Nutrition in pregnancy

F. E. HYTTEN
M.D., Ph.D., F.R.C.O.G.

Division of Perinatal Medicine, Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ

Summary

Epidemiological evidence shows that women living in affluent circumstances have bigger babies with a lower mortality than underprivileged women. How much of that effect is due to nutrition alone is not known but supplementary feeding in pregnancy of chronically ill nourished women does appear to increase mean birth weight, and famine conditions in a basically well nourished community reduce the birth weight; in both cases the birth weight difference is relatively small and could be accounted for by no more than fetal adipose tissue.

The fetus may be much less vulnerable to vagaries of maternal diet than has been thought because of protective physiological mechanisms associated with pregnancy. Firstly the mother's energy balance changes, so that if she has access to extra food in the first half of pregnancy she will store large amounts of depot fat as an energy buffer against possible privation later. Secondly, there are widespread changes in nutrient metabolism one of which is to lower plasma levels of most nutrients, and that may tip the balance of advantage away from maternal tissue towards the placenta. Finally, the placenta itself has developed elaborate mechanisms to acquire nutrients from the maternal circulation. A notable exception to that rule is glucose for which no active transport mechanism has evolved and which might therefore be regarded as a low priority nutrient; it may be that the generous supply of glucose for the fetus which would be provided by a well fed woman does little more than allow the fetus to build up its fat stores.

Introduction

The subject of nutrition embraces everything from population statistics to the subtle activities of intracellular enzymes. Information throughout that range is particularly thin and fragmentary in pregnancy, but with a bravery born of ignorance the author would like to collect together some of the phenomena associated with nutrition in pregnancy and try to make some kind of coherent if superficial picture.

Although it is obvious to the clinician that most poorly nourished and socially deprived women re-

produce easily, and that healthy well fed mothers may produce poorly grown infants, it is nevertheless part of medical folk-lore that successful reproduction depends on good nutrition. Large scale statistics support that idea: women in affluent circumstances have bigger babies and fewer perinatal deaths than socially under-privileged women, but interpretation of those differences is bedevilled by the fact that nutritional variables never operate in isolation. Affluent mothers are not only better fed, they enjoy and have had a life-long experience of superior health, education, housing and medical care; they plan their families advantageously and they smoke less. Thus, the large differences in perinatal mortality which occur within a single small country such as Britain from the high rates in Clydeside and Merseyside to the low rates in South-East England undoubtedly reflect more than simple differences of diet during pregnancy.

The most persuasive evidence that diet itself may have an effect on reproductive performance was provided by the involuntary 'feeding experiment' made on a national scale in Britain during World War II. A dramatic fall in the stillbirth rate (per thousand total births), from 38 in 1940 to 28 in 1945 was considered by Duncan, Baird and Thomson (1952) to be due mainly to improved maternal nutrition which followed an enlightened food-rationing policy under which pregnant and lactating women received priority; civilian medical services were attenuated and there was no advance in treatment that would plausibly have reduced stillbirths so substantially at that time.

But even in a wholly nutritional context interpretation is not straightforward. How much of an effect is due to 'nutritional status', that elusive concept of being well grown and well nourished which is so difficult to define and measure, and how much to the actual diet taken during pregnancy? Again the two overlap. Women who live in socio-economic circumstances where they are poorly fed as children, grow poorly, and eat poorly as adults, are the ones who eat poorly in pregnancy.

The combined effect is not as great as one might

expect. Gambian women who are small and, by Western standards, ill nourished, also have small weight gains in pregnancy; when most of pregnancy coincides with the wet season with its associated load of increased agricultural work and infectious disease the mean weight gain can be as little as 2.2 kg (Thomson *et al.*, 1966). Yet the seasonal fluctuation in birth weight is small and not statistically significant, and the infants generally thrive.

In spite of the apparently unspectacular effects of chronic under-feeding there is evidence that dietary supplements in such circumstances may improve fetal size. In a carefully controlled study of a chronically malnourished Guatemalan community, Lechtig *et al.* (1975) were able to increase mean birth weight by over 100 g and halve the incidence of low birth weight babies with a dietary supplement during pregnancy exceeding 20 000 cal (84 MJ) (Fig. 1). Whether the supplement had a substantial protein component, or no protein, made no difference to the result, and Lechtig *et al.* speculated that the increase in birth weight might be 'a function of the accumulation of fetal adipose tissue'.

What of the reverse situation where, because of war or famine, severe dietary deprivation occurs in pregnancy to previously well nourished women? Communities engaged in war or faced with famine have other things to do than record detailed obstetric observations but substantial data exist for the severe famine which occurred in North-West Holland from mid-September 1944 until liberation in May 1945 when during an unusually severe winter mean daily calorie intake fell to well below 1000 cal and other necessities of life such as fuel were extremely scarce (Smith, 1947).

The most obvious effect on reproduction of sudden severe under-nutrition is infecundity so that the famine was followed 9 months later by a massive fall in the birth rate (Stein and Susser, 1975a) (Fig. 2), but large numbers of women were pregnant for all or part of the famine. When the last third or last two thirds of pregnancy coincided with the famine the birth weight of the infants was conspicuously

reduced by an average of about 350 g; but if the last third of pregnancy escaped the period of famine, birth weights were not affected (Stein and Susser 1975b) (Fig. 3).

The infants born after exposure *in utero* to the Dutch famine were a little shorter than before although the effect was much less than the effect on birth weight and not statistically significant. Perhaps the fetus which is deprived because its mother does not eat enough is not particularly stunted, merely thin, and the 300- or 400-g deficit which distinguishes it from the fetus of a well fed mother may be largely the luxury of a subcutaneous fat store.

It is true that where dietary deprivation is severe and prolonged, with manifest vitamin deficiency and where the population is subject to continuous cold and physical and nervous stress, as occurred in the German siege of Leningrad (Antonov, 1947) the effects appear to be more profound with devitalized babies and a high mortality, but those circumstances are more complex than simple dietary deficiency.

In summary, therefore, apart from such extremes as the siege of Leningrad, there is epidemiological evidence that poor nutrition and all that goes with it is linked to a reduced reproductive performance with somewhat smaller infants; that supplementary feeding during pregnancy of chronically ill nourished women increases the weight of their infants; and that starvation in pregnancy of women who are basically well nourished reduces birth weight.

Those generalities must be kept in perspective. The relatively poor reproductive performance in countries where nutritional standards are chronically low is not sufficient to prevent an embarrassing growth of population. And as Thomson (1959) pointed out, the dramatic and unprecedented fall in the stillbirth rate over 5 years in wartime Britain was only 1% and if a similar change was expected in a controlled feeding experiment, it would require more than 10 000 experimental and control subjects to be reasonably sure of obtaining a statistically convincing result. Even the very large depression in

FIG. 1. The effect of dietary supplementation on birth weight in a Guatemalan community (from the data of Lechtig *et al.*, 1975). By permission of the editor of *Pediatrics*.

FIG. 2. The effect of the famine in North-West Holland in 1944-45 on fertility (from the data of Stein and Susser, 1975a). — Calorie ration; ---- total births.

birth weight of the infants born to the starving Dutch women appears to have had no permanent effect on their subsequent growth and intellectual development (Stein *et al.*, 1975).

Throughout evolution pregnant women will have been subjected to nutritional deprivation from food shortage, and pregnant women seem always to have been subject to a range of nutritional taboos and restrictions. Even today nutritional advice given by obstetricians to their patients is generally restrictive rather than generous. The obvious ability of the pregnant woman and her fetus to weather the gamut of hazards from crop failure to obstetrical advice may well be due to physiological changes in nutrient metabolism which makes her more resilient to deprivation and her fetus less vulnerable than perhaps has been believed.

Changes in energy balance

Physiological changes in pregnancy are characteristically anticipatory and a good example is provided by a major change in energy balance. The average healthy woman eating to appetite gains 12.5 kg of body weight, a weight gain associated with the best clinical outcome, and this is considerably more than can be accounted for in the product of

FIG. 3. The effect of the famine in North-West Holland in 1944-45 on birth weight (from the data of Stein and Susser, 1975b).

conception, the growth of uterus and breasts and the expansion of volume of blood and other body fluids (Hytten and Leitch, 1971). The balance amounts to about 3.5 kg and is body fat. Figure 4 shows the

FIG. 4. Components of the weight gained by the normal pregnant woman (from Hytten and Leitch, 1971). Uterus and contents; ---- maternal stores; — blood and body fluids.

various components of weight gain separately; the pattern of accumulation of the extra body fat differs from that of the other components, beginning early in pregnancy, showing maximum rate of gain in mid-pregnancy and almost stopping in the last trimester. That pattern is confirmed by measurements of skin fold thickness which further shows the characteristic centripetal distribution of fat accumulation in pregnancy: over the abdomen, back and upper thighs there is a progressive increase in skin fold thickness up to about 30 weeks after which there is no further increase; over the arms and lower part of the thighs there is no increase or even a loss.

The accumulation of depot fat on a scale otherwise unknown in healthy adult life makes obvious biological sense. The average woman will enter the last trimester of pregnancy with a very considerable buffer against possible deprivation of food amounting to more than 30 000 cal (126 MJ). In Western society the healthy pregnant woman needs no such buffer, but the majority of the world's women do arduous manual labour until the day they give birth and it is generally in those parts of the world that food supplies are uncertain; such conditions were presumably the rule when mammalian reproduction was evolving. Analogous anticipatory fat storage occurs in mammals before hibernation and in birds before migration. Figure 5 shows that the energy accumulated in body fat by the average pregnant woman in the first 2 trimesters of pregnancy could completely subsidize the extra maintenance costs of late pregnancy.

The evidence suggests that the stimulus to accumulate body fat is not simply through the appetite-satiety centres driving the mother to eat more but by a more fundamental change in the control of energy balance. The total quantity of body fat is controlled by a central 'lipostat' and if this is set higher, as it can be, e.g. in female rats by progesterone, then the new level of body fat is achieved either by eating more, or expending less energy, or both. The pregnant woman normally does both, although to what extent either is possible in some developing communities is not known. Appetite usually increases within the first trimester, but even without a conscious increase almost all women eat more than usual by a daily average of some 200 cal (840 kJ), about half the specific requirement shown in Fig. 5.

FIG. 5. The cumulative energy costs of pregnancy (from Hytten and Leitch, 1971). ▨ Maintenance; ▨ fat; ■ protein.

They also reduce energy output in several ways: women are relatively listless in pregnancy, they spend more time at rest and they perform fewer strenuous tasks; moreover they appear to perform those tasks with more economy of effort than when they are not pregnant and there is a general relaxation of voluntary muscle. A reduction in circulating free thyroid hormone also suggests that all maternal tissue may be metabolizing at a somewhat reduced tempo.

Changes in nutrient metabolism

Much less is understood about the many changes in nutrient metabolism. One of the most studied is glucose and Dr Lind (1979) will be dealing with that aspect in detail. The fasting level of glucose in plasma falls within the first few weeks of pregnancy to a new level some 10–15% below the non-pregnant concentration (Lind, 1975) and that has been interpreted (e.g. by Freinkel, 1969) as 'accelerated starvation'

due to the continuous withdrawal of glucose and amino acids by the fetus. The concept is unconvincing because the fall occurs at the beginning of pregnancy when competition by the fetus weighing only a few milligrams cannot be seriously entertained, and because prolonged starvation in pregnancy (Felig and Lynch, 1970; Tyson *et al.*, 1976) fails to show a progressive disadvantage to the pregnant woman (Fig. 6). Whatever its explanation, the reduced fasting glucose concentration stands in curious contrast to the progressive relaxation of glucose tolerance following a glucose load in spite of an increasing insulin response. It is difficult to see what purpose might be served by this change of control but presumably the fetus has a better chance of sharing the maternal meal if glucose levels in the plasma perfusing the placenta remain higher for longer.

Glucose is not alone in showing reduced fasting levels; the plasma levels of most nutrients fall in pregnancy (Fig. 7). Only lipid fractions tend to rise, and while it is possible to explain some of the changes in the figure the majority are enigmatic (Hyttén, 1978a).

The homeostatic control of nutrient levels in blood and tissue fluids reflects two kinds of physiological need: the need to have a certain *total quantity* of a substance available in the circulation, and the need to have a substance at a *particular concentration*. Thus it is the total quantity of some protein fractions in the circulation which matters; of fibrinogen for effective haemostasis, of γ -globulin for effective control of infection and of haemoglobin where the total is matched with some precision to the

need for oxygen carriage. For other substances the efficient function of the body requires a precisely controlled concentration: ionized calcium and hydrogen are examples.

In pregnancy both types of control are affected. For example Ca^{++} and H^{+} are preserved at the usual non-pregnant concentrations, but osmolality and PCO_2 whose levels are subject to equally careful control are maintained during pregnancy at much lower levels. As examples of changes in total quantity, there is a greatly increased amount of fibrinogen in the circulation, enough to raise the concentration considerably even in the expanded plasma volume; and there is also a considerable rise in the total circulating haemoglobin, quite sufficient to cover the needs for extra oxygen carriage but not enough to prevent a fall in concentration as the plasma volume rises; on the other hand the total quantity of circulating albumin falls, and with it albumin concentration and colloid osmotic pressure.

How the levels of most nutrients are controlled is a mystery. Why do the fat-soluble vitamins tend to rise in concentration while the water-soluble vitamins invariably decline? Why does fasting glucose fall in early pregnancy to a new level, and why do amino acids show a complex pattern of change where some remain unchanged, but the majority fall?

The answers to those, and many other questions, are unlikely to be found before the fundamentals of control are understood at least for the non-pregnant; at present there is no information about how nutrient levels in the blood are governed. For example, until one knows what controls the 'fasting' blood sugar in

FIG. 6. The effect of starvation on plasma levels of glucose and alanine in normal pregnancy (data (a) and (c) from Tyson *et al.*, 1976; (b) Felig and Lynch, 1970; (d) Felig *et al.*, 1972). The dotted lines refer to pregnant subjects the solid lines to non-pregnant women.

FIG. 7. Changes in pregnancy of the plasma concentrations of some nutrients. The levels shown in this figure are percentages of the non-pregnant level taken as 100% (Hytten, 1978a).

the normal person – why one woman should preserve a level of 5, and another a level of 4 mmol/l, one is not likely to be able to interpret the fall in level which occurs in early pregnancy. And that is even more true of nutrients like folate where there is no certainty that any homeostatic control exists at all.

The preponderant pattern of reduction in the plasma levels of nutrients suggests a common mechanism or perhaps a common purpose. No mechanism is known and because of the differences of pattern of fall none seems likely. Dilution by the increasing plasma volume cannot explain the sudden drop in concentration shown by glucose and amino acids in early pregnancy, although it could explain the more gradual change in folate concentration. Dietary deficiency or failure of absorption is cer-

tainly not responsible at least for most of the low levels described, although many can be artificially raised by large dietary supplements. Nor is it likely that excessive excretion in the urine plays more than a marginal role: all women show a reduced fasting blood sugar but not all have glycosuria and there is little relation between amino acid excretion and blood levels. For example, histidine, which is lost in greatest amounts in the urine, has an unchanged plasma level in pregnancy.

Although dietary deficiency is the popular scapegoat for the reduced nutrient levels in normal pregnancy it is worth emphasizing its implausibility: it seems excessively unlikely that a phenomenon affecting all healthy well nourished women having normal pregnancies and healthy babies is due to an inadequate diet, and the reduced concentrations often

and it seems strange that the fetus should have to rely on a favourable concentration gradient from occur in the presence of greatly increased total circulating quantities. Moreover, it is surely illogical to believe that lower levels of some nutrients such as folate or iron indicate dietary deficiency requiring supplements, when other nutrients with equally reduced levels such as glucose and some amino acids are ignored.

The changes in nutrient level are so widespread and varied in detail that it would appear that levels of many different nutrients are reduced by a resetting of many different mechanisms, and that suggests a common purpose. Could it be that a general lowering of nutrient levels produces a balance which favours transfer to the fetus rather than to maternal tissues? The placenta is clearly capable of taking up most nutrients with considerable efficiency and is perhaps better able to do so than the maternal liver at the low levels which are usual in pregnancy.

It is characteristic of many nutrients that the reduced maternal plasma levels are matched by a higher level in the fetal plasma with a level in the placenta considerably in excess of either circulation (Table 1). The placenta is clearly capable of extracting a large store from the maternal circulation to provide a consistent gradient towards the fetus. It appears to achieve this, at least for some nutrients, by operating a 'biochemical valve'. Nutrients taken into the placenta are transformed into derivatives which cannot return to the mother, a system which offers great advantage to the fetus, in the last resort at the expense of maternal nutrition. For example, the fetus may maintain normal folate levels while its mother becomes grossly anaemic from folate deficiency.

That is to say, the nutritional symbiosis between mother and fetus seems to involve the 'deliberate' change of nutrient levels in the maternal blood to shift the balance of advantage to the fetus. In a well

fed society the fetus has no need of this advantage, but if the mother is deficient then the fetus will exercise it to the detriment of the mother and it becomes a true parasite.

The relative sizes of mother and fetus allow the fetus to take such essential nutrients as amino acids from the mother, even if she is having to mobilize them from her own tissues, without serious embarrassment. Some other nutrients such as folate, however, may be in such short supply that the relentless fetal mechanism of acquisition can threaten the mother's life.

Conclusion

Although poor nutrition leads to a reduced reproductive performance the effect is marginal and requires large population groups to demonstrate it. The starvation of previously well nourished women during pregnancy, and the dietary supplementation of chronically ill nourished women has a relatively trivial effect, a change in mean birth weight of no more than about 300 g with an otherwise unconvincing effect on fetal size.

It is suggested that, in general, the fetus which is deprived only because its mother does not eat enough is not particularly stunted, merely lean, and the 300-g deficit which distinguishes it from the fetus of a well fed, or a supplemented mother may be largely the luxury of a subcutaneous fat store.

From the point of view of the fetus, nutrients appear to be separated into two main groups. Those which are vital to its growth and development and for which mechanisms have evolved to ensure supplies at all costs, and those which are in a sense optional extras, used if available but depending upon favourable concentration gradients from the mother.

In the latter group are glucose and fatty acids. Obviously some fatty acids are essential for the fetus

TABLE 1. Approximate plasma levels of 4 water soluble nutrients in the mother before pregnancy and in late pregnancy, and in the fetus, compared to tissue levels in the placenta

Substance	Maternal plasma		Placental tissue	Fetal plasma	Reference
	Before pregnancy	Late pregnancy			
	Per litre	Per litre	Per kg	Per litre	
Free amino acids (μmol)	2800	1800	10 000	3300	Lindblad and Baldesten, 1967 Pearse and Sornson, 1969
Ascorbate (mg)	20	10	90	20	Barnes, 1947
Total riboflavin (μg)	60	30	2140	40	Lust, Hagerman and Vilee, 1954
Folate (μg)	7	3	750	15	Landon and Hytten (unpublished)

and it seems strange that the fetus should have to rely on a favourable concentration gradient from the mother for its supplies (Elphick, Hull and Sanders, 1976; Elphick, Edson and Hull, 1978). However, since free fatty acids in the plasma rise when the mother starves it seems unlikely that the fetus would ever be seriously deprived. Glucose, in contrast, is something of a luxury food, and the infant's fat store, built from glucose, is largely a function of the mother's plasma levels, high in the well fed and low in the starved. When the mother eats well then the relaxed glucose tolerance allows the fetus a generous share; when she does not then the fetus gets enough glucose for its immediate needs or can make it from non-carbohydrate precursors. If a generous supply of glucose were essential to fetal growth and survival then evolution would presumably have seen to it that the placenta acquired glucose actively, but glucose crosses to the fetus by facilitated diffusion and depends for its placental transport on a gradient from the mother (Hytten, 1978b).

It seems unlikely that fetal growth would be noticeably affected by marginal supplies of glucose, although it is possible that if the fetus does have increased levels of plasma glucose then the insulin which it may release to control it will have a minor growth-promoting effect. But the essential nutrients such as amino acids and the vitamins are actively transported to the fetus by a placenta which will acquire them inexorably regardless of the mother's state of nutrition, ensuring a reasonably well grown if lean baby.

The author must reiterate that he is speaking as a physiologist about the physiological safeguards against maternal deprivation enjoyed by the fetus of a basically healthy woman and which he believes it is very difficult to damage by overall restriction of diet. However, for the fetus of an apparently normal woman which is growth-retarded perhaps because of some pathology affecting placental function, these safeguards may not be effective and dietary supplements are probably inappropriate.

In communities such as rural Guatemala, where most mothers are deprived, undergrown and generally unhealthy, extra feeding in pregnancy may help to support the infant's undoubted capacity to survive by parasitism, but the basic defect of prolonged underfeeding of the mother must be tackled at a social rather than a clinical level.

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