight lengthening of gestational age (2 days) and a slight fall in the number of preterm births (from 13% to 10%). Small as these changes are they contributed 23 g to the overall increase in birthweight of 139 g.

Perhaps more attention should be paid to gestational age. Possibly even small increases would have a measurable effect on birthweight.

TABLE 3. *Comparison of studies of effect of parental consanguinity on fetal growth*

Study	Country (population studied)	Numbers: Total	Numbers: Consanguineous	Numbers: Unrelated	Birthweight (g): Mean consanguineous	Birthweight (g): Mean unrelated	Birthweight (g): Difference (consanguineous-unrelated)	Birthweight (g): Significance of difference	Birthweight (g): Weight for gestational age, parity, sex, and maternal height (% < 10th percentile)	Other factors affecting birthweight allowed for in statistical analysis	Other body measurements
			126	196	2,731	2,834	− 103	$p < 0.01$			
Siben (43)	India (Tamil Nadu)	322	UN 52		UN 2,650					Gestational age—term babies only included	Length, head circumference, skinfold thickness
			C1 61		C1 2,794						
			C2 13								
Morton (44)	Japan	75,180	C1 2,928	70,088	C1 3,046	3,074	− 28			Gestational age, parity, city	
			C2 2,144								
Schork (45)	Japan	2,314	230	2,084	3,099	3,091	+ 8	NS		Parity, sex, maternal age, paternal age, month of birth	Head circumference, chest girth

Rao (46)	India (Tamil Nadu)			Rural									
				3,889	4,449		2,740	2,772	− 32	NS			Length, head circumference, chest girth
		14,243	UN	1,308									
			C1	1,991									
			C2	590									
				Urban									
				1,654	4,251		2,883	2,867	+ 16	NS			
			UN	371									
			C1	989									
			C2	294									
Slatis (47)	United States (white)	108		63	45		3,247	3,352	− 105	NS			
Paddaiah (48)	India (Andhra Pradesh)	1,823		1,821	3,002		2,820	2,880	− 60	$p < 0.001$		Sex, socio-economic state	Length, head circumference, chest girth, calf girth
Honeyman (17)	United Kingdom (Pakistani Moslems)	260	C1	122	76	C1	3,178	3,258	− 80	NS	C1 (17)*	Gestational age, sex, parity, maternal height	Length, head circumference, skinfold thickness
			C2	62		C2	3,192		− 66	NS	C2 (6)		
											Unrelated (5)		

*$p < 0.05$.
NS = Not significant.
C1 = first cousins; C2 = more distant than first cousin. UN = uncle/niece.
From ref. 17.
Since preparing this table Khoury et al. (49) have published their study of consanguinity in the Amish. They also found an increased prevalence of intrauterine growth retardation, but their method of presenting their results makes it difficult to summarize them in this table.

Anemia

It may be that anemia has not received sufficient attention as an indicator of poor intrauterine growth. The situation is complex, however. In normal pregnancy the hemoglobin falls, and this is partly but not wholly explained by hemodilution. We and many others have observed that this "normal" fall in hemoglobin does not occur in European mothers who produce a poorly grown baby (25, and see also Marini in this volume). However, a low hemoglobin may also be a marker of poor maternal reserves. A large study in Indonesia showed that primiparous mothers of low birthweight babies had a hemoglobin level 0.3 g below those having babies weighing 3.0–3.499 kg and this difference increased with increasing parity up to a difference of 0.6 g at parity 5 or more (26). There have been other recent studies on this subject (e.g., 27). Reduced hemoglobin is not necessarily evidence of a specific deficiency—only an intervention study with iron supplements could determine that. It is more likely to be just one component of the mothers' poor environment.

Hypertension

It is well-established that maternal hypertension, whether it is the pregnancy-specific variety developing after the 20th week (i.e., preeclampsia) or due to some pre-existing problem, is associated with poor intrauterine growth and an increased perinatal mortality. In the British Perinatal Mortality Survey of 1958, severe preeclampsia (i.e., diastolic pressure above 110 mm Hg, or above 90 with proteinuria) was associated with a reduction in mean birthweight of 225 g (28).

The prevalence of preeclampsia in different communities varies. The reason for this is not clear, although two of our colleagues contributing to this volume have suggested a relationship between calcium intake and pregnancy hypertension (29). In Birmingham we found that fewer of our primiparous Asian mothers (25%) had hypertension when compared with our European mothers (46%) and with the UK national average (34%) (30). Interestingly, this difference was not apparent in the multiparae (20%, 24%, and 24%, respectively).

Smoking

Again, it is well-established that smoking in later pregnancy is associated with poor intrauterine growth. There has been considerable discussion as to whether smoking itself is the true cause or whether it is merely a marker for poorer socioeconomic circumstances, poorer diet, and perhaps a higher alcohol intake. However, one study of a health education intervention did result in increased birthweight (31). Maternal smoking is uncommon in most rural areas of the developing world but it is becoming increasingly frequent in urban areas. I have not been able to trace studies concerned with the effects of smoking on birthweight specifically in developing countries, though Verma et al. (32) have described the effect of tobacco chewing on fetal outcome in India. I suspect, to use a vernacular phrase, that this would be "one more nail in the coffin," but this may not necessarily be the case. Perhaps, in developing countries, major influences such as nutrition act as the limiting factors, and so other environmental influences have little effect.

Malaria

The association of malaria with perinatal pathology is well established (33), but just as with smoking it has not been made absolutely clear whether the relationship between maternal malaria and low birthweight is causal or merely an association. More affluent mothers would tend to avoid malaria and these mothers could have larger babies for other reasons. Perhaps the best evidence of a direct cause and effect association is the experience in the Solomon Islands (34) where an anti-mosquito campaign, though relying on a historical control technique, was quickly followed by a substantial reduction in the number of low birthweight babies.

We are certainly not winning the battle against malaria at present, and the result of this is that more low birthweight babies are likely to be born. Robyn, elsewhere in this volume, discusses malaria in more detail.

Energy Balance

A report of the discussion on maternal supplementation appears later in the volume. I have therefore reviewed supplementation in more detail there.

I would in this chapter, however, like to develop in more detail the concept of energy balance in mid-pregnancy. During the second trimester a substantial amount of the mother's weight gain is due to an increase in her own fat stores—not only is her fetus growing, she is growing too. In later pregnancy most of the weight gain is due to the rapidly growing fetus and placenta. The mother herself has stopped growing, her fat stores are no longer increasing; in fact they decrease a little.

We noted that Asian mothers who went on to have poorly grown babies had put on little fat in the second trimester (35); indeed, their triceps skinfold thickness hardly increased at all. The increment in triceps skinfold also indicates which mothers will benefit from nutritional supplementation (36,37). In a larger and more recent study (38) we have confirmed the value of triceps skinfold increments during the second trimester in predicting intrauterine growth (See Table 4).

We consider that the increment in skinfold thickness represents the state of energy balance, i.e., intake minus output over a 10-week period at a crucial time in mid-pregnancy, when the mother is laying down stores in anticipation of later fetal demands. Nutrition in pregnancy is concerned with the input side of the balance. There is little point in increasing the input if there is not a potential negative balance and, indeed, there is some evidence of an adverse effect.

The output side of the balance is concerned with energy expenditure, and in recent years this has received increasing attention. It seems that many women in de-

TABLE 4. *Birthweight, birthweight percentile,[a] and placental weight in mothers who accumulate fat inadequately (triceps skinfold increment ≤ 20 μm/week) and in mothers who accumulate fat adequately (triceps skinfold increment > 20 μm/week) during the second trimester of pregnancy. From Viegas et al. (38). Results are means (SD).*

Measurement	Babies born to mothers who accumulate fat inadequately n = 35	Babies born to mothers who accumulate fat adequately n = 46	*p*
Crude birthweight (kg)	2.96 (0.33)	3.14 (0.42)	< 0.05
Gestational age (weeks)	39.2 (1.2)	38.9 (1.1)	NS
Thomson SD score[a]	− 0.685 (0.66)	− 0.255 (0.80)	< 0.02
Sorrento SD score[a]	− 0.411 (0.79)	0.198 (0.81)	< 0.005
Other baby anthropometry			
Head circumference (cm)	33.8 (1.2)	34.6 (1.2)	< 0.005
Length (cm)	49.8 (1.9)	50.3 (2.1)	NS
Triceps skinfold (mm)	3.62 (0.63)	3.80 (0.76)	NS
Biceps skinfold (mm)	3.33 (0.62)	3.93 (0.76)	NS
Suprailiac skinfold (mm)	3.17 (0.75)	3.93 (0.85)	NS
Mid upper arm muscle circumference (cm)	8.83 (0.59)	9.13 (0.72)	< 0.05
Placental weight (g)	551 (98)	616 (112)	< 0.01

p values indicate significance of difference between the two groups. NS: $p > 0.09$.
[a]*Birthweight percentile for gestational age, sex, parity, and maternal height according to data from refs. 36, 37, and 50.*

veloping countries carry on doing strenuous work throughout their pregnancies (39). There have also been a number of accidental "experiments" suggesting that work in later pregnancy is deleterious, e.g., flooding in Tanzania led to less work in the fields, a strike in Bombay led to less work in the cotton mills, and in both instances, birthweight was improved (40,41).

CONCLUSIONS

Low birthweight is commoner in developing countries than in the remainder of the world. There is a tendency to relate this difference solely to differences in maternal nutrition. Undernutrition makes a contribution to the problem, and I have no doubt it makes a considerable contribution. Nevertheless, it is not realistic to brood over nutrition alone without due consideration for other genetic and environmental characteristics of the developing world, such as parity, birth interval, consanguinity, smoking, malaria, hypertension, anemia, and so on.

The ills of geographical pathology are not susceptible to isolated nutritional explanation.

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