PROCEEDINGS OF THE NUTRITION SOCIETY

VOL. 2, NOS. 1 and 2 1944

TENTH SCIENTIFIC MEETING—SIXTH ENGLISH MEETING

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE,
FEBRUARY 6TH, 1943

NUTRITION IN PREGNANCY

Morning Session: Chairman, Dr. F. H. A. MARSHALL

In opening the proceedings, Dr. F. H. A. Marshall (Christ's College, Cambridge) commented on the remarkable adaptability during pregnancy of the maternal organism and of the developing young. This was shown in the great variation in the length of pregnancy in different species and still more in the same species when pregnancy had been artificially extended by experimental means. He also referred to multiple pregnancies in which young were able to develop in increased numbers. The increase was, however, strictly limited and *corpora lutea* were, undoubtedly, indirectly a factor in foetal nutrition.

Foetal Development

Mr. A. W. Bourne (12 Wimpole Street, London, W.1)

In such an immense field of knowledge and work as that of foetal development it is possible to discuss only one small aspect. It is proposed, therefore, to look at the subject from the point of view of the obstetrician, that is, of one who sees something of the processes of human reproduction and the quality of the child.

The factors which contribute to the ideal normal results of reproduction for both mother and child are very many and of differing importance but, of all these, we know that food, which embodies an adequate supply of all the nutrients, is the most important in the aggregate. The results of a field survey in South Wales under the direction of Lady Rhys Williams (Williams, 1936–37, 1, 2) illustrate broadly the effect of improving the food supply of pregnant women; they are set out in Table 1.

TABLE 1

MATERNAL DEATH RATE (1) AND STILLBIRTH AND NEONATAL DEATH RATE (2) PER 1000 BIRTHS IN 2 AREAS IN SOUTH WALES

	One area, 1934			Another area, 1936	
	Before experiment	After medical care for one year	After medical care and additional food for one year	Before experiment	After additional food only
(1)	7·20	11·29	4·77	6·65	3·75
(2)	92·0	84·0	59·0	—	(National rate 3·64)

A brief glance at the figures shows the enormous extent of the improvement which can be made in the saving of maternal, foetal and infant lives, mostly by food alone.

In 1938 there were in the United Kingdom 24,729 stillbirths or 3·3 per cent. of the total births. Many of these were due to inevitably fatal conditions such as deformities and congenital defects incompatible with life, or to indifferent attention during labour, but there remains a large proportion associated with, and probably caused by, a sub-optimum condition of the mother during pregnancy.

There is evidence that the state of nutrition of the mother is important for its influence not only on the development of the birth vigour of her child, by which its survival is ensured, but also on uterine action during labour. If the action is feeble, so that there is a state of uterine inertia, the risk to the child is greatly increased. For example, Bourne and Bell (1933) found that in 49 cases, when labour lasted for 48 hours or more with no other obstetric complication, the foetal death rate both stillbirth and neonatal was 42 per cent.

Causes of Neonatal Death

Some neonatal deaths during the first month of life are due to neglect and errors of feeding. In 1938 the rate during the first four weeks of life among 1101 illegitimate babies was 41·74 per 1000 against 27·69 among 16,471 legitimate babies. An undetermined and larger amount of mortality is due to lack of what may be called vigour at birth.

During 1938 there were no less than 22,634 deaths under three months of age. When allowance has been made for those infants which die from neglect and unavoidable causes there remains a large number, many of them premature, whose vigour is not sufficient for them to thrive or protect themselves against infection. It seems probable that this latter group comprises children who suffer from the handicap of being born from women whose nutrition during pregnancy was qualitatively inadequate.

It is, however, not only infant mortality which has to be considered. There is another field, that of *infant morbidity*, and of failure to develop the optimum health of childhood and adolescence. Much of this handicap also can be attributed to faults in nutrition of the woman while carrying her infant.

Factors which Influence Birth Weight

While there may yet be some factors unknown, there are certain ones which can be recognized.

1. *Hereditary influence.* A small woman fortunately usually produces a small baby. In stock breeding it has been shown that the weight or size of the mother is the chief factor determining the size of the young (Walton and Hammond, 1938). Clinical experience supports the extension of this observation to man.
2. *Relative placental insufficiency.* This can be due to destruction of placental tissue by necrosis (infarction), caused by separation of an area of placenta from the maternal connexion, or possibly to a placenta being abnormally small for the foetus it has to carry. The majority of all necrotic cases are associated with albuminuric

toxaemia. Abnormal smallness of the placenta is a possible cause of dead birth, but is less common than might be thought. Holland (1922) found that among 300 foetuses dead from all causes, 17 deaths were ascribed to the abnormal smallness of the placenta with no obvious placental disease. It is interesting that 10 of the 17 were macerated foetuses which therefore died before labour, and all foetuses but one were of normal size showing that this cause of foetal death operated late. Holland says "Whether it is due to arrest of growth of the placenta or to a placenta, small from the beginning, it is impossible to say".

3. *Nutritional state of the mother.* This factor is acknowledged by all to have an important influence on the birth weight but only when the nutrition is on an unusually low plane. It may be that low maternal nutrition acts most forcibly in those species which have the longest gestation, *i.e.*, those in which the influence of dietary depletion has the longest time to act. Apart from general malnutrition, the lack of specific nutrients such as iron and calcium may be reflected in the foetus by the development of similar deficiencies. It is also possible that other specific deficiencies such as those of vitamins and trace elements may have an influence on foetal death *in utero*, and especially on the onset of premature labour. Nixon, Wright and Fieller (1942) have produced evidence to show that there may be a deficiency of vitamin B_1 in eclampsia and pregnancy toxaemia. They found a marked reduction in the excretion of vitamin B_1 in the urine and in the content of the placenta.

   Protein deficiency during the last quarter of pregnancy is probably a factor governing birth weight and birth vigour. Hammond (1932) states that the diet of the latter part of pregnancy influences the birth weight of lambs and that summer lambs are heavier than early spring lambs, probably because of the higher protein content of grass during the early summer. Huggett (1941) quotes Toverud who states that August babies are heavier than January babies. If this is true it may be due to a higher summer intake of vitamins A, C and D in the human diet. In urban areas there are few seasonal variations in diet except that potatoes are fewer in summer and eggs more numerous in spring (Marrack, 1942).

   As has been stated, however, the doctor is more interested in vigour than weight, and it is probable that even minor deficiencies of protein, iron, calcium, phosphorus, vitamins and even trace elements in the mother's diet, have a greater influence on human post-natal vigour than on the birth weight.

4. *Successive pregnancies.* The birth weight usually increases in successive pregnancies. This is of no obstetric importance unless the pelvis is small enough to lose its spatial reserve.

5. *Diabetes.* The babies of diabetics are usually very large, especially if the sugar metabolism is not controlled by insulin. This is probably due to nothing more than the availability of a large amount of carbohydrate.

Influence of Prematurity

There is abundant evidence that, in animals, a high birth weight is

associated with vigour of the new born and with optimum development during the formative age after birth. The relatively small size of the foetal head in animals allows attainment of maximum weight without risk of obstetric injury which might cause death or post-natal retardation. In man, on the other hand, while there is an obvious correspondence between weight and vigour at the extreme lower end of the weight scale, there is no close correspondence within the range of about 6 to 9 lb. There are many variations in vigour between babies of 6 lb. at full term in the same hospital and under the same nursing management. Further, a child of 6 lb. born at 40 weeks will as a rule be conspicuously more vigorous than a child of the same weight born at 36 weeks.

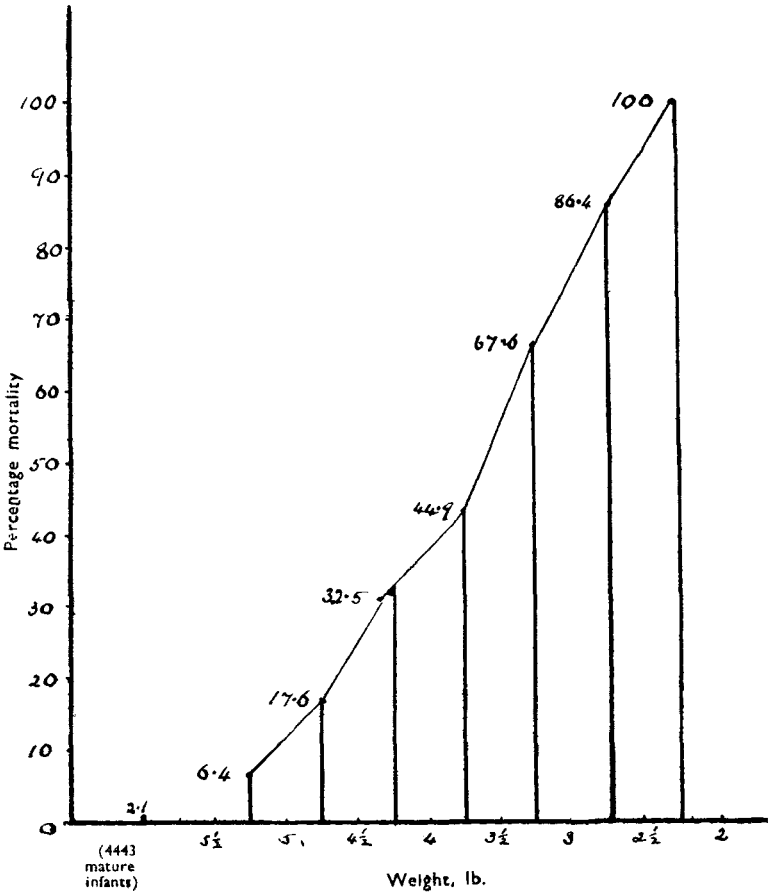

FIGURE 1. Relationship between Death Rate and Birth Weight under 5½ lb.

Stillbirth and neonatal death are due to prematurity rather than to small size. For example, Clayton (1941) in an analysis of 9649 births found that the mortality of babies of less than 5 lb. was 44·7 per cent. for 642 premature babies, while for 455 post-mature babies, *i.e.*, over

https://doi.org/10.1079/PNS19440002 Published online by Cambridge University Press

42 weeks, it was only 6·6 per cent. For 8552 mature babies the death rate was 5·47 per cent.

In a review of the data for the Scottish infant death rate, McNeil (1942) states that 50 to 60 per cent. of the total loss of infants is due to prematurity, and Spence and Miller (1941) in Newcastle found the figure to be 78 per cent. In Glasgow the neonatal mortality of premature live births was 31 per cent. The incidence of premature delivery ranges between 5 and 12 per cent. of all births.

The accompanying graph (Figure 1) made from data given by McNeil (1942) shows the relation of mortality to weight for premature babies, defined as those of 5½ lb. or less. There is a rough inverse relation between mortality and birth weight below 5½ lb. showing the effect of degree of maturity.

Neonatal deaths still form half of all the loss of infant life, and stillbirth due to prematurity contributes a large proportion of all stillbirths. Prematurity is the greatest single cause of neonatal death (Collis and Majekodunmi, 1943). It is not the handling of the premature infant when born which will be considered here, but rather those conditions which cause prematurity. There are some causes, such as deformities, over which little or no control can be exercised; they constitute about 25 per cent. of premature births (Potter and Adair, 1939), but it is possible that certain nutritional conditions of the mother may favour premature expulsion of the foetus. The relation of nutritional defects to abortion and premature labour needs further study.

Association of Birth Weight and Post-Natal Progress

The following is the clinical experience of most of those who have watched infant progress:

1. The baby below 5 lb. is very slow in gaining weight after birth and, though quite healthy, may remain *in statu quo* for a week or more. The 3 lb. baby will reach 4 to 4½ lb. in 6 weeks.
2. The baby of 5 lb. will grow to normal stature in 4 to 5 years, but the child of 4 lb. or under will always be a small individual though it may reach a high grade of mental development.
3. The post-natal loss of weight of 6 to 8 oz. shown by normal mature children is not altered by the amount of post-natal feeding, but it is believed that some nourishment given before lactation is established maintains vigour despite loss of weight.
4. Small women have small babies and the 5 lb. mature baby of a small woman thrives better than the 5 lb. baby of a big woman. Also a 5 lb. baby born at term thrives better than a 5 lb. baby born at 36 weeks.
5. Very young adolescent mothers usually have babies of normal weight, despite the metabolic competition.
6. Overweight children lose more weight, from 12 to even 18 oz., and are slower in regaining it than normal ones but, after 6 months and subsequently, they grow to bigger individuals than the average.

What the Obstetrician Wants

The experimental work on animals has led the stockbreeder to measure the optimum standard by birth weight, and there is a danger

that the specialists in nutrition who are not in clinical contact with the human young may lay an undue emphasis on birthweight as opposed to birth vigour. For example, it is true that piglets of good weight at birth will make the best progress after birth, but this is not always true of babies.

The doctor is less interested in weight than in vigour. The fundamental difference between human and animal breeding is that the size of the head of the human foetus determines the size of the baby from the angle of safety of delivery. Therefore, the prognosis of infant life will depend among other things on the size of the head in relation to the pelvis more than on the maximum birth weight, in so far as a very large head will increase the hazards of labour and, therefore, the danger of stillbirth or neonatal death.

A birth weight between 7 and 8 lb. is the most desirable. It is true that wide ranges of weight are compatible with safety provided that the pelvis is of normal shape and size. The progress of the heavy baby may be no better than that of the child of $6\frac{1}{2}$ lb.; the loss of weight after birth is considerable and the baby is not necessarily more vigorous than a child of $7\frac{1}{2}$ lb. The doctor wants above everything "birth vigour" rather than birth weight. This can be defined by the word "performance." It means, for example, immediate, lusty crying within a few seconds of delivery, normal functioning of the stomach, intestine, and heat regulating mechanism, hungry suckling, tranquil sleep, loss of not more than 6 oz. weight, and ability to regain the birth weight at least by the tenth day. After re-attainment of the birth weight the increase of weight should be steady and optimal. The newborn body should also contain enough iron and calcium together with an endowment of endocrine activity and perhaps of vitamin reserves.

The Outstanding Problem

More exact knowledge is wanted of the influence of the general plane of nutrition and of the intake of individual nutrients on :

1. The incidence of premature labour, pregnancy toxaemia and placental infarction in the mother.
2. The birth vigour, birth weight and post-natal progress of the child.

REFERENCES

Bourne, A. W. and Bell, A. C. (1933). *J. Obstet. Gynaec.* **40**, 423.
Clayton, S. G. (1941). *J. Obstet. Gynaec.* **48**, 480.
Collis, W. R. F. and Majekodunmi, M. A. (1943). *Brit. med. J.* i, 31.
Hammond, J. (1932). *Growth and the Development of Mutton Qualities in the Sheep.* Edinburgh: Oliver and Boyd.
Holland, E. (1922). *Rep. publ. Hlth med. Subj., Lond.*, no. 7.
Huggett, A. St. G. (1941). *Physiol. Rev.* **21**, 438.
McNeil, C. (1942). *Glasg. med. J.* **19**, 87.
Marrack, J. R. (1942). *Food and Planning.* London: Gollancz.
Nixon, W. C. W., Wright, M. D. and Fieller, E. C. (1942). *Brit. med. J.* i, 605.
Potter, E. L. and Adair, F. L. (1939). *J. Amer. med. Ass.* **112**, 1549.
Spence, J. C. and Miller, F. J. W. (1941). *Infantile Mortality in Newcastle upon Tyne during 1939.* Newcastle upon Tyne: Christie and Malcolm.
Walton, A. and Hammond, J. (1938). *Proc. roy. Soc.* (B), **125**, 311.
Williams, Lady (1936–37, 1). *Publ. Hlth, Lond.*, **50**, 11.
Williams, Lady (1936–37, 2). *Publ. Hlth, Lond.*, **50**, 231.

Discussion

Dr. A. S. Parkes (National Institute for Medical Research, Hampstead, London, N.W.3), opener: I wish to bring to your notice just one piece of information concerning the subject of foetal development, namely the effects of superfecundation, the attempted development of a much larger number of embryos than is normal. It is well known that the administration of hypophyseal and other gonadotropic preparations will cause stimulation of the ovary. When appropriate preparations are used this stimulation takes the form of superovulation, the ovulation of a number of ova far in excess of that normally produced. Such eggs, liberated artificially in unusual abundance, are apparently quite normal and can be readily fertilized. Early segmentation proceeds as usual and a highly excessive number of blastocysts may become implanted in the uterus. This excessive number survives through the early stages of pregnancy; Engle (1927), for instance, found up to 29 implantations in treated rats at the 10th day of pregnancy. Cole (1937) found that nearly 40 per cent. of treated rats had more than 20 embryos at the 10th to 12th day of pregnancy; he made the curious observation that such superimplantation was more easily achieved in immature than in adult animals. Evans and Simpson (1940) secured up to 34 implantations in treated rats. The phenomenon is very easily produced in the rabbit, in which we have obtained as many as 38 implantations on the 9th day of pregnancy.

The subsequent history of animals thus treated is extremely curious. One might expect that, on merely mechanical grounds, a doe would have difficulty in carrying to full term such an excessive number of young, and one would expect, for a variety of reasons, that in the later stages of pregnancy the number would be reduced to something approaching normal. In both the rat and the rabbit such a reduction could take place without terminating the pregnancy, since re-absorption of some foetuses concurrently with the normal development of others is well known in both these species. In the animals with superimplantations, however, the sequence of events is somewhat unexpected. Evans and Simpson (1940) noted that, far from there being any increase in the average number of young born, few or none might be born where a very large number of embryos had become implanted. My own experience with rabbits is similar to that of Evans and Simpson with rats. In spite of many attempts I have not yet produced in rabbits an abnormal number of young at one birth. In fact, rabbits known to have implanted a very large number of embryos at 9 to 10 days have subsequently given birth to no more than two or three young, or have even failed to carry any at all to term.

At first sight one is inclined to postulate some endocrine basis for this disappearance of not merely the excess, but of actually the greater part or even all of the abnormal number of embryos. For instance, it might be supposed that progesterone, the hormone of the *corpus luteum*, necessary for the maintenance of pregnancy, may not be produced by the animal in quantity sufficient to maintain the excessive number of embryos. Attempts to maintain such pregnancies by the injection of progesterone have, however, so far failed. It seems, therefore, relevant to consider whether some other factor is involved, especially whether some nutrient

essential for the proper development of the embryo and foetus is present in such limited amount that its inadequacy for the large number of embryos leads to its deficiency for all of them, and to their eventual death.

REFERENCES

Cole, H. H. (1937). *Amer. J. Physiol.* **119**, 704.
Engle, E. T. (1927). *Proc. Soc. exp. Biol., N.Y.*, **25**, 84.
Evans, H. M. and Simpson, M. B. (1940). *Endocrinology*, **27**, 305.

Dr. A. A. Moncrieff (Hospital for Sick Children, Great Ormond Street, London, W.C.1): The agreed international standard of prematurity is now $5\frac{1}{2}$ lb. (2500 g.) and not 5 lb. as indicated in the table by Clayton (1941), quoted by Bourne. It would be interesting to know whether deprivation of meat protein produces the smaller babies promised by the "vegeterian" school of obstetrics, and whether this would ultimately have an adverse effect on the quality of the baby and child.

REFERENCE

Clayton, S. G. (1941). *J. Obstet. Gynaec.* **48**, 480.

Physiological Factors Affecting Birth Weight

Dr. J. Hammond (School of Agriculture, Cambridge)

The present state of knowledge on this subject is still in a rather nebulous condition, consisting of a number of detached facts. The main underlying basic principles are only just beginning to take shape. A theory of foetal nutrition will, therefore, first be put forward and, later, it will be shown how many of the facts fit into it.

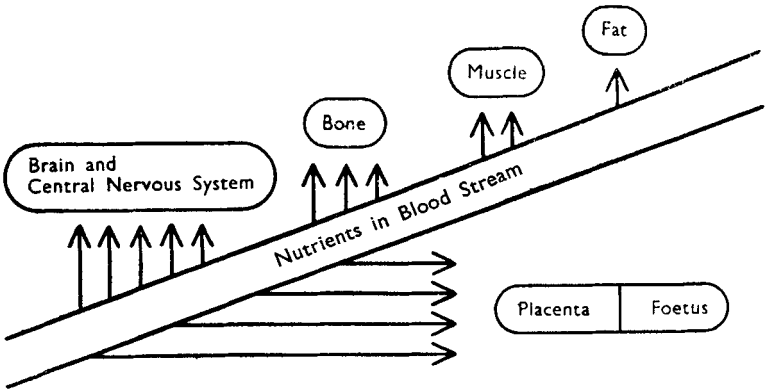

FIGURE 1. Priority of Partition of Nutrients According to Metabolic Rate.

In answer to the question "What determines the distribution or partition of the nutrients in the maternal bloodstream between foetus and maternal tissue?" it is suggested that the cause is the same as that which determines the partition of incoming nutrients between the different maternal tissues. As Child (1920) first showed, this is determined by the metabolic rate of the tissue concerned, the tissue or part with the

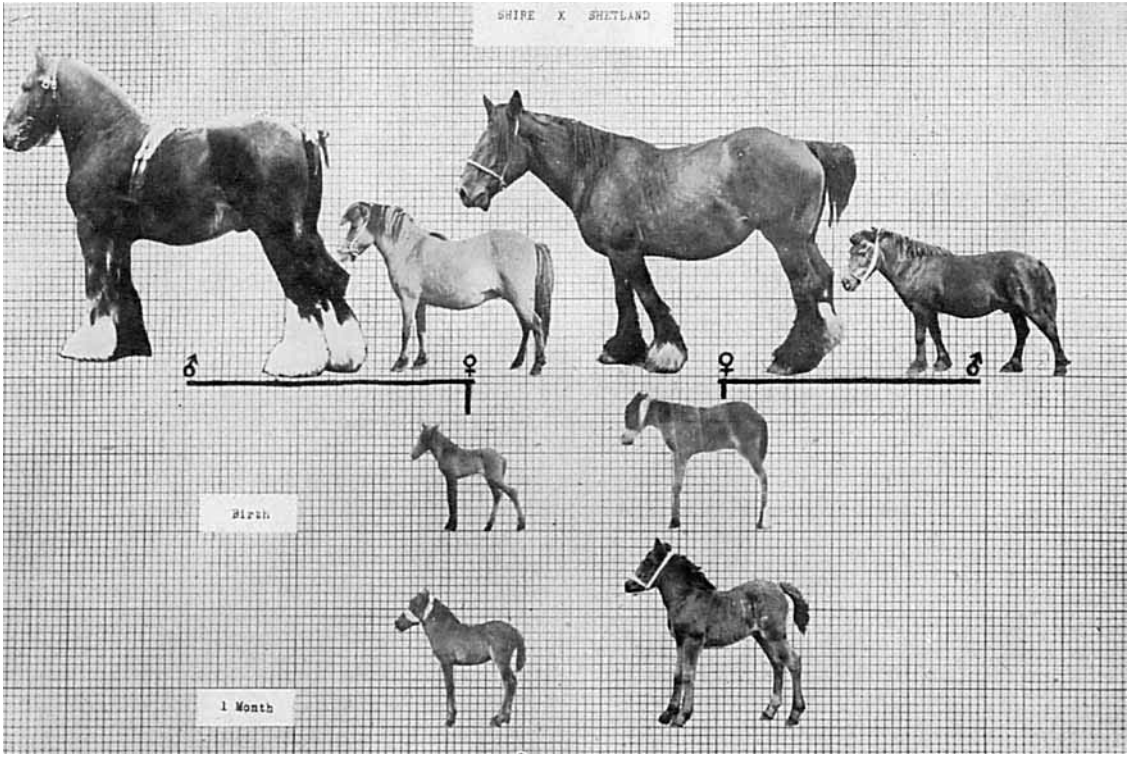

FIGURE 2. Reciprocal Crosses between the Large Shire Horse and Small Shetland Pony, Showing how the Size of the Offspring at Birth is Affected by the Size of the Mother (Walton and Hammond, 1938).

highest metabolic rate having priority in supply over tissues and parts with a lower metabolic rate. This can be illustrated by a diagram (Figure 1) in which the number of arrows denotes the metabolic rate. There is experimental evidence for this method of the distribution of nutrients in McMeekan's (1940, 1941) and Pomeroy's (1941) work on pigs and Verges' (1939) work on sheep.

When the supply of nutrients in the bloodstream is limited we may suppose that one arrow is deducted from each tissue and, whereas growth of fat is now completely stopped, brain and bone growth continues; at a still lower level of nutrition the direction of the arrow for fat may be reversed and brain and bone may, notwithstanding, continue to grow, though at a reduced rate.

At the onset of pregnancy the foetus comes into the picture with at first a very high metabolic rate and competes with the maternal tissues on a level, as far as can be judged, slightly below that of the central nervous system. As the foetus grows, however, it seems likely that its metabolic level as a whole falls and, as pregnancy proceeds, the competition between the foetus and certain other maternal tissues becomes more severe. Further details concerning this will be given later.

Let us now turn to some of the facts concerning foetal growth and birth weights. In reciprocal crosses between large and small breeds, such, for example, as the large Shire horse and the small Shetland pony, the size of the offspring and weight of the placenta are directly proportional to the size of the mother and are not just intermediate between the sizes in the parent breeds (see Figure 2). It is possible that the limitation of the size of the crossbred foetus in the small mother is brought about by a higher rate of metabolism of the maternal tissues in the small breed than in the large breed, that is, by the greater competition of the maternal tissues. There is, however, another possible explanation, namely that special growth substances of maternal origin may be involved.

A somewhat similar case of the limitation of birth weight is to be found in animals which have a varied number of young at a birth. For example, in sheep, single lambs at birth are on the average 28 per cent. heavier than individual twin lambs (Hammond, 1932). Incidentally the ratio between single and twin weights increases while milk is the sole source of nutrition, but narrows as soon as the lamb is able to eat for itself.

A still more striking example is met with in rabbits, in which it is possible to control the number of young at a birth by timing the mating in relation to the time of ovulation (Hammond, 1934). Rabbits which normally produce litters of 8 to 11 young give individual young averaging 45 g. at birth while, if made to produce litters of 1 or 2 young only, they will give young which weigh 95 g. or more at birth (Wishart and Hammond, 1933). By giving a mother bearing a large litter unlimited food during pregnancy it is not possible to increase the weight of the individual young in large litters to this extent. This fact seems to point to some limiting internal secretion or metabolic substance produced by the mother, as a controlling factor in foetal growth. Possibly the key substance may be glutathione an amino-acid, as suggested by Gregory and Goss (1933), or some substance related to glycogen, or a glycoprotein, reference to which will be made later. The principle of partition of nutrients, as already

outlined, is as applicable to special growth substances in the bloodstream as to nutrients in general.

It might be argued that limitations of uterine space cause the decreased weight of the individual young in large litters, but this is not so, for the uterus is capable of growing to accommodate all the young contained in it. For example, in rabbits at the 32nd day the uterine horn weighs 35 g. when 6 foetuses are contained in it, as compared with 25 g. when there are only 2 young (Hammond, 1935). Moreover, in pregnant does containing an equal number of embryos, the weight of the individual foetus is no larger in uterine horns containing only one young averaging 50 g. than in horns containing 5 young averaging 51 g.

Another factor which influences birth weight is the age of the mother. Young mothers which are themselves still growing usually produce smaller young at birth than do adult mothers. For example, the average weight of twin Suffolk lambs from young ewes is 11 lb. as compared with 12 lb. from adult ewes (Hammond, 1932), while in the Southdown breed the average weight is 2·4 kg. for young, as compared with 3·0 kg. for adult, ewes (Prawochenski and Kaczkowski, 1926). This fact is explicable on the theory of partition of nutrients outlined earlier, for in a young mother the competition of the maternal tissues for nutrients would be more severe.

When the effect of feeding during pregnancy on the growth and birth weight of the young is considered, it is necessary to discuss also the distribution of nutrients between the different components of the pregnant uterus. For example, in the rabbit up to the middle of pregnancy the growth of the maternal and foetal placentas far exceeds the growth of the foetus itself, while in the later stages the increase in weight of the foetus far exceeds that of all other components combined. The placenta supplies the nutrients to the foetus and, on the development of the placenta, depends the growth of the foetus. At an early stage of pregnancy, about the 16th day in the rabbit, there is little or no correlation between the weight of the foetal placenta and of the foetus itself but, by the 32nd day of pregnancy, there is a strong correlation (Hammond, 1935). McKenzie and Bogart (1934) found too in sheep that the foetal placenta gave a very good indication of the strength and vitality of the lamb after birth.

It has been shown by several investigators (Verges, 1939; Hammond, 1932; Underwood and Shier, 1942) that the plane of nutrition of the ewe during the latter part of pregnancy has a marked effect on the birth weight of the lambs. From these experiments it is now becoming evident that the effect is graded according to the level of nutrition during this period. With the body of the pregnant ewe gaining about 1 lb. during the last 60 days of pregnancy, the single lambs born are no smaller than those of pregnant ewes fed to gain 39 lb. during this period, that is, a single foetus can draw on the mother's own tissues to supply its needs. With twin lambs this is not so, however, and, under these conditions, while the ewes fed on a high plane produce lambs weighing 9 lb. those fed on a low plane give lambs weighing only 6 lb. Under feeding conditions where the pregnant ewe loses more weight during the later stages of pregnancy the weight of the single lambs at birth is also affected, while, as Fraser, Godden, Snook and Thomson (1939) have found, ewes bearing

twins frequently die from the so called twin lamb disease which is common in the drought areas of Australia (Underwood and Shier, 1942) and the mountainous area of Scotland and Wales. These graded effects of the plane of nutrition are explicable on the theory of the partition of nutrients outlined earlier. Fraser, Godden, Snook and Thomson (1939) found that in this twin lamb disease carbohydrate deficiency is probably the limiting factor concerned. The fact that a very high plane of nutrition as compared with a maintenance ration will not increase the birth weight of single offspring has been found by Eckles (1919, 1920) to be true also for cattle. In cattle also I have seen one case of twin disease when the cow was on a sub-maintenance ration.

It may be argued that birth weight as such does not matter very much and that the weight can be made up later. There is, however, a relation between weight and development, and this is important, for the viability of the newborn is much affected by the stage of development reached at birth. Just as a lowering of the plane of nutrition in a growing animal affects the later developing parts and tissues more than the early developing parts and tissues, so in foetal life the same effect is seen (Verges, 1939). For example, in rabbits of the same litter at birth the larger ones are in a more advanced state of development than the smaller ones, having a higher proportion of body to head, and better developed hair. Appleton (1929) found too that the ossification of the bones was more advanced in the larger rabbits of the same birth age. In addition to the development of such anatomical characters, the development of physiological functions also is affected by the birth weight, and functions which develop late in foetal life, such as that of the regulation of body temperature, are very important in the viability of the young after birth. In such circumstances of the late development of a function in foetal life, a slight deficiency in development at the time of birth may make a very great difference in the viability of the young. From this point of view the proper feeding of the mother during the latter part of pregnancy is important; thousands of lambs, and probably of the young of other species also, are lost each year due to neglect of this factor.

Since the different tissues and parts of the foetus itself compete with one another for nutrients incoming from the placenta, in the same way as has already been described for the maternal tissues, it is the later developing tissues and functions which suffer most and which, as will be seen from Figure 1, compete most with the various maternal tissues for the nutrients available in the maternal bloodstream. In other words, the later developing parts of the foetus are less able to compete with the maternal tissues than the early developing parts, and especially is this so when the mother herself is not yet fully grown.

In conclusion, we must expect differences in detail between different species of animals in their reaction to the same conditions of nutrition during pregnancy, because of the fact that different species are born in different states of development; the horse, for example, is born at a comparatively advanced stage of development while the rat is born in a relatively immature condition.

References

Appleton, A. B. (1929). *C. R. Ass. Anat.* 24th meeting, Bordeaux, p. 3.
Child, C. M. (1920). *Biol. Bull. Wood's Hole*, **39**, 147.

Eckles, C. H. (1919). *Res. Bull. Mo. agric. Exp. Sta.* no. 35.
Eckles, C. H. (1920). *Res. Bull. Mo. agric. Exp. Sta.* no. 36.
Fraser, A. H. H., Godden, W., Snook, L. C. and Thomson, W. (1939). *J. Physiol.* **97**, 120.
Gregory, P. W. and Goss, H. (1933). *Amer. Nat.* **67**, 180.
Hammond, J. (1932). *Growth and the Development of Mutton Qualities in the Sheep.* Edinburgh: Oliver and Boyd.
Hammond, J. (1934). *J. exp. Biol.* **11**, 140.
Hammond, J. (1935). *Trud. Dinam. Razvit.* **10**, 93.
McKenzie, F. F. and Bogart, R. (1934). *Proc. Amer. Soc. Anim. Prod.* 221.
McMeekan, C. P. (1940). *J. agric. Sci.* **30**, 276; 387; 511.
McMeekan, C. P. (1941). *J. agric. Sci.* **31**, 1.
Pomeroy, R. W. (1941). *J. agric. Sci.* **31**, 50.
Prawochenski, R. and Kaczkowski, B. (1926). *Mém. Inst. polon. Écon. rur.* 7, 139.
Underwood, E. J. and Shier, F. L. (1942). *J. Dep. Agric. W. Aust.* **19**, 37.
Verges, J. B. (1939). *Yearb. Suffolk Sheep Soc., Ipswich.*
Walton, A. and Hammond, J. (1938). *Proc. roy Soc.* (B), **125**, 311.
Wishart, J. and Hammond, J. (1933). *J. agric. Sci.* **23**, 463.

Discussion

Professor J. Young (British Postgraduate Medical School, Ducane Road, Hammersmith, W.12), opener: There are no reliable data on the influence of maternal nutrition on the birth weight of the human infant. It is generally stated that in ordinary conditions there is no correlation between the scale of the mother's diet and the birth weight. If this be true it would correspond with the findings to which Dr. Hammond refers of the ewe producing a single lamb. There is a further analogy with the pregnant ewe in the case of the woman whose increment of weight during pregnancy is greatly reduced or abolished because of starvation or illness and who yet gives birth to an infant of normal weight. It has been stated that in famine areas the average birth weight of the children may be maintained. There do not seem to be any accurate figures, however, from which quantitative relations can be studied.

In the full term human infant the factor of maturity is important in the determination of birth weight. In the investigation by the People's League of Health (1942) a large group of pregnant women was given a supplement of minerals including iron and calcium and of vitamins A, B complex, C and D. The results are summarized in Table 1. It is

TABLE 1

	Number	Mean birth weight lb.	Difference lb.	Standard error
Primiparae				
Controls	1463	7·17	−0·01	±0·04
Treated	1485	7·18		
Multiparae				
Controls	973	7·54	−0·07	±0·05
Treated	956	7·61		

seen that the supplements made no appreciable difference to the average birth weights. The table also demonstrates the marked difference between the birth weights of the offspring of primiparae and multiparae.

This difference did not depend upon age as was found by plotting the birth weights under different age groups within the classes of primiparae and multiparae; in no age group did the birth weights differ appreciably from those for all ages.

In the People's League of Health investigation it was found that there was a significant difference in the mean birth weights in different hospitals. This suggested that economic factors might be operative.

REFERENCE

People's League of Health (1942). *Lancet*, **243**, 10.

Sir Joseph Barcroft (Physiological Laboratory, Cambridge): The foetus like the mother is made up of organs. In the goat, on the basis of tissue sections, the metabolic value of the brain and muscle of the foetus is found to be higher than that of the mother. The metabolic values of glandular tissue could with interest be brought in. It would be interesting to know why bone should be regarded as of high metabolic value.

Dr. S. K. Kon (National Institute for Research in Dairying, University of Reading): Is there a difference in weight between the first and subsequent children only or are there also weight differences between consecutive births after the first?

Dr. W. H. Newton (Department of Physiology, Pharmacology and Biochemistry, University College, Gower Street, London, W.C.1): If the foetuses but not the placentas are removed from mice one week before the end of gestation, the mothers do not lose weight. On delivery of the placentas a dramatic loss of weight occurs, not to be accounted for by the removal of the placentas. One of the many possible explanations is that the placenta secretes a substance which promotes tissue growth and which, in the mouse, is sufficiently non-specific to affect maternal weight.

Mr. A. W. Bourne (12 Wimpole Street, London, W.1): Is there any evidence that serious undernutrition of a pregnant animal is associated with delayed or abnormal labour?

Dr. J. Yudkin (Dunn Nutritional Laboratory, Cambridge): The difference in birth weights in different hospitals, as reported by the People's League of Health (1942), might perhaps be due to differences in the technique of weighing, whether, for example deduction was made for weight of the cord or not.

REFERENCE

People's League of Health (1942). *Lancet*, **243**, 10.

Professor O. Kestner (School of Agriculture, Cambridge): In newborn puppies and kittens heat regulation and oxygen consumption are well developed when there are only one or two in the litter, but irregular and abnormal, if there are four or five.

Professor W. J. Hamilton (St. Bartholomew's Hospital Medical School, West Smithfield, London, E.C.1): What effect has genetic influence on the size of the foetus, especially in relation to the crossing of Shetland ponies with Shire horses?

Mr. J. Francis (Foot and Mouth Disease Research Station, Pirbright, Surrey): In the horse the sire has a profound influence on the size and type of progeny; at what age does this effect become manifest? There is

a firm belief among shepherds that when a large headed ram, such as the Oxford Down, is used there is more trouble at lambing time than with a small headed ram. Could Dr. Hammond say whether this is true?

Dr. J. Hammond gave the following replies:

To Sir J. Barcroft: The diagram was intended to represent the metabolic rate of the bone cells and not that of the bone as a whole including the storage matter.

To Dr. Newton: In mice the placenta is probably responsible for the laying down of storage tissue by the pregnant mother because of the effect on metabolism of its internal secretions, oestrin and progesterone.

To Mr. Bourne: Ease of labour in domestic animals depends not so much on the size of the young, for in rabbits young of twice the normal weight are born quite easily, as on the proper muscular development of the uterus and vagina, which is affected by the plane of nutrition of the mother during the latter part of pregnancy and by the presence of sufficient oestrin in the blood.

To Professor Hamilton: With the Shetland and Shire crosses the limited nutrition of the small Shetland mare limits the size of the crossbred foetus to the size of a purebred Shetland foetus, but the genetic constitution of the crossbred foetus in the large Shire mare prevents its reaching quite the same size as a pure Shire foetus, in spite of the good nutritional conditions.

To Mr. Francis: It is said that the use of rams of large breeds on small ewes causes difficulty at lambing, but I have never seen a case myself. If it is so, it may be that the head shape, rather than the size of the lamb as a whole, is the cause.

Nutritional Functions of the Placenta

Sir Joseph Barcroft (Physiological Laboratory, Cambridge)

The title assigned to me does not offer an easy problem. Taken strictly it may be questioned whether the placenta has any functions in the active sense, or whether as Needham (1942) thinks it is merely an ultra-filter.

If it is merely an ultra-filter, then the fundamental processes on which the nutrition of the embryo is based must reside in the mother or in the foetus or in both. The only role which the placenta could play would be the blocking of this or that material which might be injurious to the development of the foetus, for it is obvious that everything necessary for the development gets through.

In spite of much that is said about the efficiency of the placenta in this or that mammalian species, the fact remains that, judged by the resulting foetus, they all seem equally efficient. The sheep, for instance, compared with man, produces a foetus at a higher stage of development, equally large and in a shorter time. The horse yields to no animal in the efficiency of its offspring at birth; it is alleged that a foal which Dr. Hammond desired to weigh at birth, promptly ran away, and was only caught with great difficulty. If, therefore, we find that the efficiency

of the placenta in species A appears on one count, such as, for instance, the reduction in the layers which form the placental barrier, to be greater than that of species B, it behoves us to examine whether, in species B, there is not some other factor which enhances the efficiency in that species.

There are three questions to which I should like to be able to give answers:

1. What role a placenta plays with regard to each important material which passes across it.
2. How these roles can be and are upset.
3. What troubles would supervene in the case of such impairments.

Frankly I cannot do this. While a great deal is known about the placenta, very little is known about the meaning of all this information. Thus, the placenta is known to harbour a vast population of chemical substances the functions of which, if indeed they have any, are a matter of sheer conjecture. Let me commence by saying something about the formidableness of the placental barrier.

Comparisons have been instituted between the effectiveness of this barrier, compared with that separating the cerebrospinal fluid from the blood, the blood from the urine in the kidney, or the alveoli from the pulmonary circulation. The first two of these comparisons has been made by Flexner and Pohl (1941, 1, 2), Pohl and Flexner (1941) and Pohl, Flexner and Gellhorn (1941). The method of approach was the use of heavy sodium, the passage of which from the mother to the foetus could be traced quantitatively. It was found that the rate of transport of heavy sodium per g. of placenta was of the same order in the goat as in the cat, although the goat has morphologically the thicker barrier.

In the goat the growth curve of the foetus resembles the curve relating the rate of transfer of heavy sodium to a unit of foetus at different periods of pregnancy.

In the rat and cat the foetus receives across the placenta on an average about 27 times as much sodium as is incorporated in the growing tissues.

In the guineapig foetus, sodium comes to within 10 per cent. of equilibrium with sodium in the maternal plasma in from 5 to 7 hours. This is in striking contrast with the behaviour of the mother's organism where the extracellular fluid comes to within 10 per cent. of equilibrium with the plasma in about 5 minutes. This last observation shows how great is the barrier even for so simple a substance as sodium.

For another simple but all important substance, oxygen, it is now possible to calculate the diffusion coefficient; in the sheep, for every millimetre of difference in pressure between the oxygen in the blood of the mother and in that of the foetus, about one-tenth of a cubic centimetre of oxygen passes per minute from one to the other. Indeed, in the sheep at the end of pregnancy it seems very difficult to maintain a gradient between the vessels of the foetus and of the mother sufficient to secure the passage of the amount of oxygen essential to foetal life. By the time birth is due the possibilities have been very completely exploited (Barcroft, Flexner, Herkel, McCarthy and McClurkin, 1935; Barcroft and Kennedy, 1939; Barcroft; Kennedy and Mason, 1939).

The devices for rendering the placenta as efficient as possible may be briefly reviewed. They fall into two types, morphological and physico-chemical.

Morphological Devices for Rendering the Placenta more Efficient

1. The increase in the barrier surface which is secured by the waviness of the contact between the maternal and foetal epithelia, or the exaggeration of it by the actual growth of the foetal villi into the crypts which open in the maternal uterine surface.
2. The distribution of the foetal capillaries as a network over the surface of the villi instead of their being embedded in the general mass of the villi. This occurs in sheep (Barcroft and Barron, 1942).
3. The arrangement of the blood vessels so that the foetal and maternal bloodstreams flow in parallel but opposite directions, and the foetal blood can enrich itself from that of the mother along the whole length of the capillary, which leaves the placenta in the sphere of influence of the entering portion of the maternal capillary. This occurs in the sheep and rabbit (Mossman, 1926; Barcroft and Barron, in press).
4. The thinning of the placental barrier by reduction in the number of its layers, 6 in the horse and pig, 5 in places in the sheep, 4 in the dog and cat, 3 in man, and 1 in the rat (Grosser and Mossman, 1940).

Physico-chemical Factors Involved in the Transfer of Substances across the Placental Barrier

Oxygen. The physico-chemical mechanism of diffusion across the placental barrier is perhaps best understood for oxygen. It has already been said that only about 0·1 ml. of oxygen crosses the barrier per minute for each mm. of pressure gradient driving it across. To put the matter in another way, the average difference of pressure between the oxygen in the maternal and foetal vessels at term seems to be in the region of 50 mm. of mercury; this is attained in two ways:

1. The foetus contains a special haemoglobin which takes up oxygen at abnormally low pressures.
2. The mother undergoes an acidosis which causes her haemoglobin to give up oxygen at abnormally high pressures.

In man, in contrast with the sheep, so great a gradient would probably be impossible of attainment, if only for the reason that such an increase in the hydrogen ion concentration as the ewe undergoes would be devastating to the intellect of the woman.

The hydrogen ion concentration of the ewe increases as pregnancy proceeds, and if measured at a stage when the lamb is no more developed than the human babe at birth, the acidosis is not nearly so great, and the gradient for the oxygen transfer not so large. Herein may be one reason why woman falls out of the general rule that the larger the animal, the longer the period of gestation and the more developed the young at birth.

Sugar. It is proved that sugar will diffuse across the placenta in most animals, and there is less sugar in the foetal than in the maternal blood, so that the basis of the gradient exists.

In some animals, the horse, cow, pig, sheep and goat, however, there appears to be more sugar in the foetal than the maternal blood (for literature see Passmore and Schlossmann, 1938). For this some explanation is necessary, and the mind naturally recurs to Claude Bernard's suggestion that the placenta with its considerable glycogen content is a sort of liver.

Knowledge of the distribution of glycogen has been extended by

Szendi (quoted by Needham, 1942), who showed that there were peak situations for glycogen at different periods of foetal life (1) in the maternal placental epithelium; (2) in the foetal placental epithelium; (3) in the foetal lung; (4) in the foetal liver.

While, therefore, a very pretty theory can be built up, correlating the resistance of the placental barrier, the glycogen content of the placenta, and the passage of sugar, such a theory is quite conjectural.

Water. If sugar is the fuel of the body, water, by a curious paradox, is the material on which all life is based, and the mode of passage of water across the placental barrier is still a mystery.

Of the substances which pass to the foetus, water, as far as we know, is delivered in the greatest quantity, but by what mechanism? There is no gradient at present known.

One might expect the following sequence: the foetal cell in its growth would multiply the number of its molecules, and so raise its osmotic pressure, when the secondary reaction would be a rise in the osmotic pressure of the foetal plasma, and an attraction of water from the mother. Actually, the concentration of protein in the maternal plasma is greater than that in the foetal plasma. As, however, the maternal plasma proteins have a lower molecular weight than those of the foetus, the molecular concentrations of the two are not very different (McCarthy, 1942-43) but, what difference there is, is still in the direction of possession by the maternal plasma of the higher osmotic pressure.

When the possibility of hydrostatic pressure is considered, the question might be asked: Is the maternal capillary pressure higher than that in the foetal vessel? The old determinations of Cohnstein and Zuntz (1884) of pressure in the umbilical vein, which must of course be less than in the foetal capillaries, placed this as high as 27 mm. of mercury. That estimate is I think quite wrong, and must be replaced by a figure more near to 10, but the corresponding estimate of pressure on the maternal side is lacking (Barcroft, Barron and Forsham, 1942).

Salts. Something has already been said about sodium; on account of its solubility and small molecular weight, the placental barrier probably presents less resistance to it than to most other materials.

Iron presents an interesting and more difficult problem. The haemoglobin alone of the sheep's foetus, which is about the same size as a baby at birth, contains about 0·2 g. of iron.

The dog contains in its placenta large quantities of uteroverdin, derived from the breakdown of blood, and certainly inorganic iron can be seen there in sections stained for the purpose, but can it be said with certainty that this iron is on its way to form haemoglobin? Moreover, the dog is exceptional in the amount of broken down haemoglobin which its placenta contains. I find it difficult, however, to suppose that the placenta can form any real barrier to the passage of 0·2 g. of iron, most of it in the last month of pregnancy.

The best example of the imperious power of the foetus to secure the materials which it requires, even at the expense of the mother, is furnished by the way it obtains calcium. The embryo will, if necessary, reduce the quantity of that element in the bones of the mother, but here again the whole quantity of calcium involved is so tiny, and its molecular weight so small, compared with that of, say, sugar, that I cannot fancy the

placenta standing in its way and, in support of this, although, as Dr. Hammond has said, the foetus of a twin is lighter at birth than that of a singlet, my experience of sheep leads me to suppose that the twin is not shorter than the singlet (Barcroft and Kennedy, 1939).

A discussion of what limits the size of the foetus at birth is Dr. Hammond's subject and, though the subject is not mine, I shall perhaps be forgiven if I put forward the view to which my own observations were leading me. It is that a factor limiting the size of the foetus is the size of the placenta, and more particularly of its vascular bed.

When comparison is made of the placental weight per foetus in singlets and twin sheep the relative lightness of the latter becomes apparent probably as early as the eightieth day, and certainly as early as the hundred and twentieth.

It will have been evident from what has been said, that oxygen is the element to which the placenta seems to present the most formidable barrier and, as a further proof that the possibilities for the foetus of getting oxygen are almost exhausted at birth, there is the fact that, in the rabbit, the blood emerging from the uterine vein becomes increasingly reduced as pregnancy proceeds, till, at term, it is almost devoid of oxygen.

The opinion to which I am being forced is, that the size of the foetus is limited largely by that of the placenta, more particularly by that of the placenta as a barrier to oxygen. What it is, however, which limits the size of the placenta is still a question.

References

Barcroft, J. and Barron, D. H. (1942). *J. Physiol.* **100**, 20 P.

Barcroft, J., Barron, D. H. and Forsham, P. (1942). *Science*, **96**, 179.

Barcroft, J., Flexner, L. B., Herkel, W., McCarthy, E. F. and McClurkin, T. (1935). *J. Physiol.* **83**, 275.

Barcroft, J. and Kennedy, J. A. (1939). *J. Physiol.* **95**, 173.

Barcroft, J., Kennedy, J. A. and Mason, M. F. (1939). *J. Physiol.* **97**, 347.

Cohnstein, J. and Zuntz, N. (1884). *Pflüg. Arch. ges. Physiol.* **34**, 173.

Flexner, L. B. and Pohl, H. A. (1941, 1). *Amer. J. Physiol.* **132**, 594.

Flexner, L. B. and Pohl, H. A. (1941, 2). *J. cell. comp. Physiol.* **18**, 49.

Grosser, O. and Mossman, H. W. (1940). Quoted by Windle, W. F. (1940). *Physiology of the Fetus.* W. B. Saunders Co.: Philadelphia and London. p. 5.

McCarthy, E. F. (1942-43). *J. Physiol.* **101**, 314.

Mossman, H. W. (1926). *Amer. J. Anat.* **37**, 433.

Needham, J. (1942). *Biochemistry and Morphogenesis*, 90. Cambridge: University Press.

Passmore, R. and Schlossmann, H. (1938). *J. Physiol.* **92**, 495.

Pohl, H. A. and Flexner, L. B. (1941). *J. biol. Chem.* **139**, 163.

Pohl, H. A., Flexner, L. B. and Gellhorn, A. (1941). *Amer. J. Physiol.* **134**, 338.

Discussion

Dr. T. Moore (Dunn Nutritional Laboratory, Cambridge), opener: Dann (1934) has shown in experiments with rats that only small amounts of vitamin A are normally transferred to the foetus and that the foetal reserves are only slightly increased by giving the mother massive doses of the vitamin. In cows and human beings a substantial contribution to the vitamin A requirements of the suckling is made by the colostrum which is much richer in the factor than the subsequent milk. The human infant which is born with a mean liver reserve of 17 I.U. vitamin A per g.

only reaches about half the typical adult reserve of 240 I.U. per g. at the age of six months.

REFERENCE

Dann, W. J. (1934). *Biochem. J.* **28**, 634.

Dr. H. Hoch (London Hospital, Whitechapel, London, E.1): I have analysed for vitamin A and carotenoids samples of blood from mother and infant taken at parturition. The foetal blood was obtained from the umbilical cord immediately after it was cut. About equal amounts of vitamin A were found in the serum of mother and infant, but there were exceptions in both directions. The value for carotenoids in the infant's serum was always low, between 9 and 35 μg. per 100 ml., or 6 to 24 per cent. of the concentration in the serum of the mother; in one case only was the value in the infant's serum as high as in the mother's. It would seem that the human placenta is permeable to vitamin A but it is conceivable, though very unlikely, that the foetal vitamin A is derived mainly from carotene which has passed through the placenta.

Professor J. R. Marrack (Haymeads Emergency Hospital, Bishop's Stortford, Herts.): Is the acidosis which occurs in pregnant sheep due to a deficiency of base or to excess of some acid? There appears to be a deficiency of base in the plasma of pregnant women, although the hydrogen ion concentration is kept down by overbreathing.

Professor P. Ellinger (Lister Institute, Chelsea Bridge Road, London, S.W.1): The strong barrier action of the placenta towards small ions with high electric charge such as sodium is probably due to electrostatic conditions (Donnan equilibrium). Is anything known about barrier effects on small anions like chlorine or on neutral molecules? The problem of water transport through the placenta is, like that in the proximal tubules of the kidney, a question of transport against the osmotic pressure. This is probably governed by electrostatic charges in the epithelial cells. What is known about the influence of foetal and maternal hormones on filtration through the placenta?

Professor W. J. Hamilton (St. Bartholomew's Hospital Medical School, West Smithfield, London, E.C.1): In dealing with questions of permeability, the type of placenta and the period of gestation should be considered.

Mr. A. L. Bacharach (Glaxo Laboratories, Ltd., Greenford, Middlesex): Mason and Bryan (1940) have shown by indirect but unequivocal experiments that there is a marked placental barrier to the passage of vitamin E which, in this matter, behaves like vitamin A.

REFERENCE

Mason, K. E. and Bryan, W. L. (1940). *J. Nutrit.* **20**, 501.

Mr. A. N. Worden (Institute of Animal Pathology, Cambridge): The transference of vitamin A to the newborn may be an example of what is probably a generalization that the nutritional functions of the placenta are but complementary to those of the colostrum. The recent work of Barron (1942) at Reading provides an even better example of vitamin A transference than those already mentioned. This worker has shown that lambs are born without any vitamin A reserves in the liver but that

the ewe's colostrum is a rich source of the factor and that within a few days of birth the lamb acquires an adequate reserve. Several years ago Mason, Dalling and Gordon (1930) demonstrated that passive immunity to lamb dysentery was transferred not through the placenta but through the colostrum. When it is being considered which factors do or do not traverse the placental barrier it should be remembered that nature has provided the colostrum to convey factors which cannot be obtained by the foetus *in utero*.

REFERENCES

Barron, N. S. (1942). *Vet. Rec.* **54**, 29.
Mason, J. H., Dalling, T. and Gordon, W. S. (1930). *J. Path. Bact.* **33**, 783.

Professor A. St. G. Huggett (St. Mary's Hospital Medical School, Praed Street, London, W.2): The term placenta alone means nothing. It is necessary to state species, type, and age of pregnancy since properties of permeability differ in every case. For example, in the epithelio-chorial placenta of the horse the foetal blood sugar content is higher than in the mother; the reverse holds in the endothelio-chorial type. Corey (1932) showed that the endothelio-chorial placenta of the rat becomes at full term permeable to insulin. After six months the human placenta becomes permeable to organisms.

REFERENCE

Corey, E. L. (1932). *Physiol. Zoöl.* **5**, 36.

Sir Joseph Barcroft gave the following reply:

To Professor Ellinger: In the sheep the placental barrier is as formidable against neutral molecules as against sodium.

Afternoon Session: Chairman, Brigadier F. A. E. CREW

Diet in Pregnancy

Professor A. St. G. Huggett (St. Mary's Hospital Medical School, Praed Street, London, W.2)

In the last three months of pregnancy the human foetus deposits 70 per cent. of its total birth weight. It lays down in this same period two-thirds of its calcium phosphate, three-quarters of its protein, four-fifths of its iron, and all but 7 per cent. of its fat. At the same time, the mother is enlarging her uterus and storing tissue and water throughout her body.

There appear to be two principal processes which govern this development of the foetus, namely its growth and its parasitic life.

The rate of growth of the foetus is greater than that of the infant after birth, and the rate gradually becomes slower as the child gets older. This fast growth rate in embryonic life is due to an inborn power for growth, the rate of which depends upon the species. In consequence, the growing foetus, if not supplied with its requirements when able to use them, may lose weight and be unable to make this up later, unless extremely well supplied by supplementary feeding over a long period. Illingworth (1939) has shown that the modern conditions of civilization

may result in underweight infants failing to catch up to the normal weight. Hess and Chamberlain (1927) have demonstrated that underweight, premature infants can be made to regain a normal weight if this supplementary feeding is maintained over a period of four years.

Another important fact is that in mammalian development it is only in the rodent and in the primate, that is man, that the placental development at the last stages of pregnancy permits the intra-uterine embryo to acquire its food, not from local stores or by secretory mechanisms, but from the maternal blood and food; it is, in fact, treated as one of her own organs, but, ironically enough, it repays this generosity by sacrificing its mother to its own needs. When there is an inadequate supply of food, the mother is affected before the embryo. From animal and human experiments we know that a dietary deficiency of progressive severity reveals itself by affecting in the following order: the maternal well being, the maternal health and blood, the maternal food stores and reserves, the foetal stores and the infant's post-natal health, and the foetal health and bodyweight; finally, if the deficiency progresses still further, abortion and death ensue. The condition of the foetus is, therefore, a less sensitive, but in some respects a more important, measure of undernourishment than that of its mother, since strong measures need to be taken after birth to produce a healthy robust child, if subnormal at birth.

The Criteria of Adequate Diet in Pregnancy

These can be divided into two groups, the maternal and the foetal. The maternal criteria include those signs visible in pregnancy, at labour and, after the confinement, in the puerperium and during lactation. They are given in Table 1.

TABLE 1

MATERNAL CRITERIA OF ADEQUACY OF DIET

1. *During pregnancy*	2. *During labour*
Presence of symptoms	Occurrence of obstetric difficulties
Subjective	Occurence of haemorrhages
Objective	
Occurrence of physical signs	3. *During the puerperium and lactation*
Results of blood and urine analyses	State of general health
Haemoglobin	Occurrence of complications
Red cells	State of breasts
Blood volume	State of milk supply
Plasma protein	Condition of teeth and bones
Vitamin tests	
Occurrence of haemorrhages	
Occurrence of absorption	
Occurrence of abortion	

The foetal criteria are shown in Table 2. Some of those included are not generally accepted as indices of nutrition but are capable of being, or have been, used for that purpose.

Effects on the Foetus of Shortage of Food

Deprivation of certain nutrients seems to be of outstanding importance.

Iron. In studying anaemias it should be remembered that it is considered normal for the maternal blood to show a hydraemia (Dieckmann and Wegner, 1934).

Premature infants born with a subnormal amount, less than 33 mg., of iron in the liver develop anaemia quicker than full term infants (Davidson and Leitch, 1934). Fetzer (1913) deprived pregnant rats of iron and found shortages in the foetal liver. Strauss (1933) showed that while infants very frequently developed anaemia at the breast, milk being almost devoid of iron, they could be protected against this by giving iron to the mother in large doses during the last three months of pregnancy; no anaemia developed in the first year of life. This effect of iron administration to pregnant women has been confirmed by Smallwood and Gittins (Smallwood, 1936).

TABLE 2

FOETAL CRITERIA OF ADEQUACY OF DIET

1. *In the embryo*	3. *In the infant*
Degree of intra-uterine activity	At birth
Degree of intra-uterine ossification	Weight
	Degree of ossification
	State of bones and teeth
2. *In the placenta*	State of blood picture
Weight	Degree of prematurity
Food content	Degree of immaturity
Histological condition	Subsequent to birth
	Condition after 2 weeks
	Liability to illness in first 6 months
	Liability to death in first 6 months

There is considerable evidence that hypochromic anaemia supervenes easily in pregnancy in women apart from the hydraemia of pregnancy, but that anaemic women deliver themselves of normal infants.

Calcium, Phosphorus and Vitamin D. Maxwell (1929) showed that the children of mothers suffering from osteomalacia through shortage of vitamin D and often of calcium and phosphorus, also in bad cases have definite osteoporosis and even foetal rickets. Here the shortage is so acute that the maternal bones yield their calcium to the infant. Coons and Blunt (1930) showed that the best calcification is obtained in an infant's bones on a high maternal intake of calcium and phosphorus. It is a common experience that teeth require copious stoppings after a confinement.

Other Vitamins. Maxwell (1932) has reported keratomalacia in infants whose mothers received a diet deficient in vitamin A. Mellanby and Green (1929) first drew attention to the protective action against puerperal sepsis of vitamin A administered during pregnancy.

Shortage of vitamin B_1 (aneurin) is found in beriberi of pregnancy and often the infants of women suffering from this disease are affected with polyneuritis or are born dead. There is considerable evidence that lack of vitamin B_1 causes in the pregnant woman neuritic pains and muscular cramps which are relieved by administration of the vitamin (Nixon, 1942; Nixon, Wright and Fieller, 1942).

Administration of marmite cures a macrocytic anaemia found in pregnancy and non-pregnancy in India, and reproducible with diet in monkeys. The realization of the gravity of this anaemia in pregnancy we owe to Dr. Margaret Balfour, and the identification of the type and its cure, to her colleague, Dr. Lucy Wills.

Absence of ascorbic acid is said to cause foetal haemorrhages. It is a vitamin of which a shortage can occur very easily. Vitamin E, the magic vitamin of reproduction, has potent effects on rats but its human function, if any, is unknown.

The Plane of Nutrition. The phrase was first used by Hammond to describe the effects on cattle of ample food supplies, in contrast with those of short supply. He showed (Hammond, 1932) that moderate underfeeding depletes the mother's reserves and lowers her weight, while marked underfeeding lowers the birth weight of the offspring. Similar results have been reported for rodents.

Prochownik (1901) claimed that he could lower the birth weight of human infants by 11 to 14 per cent. by dietary restrictions. He hoped to produce easier labours with smaller babies. One notices that his teaching is not, however, practised by the profession.

During the last war the results reported from Central Europe as to the influence of war time diet on the birth weight were equivocal.

Supplementation Experiments with Women

The three most important supplementation experiments are those of the National Birthday Trust (Williams, 1939) at Rhondda and Gateshead, of Ebbs, Tisdall and Scott (1941) in Toronto, and of the People's League of Health (1942) in London. All were conducted before the war, but have been reported only since the war began. In all three, supplements of vitaminized foods or extracts were given, and the Canadian and London workers gave also foods containing iron and calcium.

The Rhondda Valley experiment was the first to be made. It was a pioneer effort conducted under difficulties and the later workers were able to profit by its experiences. Its importance is that it directed attention to the question of supplementing the diet of the pregnant woman with certain foodstuffs particularly useful to her in the present social conditions, but also often in short supply even in peace time. Dr. Margaret Balfour will describe this experiment herself.

The Toronto experiment demonstrated that easier pregnancies and labour, improved health in the puerperium, and decreased morbidity and mortality at birth and in the first six months can be achieved by improvement of the diet. The experiment has been criticized statistically because of the small number of results in the control and experimental groups. While this is important, it is to be borne in mind that the experiment forms the apex of a mass of animal experiments which it confirms, and upon which it rests.

The London experiment conducted by the People's League of Health (1942) is much more extensive, and shows two things, a protection against toxaemia, and a slight decrease in the number of cases of prematurity with a limited increase in birth weight for the women over 30 years of age. Here, again, the foetus proved the more stable of the two organisms. Lack of protective foods produced more potent effects in the mother than in the infant; the same was found in the Toronto work.

Arising out of these and other results, various recommendations have been made as to the most suitable dietary supplements for pregnancy in terms of foods and of their component foodstuffs. There is agreement on the following points:

(*a*) An increased supply of proteins to give daily from 1·0 to 1·5 g. per kg. bodyweight with a good proportion of animal protein.
(*b*) Adequate increases in the supply of calcium and phosphorus to give 1·5 to 2·0 g. daily, and of iron to give 18·5 to 20 mg. daily.
(*c*) Ample supplies of vitamins, especially of vitamins A and D and of the vitamin B complex.

To secure this end, milk, cheese, eggs, meat and fruit, and supplements of iron salts, cod liver oil and the B vitamins in some suitable form should be given.

Effect of War Time Conditions

It is possible with our rationing system to calculate the composition of the diet of the pregnant woman receiving 1 pint of milk a day and 3 eggs a week. This is shown in Table 3.

TABLE 3

CALCULATED COMPOSITION OF THE WAR TIME DIETARY OF THE PREGNANT WOMAN (56 KG.)

Protein		Salts and vitamins	
Animal	36 g.	Calcium	1·3 g.
Total	91 g.	Phosphorus ..	1·4 g.
Per kg. bodyweight	1·6 g.	Iron	13·3 mg.
Fat	74 g.	Vitamin A ..	7980 I.U.
Carbohydrate ..	324 g.	Vitamin B_1 ..	741 I.U.
Calories		Vitamin D ..	69 I.U.
Total	2408	Riboflavin ..	1·46 mg.
Per kg. bodyweight	44	Ascorbic acid ..	87 mg.

In regard to shortage of foods, there appears to be very little risk; if anything, the animal protein is low, possibly also the calcium and phosphorus and the vitamin D and ascorbic acid. The sheet anchor of the diet is the milk, 1 pint daily. If this were reduced to the 2 to 3 pints a week which the non-pregnant adult gets at present, there would be great shortages of calcium, phosphorus and animal protein. As it is, the shortage of iron is the most prominent difficulty, milk being relatively devoid of iron.

There are no figures for comparing the haemoglobin percentage of newborn infants before and during the war in comparable conditions. Sinclair (1942) alone has published for the pregnant woman values which attempt to allow for the rise in blood volume of normal pregnancy, and they do not show unequivocal anaemia over and above the "physiological" anaemia due to the hydraemia. Incidentally, this hydraemia was described at a time when the question of food supply was not considered important or allowed for by the investigators.

Birth Weights in London in War Time

The birth weights in four London teaching hospitals and one London borough for the first eight months of 1938 and 1939 have been compared with those for the same eight months of 1941 and 1942. For the statistical analysis I am indebted to Mr. W. T. Russell and Miss M. Rogers of the Department of Statistics of the London School of Hygiene,

TABLE 4

BIRTH WEIGHTS IN LONDON BEFORE AND DURING THE WAR (JANUARY TO AUGUST)

Year	No. of cases	Mean birth weight, lb.
1938, 1939	4577	7·260 ± 0·017
1941	2310	7·125 ± 0·024
1942	2445	7·216 ± 0·025
Years	**Difference, lb.**	**Significance**
1938, 1939 and 1941	−0·135 ± 0·029	Significant
1938, 1939 and 1942	−0·044 ± 0·030	Not significant
1941 and 1942	+0·091 ± 0·035	Significant

There is a significant fall in birth weights for primiparae and multiparae together in 1941 as against 1938 and 1939, but a rise of corresponding significance in 1942.

Some of these figures can be divided into values for primiparae and multiparae and when thus analysed the results show no significant change, but a progressive decline in the birth weights for multiparae is suggestive (Table 5).

TABLE 5

BIRTH WEIGHTS FOR PRIMIPARAE AND MULTIPARAE IN LONDON BEFORE AND DURING THE WAR (JANUARY TO AUGUST)

	Primiparae		Multiparae	
Year	No.	Mean birth weight, lb.	No.	Mean birth weight, lb.
1938, 1939	1151	7·128 ± 0·037	813	7·482 ± 0·047
1941	414	7·141 ± 0·052	253	7·413 ± 0·080
1942	483	7·119 ± 0·051	206	7·369 ± 0·079
	Difference, lb.			
Years	Primiparae		Multiparae	
1938, 1939 and 1941	+0·013 ± 0·062		−0·069 ± 0·093	
1938, 1939 and 1942	−0·009 ± 0·063		−0·113 ± 0·092	
1941 and 1942	−0·022 ± 0·073		−0·044 ± 0·112	

If any undernourishment exists, we might expect it to be shown more clearly in the weights of twins since three organisms would then be competing for the nourishment. The values are set out in Table 6,

TABLE 6

BIRTH WEIGHTS OF TWINS IN LONDON BEFORE AND DURING THE WAR (JANUARY TO AUGUST)

Year	No. of children	Mean birth weight, lb.	Difference, lb.	
			1938/1939 and 1941	1938/1939 and 1942
1938/1939	197*	5·237 ± 0·092	−0·112 ± 0·194	+0·211 ± 0·224
1941	56	5·125 ± 0·171		
1942	24	5·448 ± 0·204	Neither significant	

* One weight not recorded in 99 pairs

The numbers are relatively few, but there is no significant change in birth weight between the pre-war years and 1941, and there is in fact a rise if 1942 is compared with 1938–1939. It is clear that figures for twins confirm strongly those for singletons, and it appears that whatever undernourishment there may be is of too slight a grade to affect the weight at birth.

I have discussed with Mr. Howard Kershner, Director of the American Friends' Relief Service in Europe, his recent statement that the birth weight in Vichy France has fallen by one-third. He says that while there is no doubt of the shortage of food, this statement is founded on a belief of the doctors attending the confinements, and that the conditions of work preclude the collection of accurate quantitative data.

The question might be asked whether there is an increased incidence of prematurity in London in war time. Table 7 shows that the answer is in the negative.

TABLE 7

INCIDENCE OF PREMATURITY IN LONDON BEFORE AND DURING THE WAR (JANUARY TO AUGUST)

Year	No. of babies		Rate per 1000
	Total	Under 5½ lb.	
Primiparae			
1938/1939	1151	99	86
1941	414	28	68
1942	483	39	81
Multiparae			
1938/1939	813	29	36
1941	253	15	59
1942	206	10	49

Summary

The foetus, having a prior claim on food, is less sensitive to deficiencies of it than the mother. This enables it to take advantage of its great capacity for growth, since it obtains first call on the maternal food supply and even on her own reserves and tissues.

https://doi.org/10.1079/PNS19440002 Published online by Cambridge University Press

From records of birth weights in London, there is no evidence that the war time diet has caused any significant alteration in the birth weight.

I would take this opportunity of thanking numerous students of St. Mary's Hospital Medical School, who perseveringly examined records of confinements in hospital notes. In addition, I would wish also to thank Professor F. J. Browne of University College Hospital, Professor James Young of the British Postgraduate Medical School, Hammersmith, Mr. Louis Rivett and Mr. Aleck Bourne of Queen Charlotte's Hospital, Dr. Oscar Holden, M.O.H. Croydon, and Dr. Seager of Croydon Maternity Hospitals, for aid willingly given in investigating the records of cases under their care.

REFERENCES

Coons, C. M. and Blunt, R. (1930). *J. biol. Chem.* **86**, 1.
Davidson, L. S. and Leitch, I. (1934). *Nutr. Abstr. Rev.* **3**, 901.
Dieckmann, W. J. and Wegner, C. R. (1934). *Arch. int. Med.* **53**, 188.
Ebbs, J. H., Tisdall, F. F. and Scott, W. A. (1941). *J. Nutrit.* **22**, 515.
Fetzer, M. (1913). *Z. Geburtsh. Gynäk.* **74**, 542.
Hammond, J. (1932). *Growth and the Development of Mutton Qualities of the Sheep.* Edinburgh: Oliver and Boyd.
Hess, J. H. and Chamberlain, I. McK. (1927). *Amer. J. Dis. Child.* **34**, 571.
Illingworth, R. S. (1939). *Arch. Dis. Childh.* **14**, 121.
Maxwell, J. P. (1929). *Proc. R. Soc. Med.* **23**, 639.
Maxwell, J. P. (1932). *J. Obstet. Gynaec.* **39**, 764.
Mellanby, E. and Green, H. N. (1929). *Brit. med. J.* i, 984.
Nixon, W. C. W. (1942). *J. Obstet. Gynaec.* **49**, 614.
Nixon, W. C. W., Wright, M. D. and Fieller, E. C. (1942). *Brit. med. J.* i, 605.
People's League of Health (1942). *Lancet*, **243**, 10.
Prochownik, L. (1901). *Ther. Mh.* (*Halbmh.*) **15**, 446.
Sinclair, H. M. (1942). *Proc. R. Soc. Med.* **36**, 80.
Smallwood, W. C. (1936). *Brit. med. J.* ii, 573.
Strauss, M. B. (1933). *J. clin. Invest.* **12**, 345.
Williams, Lady (1939). *Publ. Hlth, Lond.*, **52**, 314.

Supplementary Feeding in Pregnancy: The National Birthday Trust Fund Experiment

Dr. M. I. Balfour (14 Sylvan Road, London, S.E.19)

The experiment here detailed began as a purely philanthropic endeavour, conceived by Lady Rhys Williams, to assist expectant mothers in the Rhondda Valley, South Wales, where maternal and infant mortality was very high and unemployment was widespread. Packets of dried foods were distributed from antenatal clinics by means of a grant given by the Birthday Trust Fund. The results were found to be good and the Commissioner for the Special Areas of England and Wales offered a further grant to enable the distribution of foods to be extended to other of the special areas. This was done with continued good results and in 1937 the Birthday Trust Fund appointed a small Committee whose members were already engaged in obstetrical or nutritional work to organize the scheme further and check the results. The figures which are given in the tables which follow are for the period beginning in the summer of 1937 and ending in the spring of 1939, when the grant from the Commissioner was discontinued.

The Selection and Classification of the Clinical Material

When the scheme was in full working order, 10 areas in the north of England under different Medical Officers of Health and 18 areas in South Wales were receiving the food supplements. In all these areas unemployment was acute and the unemployment benefit did not leave any margin for extra food for the expectant mother; indeed, the expectant mother, who catered for the family, was usually found to have less food than any other member of the family.

The women who received the foods were selected by the medical officers in charge of the antenatal clinics. These medical officers were asked to keep particulars of the condition of all mothers and infants who attended the clinics so that a control class of mothers who did not receive supplementary foods but who attended the clinics might be obtained. All cases where abortion or miscarriage occurred were excluded from both groups.

The Food Supplements Given

Each woman on the Birthday Trust roll received once a fortnight the following:

One lb. of ostermilk and one half lb. of ovaltine. In some cases a half lb. of colact was given instead of ovaltine.

One four oz. carton of marmite or a yeast extract resembling marmite. In some areas, as an alternative to the marmite or yeast, an eight oz. bottle of minadex was given.

It was intended that these foods should be in addition to the milk usually given to poor expectant mothers by the Local Authority, but in practice it was frequently found that the Local Authority kept its milk for women in the control class, many of whom were very poor. Other women of the control class who were better off financially, bought their own milk, either fresh or dried, so that the main difference between the two classes was the taking by the Birthday Trust mothers of marmite or yeast or minadex. It has been estimated that the marmite or yeast given was enough to provide each mother daily with 240 I.U. of vitamin B_1, while the minadex was enough to provide 13,500 I.U. of vitamin A and 2250 I.U. of vitamin D.

It was intended that the foods should be given for 9 weeks before and 3 weeks after delivery, but no objection was raised if they were given for 3 months before delivery or even longer. The purposes of the feeding and especially of the vitamin supplements were constantly explained to the women and the suggestion made by the Health Visitors that the supplements were likely to lead to an easier labour was a very potent inducement to continue to take them, even if they were thought to be unpalatable.

The Records

The name of each woman who received the foods was entered on an individual card which gave particulars regarding the period of pregnancy when the foods were begun, the woman's age and the number of previous confinements. The date of each food distribution was entered on the card, also the nature and amount of the food. Finally the date of the confinement was entered and the result to mother and child. Where death took place the causes as entered on the death certificate were given

and were supplemented by any additional information available from the medical officers or midwives. Similar facts were obtained about women of the control group.

The Results of the Experiment

Individual cards of over 14,000 women were examined. Some were discarded, having essential facts left out. Others were excluded as no control cases had been sent from the area. The remaining 11,618 cards were examined statistically by Mr. J. Plymen, F.I.A., whose tables and conclusions are shown as follows.

The neonatal and stillbirth rates for the treated and control groups are set out in Table 1. This table shows a statistically significant reduction

TABLE 1

INFANT MORTALITY

(NEONATAL AND STILLBIRTH RATES COMBINED)

Group	Number of cases	Deaths		Difference between death rates per mille in favour of treated group	Minimum difference required for statistical significance
		Number	Rate per mille		
England					
Treated with marmite or yeast extract ..	5364	297	55·4	10·6	9·5
Controls..	4392	290	66·0		
Treated with minadex..	2457	140	57·0	7·7	13·6
Controls..	2760	179	64·7		
Wales					
Treated with marmite or yeast extract ..	3797	249	65·6	19·2	14·0
Controls..	2760	234	84·8		
England and Wales combined					
Treated with marmite or yeast extract ..	9161	546	59·6	13·7	8·1
Controls..	7152	524	73·3		

of the infant death rate in favour of the marmite, yeast extract group. The figures for England and Wales combined are very striking, the likelihood of the difference shown arising from chance being 1 in 1300. The statistics upon which Table 1 is based are not, however, homogeneous, as the groups are compiled from four classes, subject to different rates of mortality. This is clear from an examination of Table 2, which shows the neonatal and stillbirth rates of the treated and control groups divided according to parity. From this table two facts appear, namely (*a*) the proportion of primiparae among the controls is definitely higher than among the treated cases and (*b*) the proportion of controls in the Welsh areas is slightly lower than in the English areas. While the effect of (*a*) will be to overstate, in the combined tables, the mortality of the control group as compared with that of the treated group, the effect of (*b*) will on the contrary be to understate the mortality of the control group.

In order to test the effect on the results shown in Table 1, of these differences in the composition of the groups, it has been assumed that instead of the distribution actually observed there is a different one, such that, while the total number of cases is almost identical with the original figures, the treated and control groups now consist of the four different classes in identical proportions (Table 3). Next the number of

TABLE 2

INFANT MORTALITY ANALYSED ACCORDING TO THE PARITY OF THE MOTHER

Group	Number of cases	Deaths		Difference between death rates per mille in favour of treated group	Minimum difference required for statistical significance
		Number	Rate per mille		
PRIMIPARAE					
Treated with marmite or yeast extract					
England					
Treated	1137	67	58·9	10·4	20·0
Controls	1673	116	69·3	*P = 1 in 3·4	
Wales					
Treated	849	57	67·1	26·4	25·2
Controls	1365	127·6	93·5	*P = 1 in 27	
England and Wales combined					
Treated	1986	124	62·6	17·6	15·6
Controls	3038	243·6	80·2	*P = 1 in 41	
Treated with minadex					
England only					
Treated	351	18·2	51·8	13·0	30·0
Controls	787	51	64·8	*P = 1 in 2·5	
MULTIPARAE					
Treated with marmite or yeast extract					
England					
Treated	4227	230	54·4	9·6	12·0
Controls	2719	174	64·0	*P = 1 in 9	
Wales					
Treated	2948	192	65·1	11·2	17·0
Controls	1395	106·4	76·3	*P = 1 in 5·5	
England and Wales combined					
Treated	7175	422	58·8	9·3	9·7
Controls	4114	280·4	68·1	*P = 1 in 19	
Treated with minadex					
England only					
Treated	1468	95·8	65·3	− 3·0	—
Controls	1428	89	62·3		

*P = probability.

cases in each group has been multiplied by the rates of mortality shown in Table 2 and, thereby, the number of deaths to be expected from the revised distribution has been obtained.

https://doi.org/10.1079/PNS19440002 Published online by Cambridge University Press

TABLE 3

COMPARISON OF FIGURES ACTUALLY OBSERVED WITH THOSE RECALCULATED ON THE ASSUMPTION THAT THE TREATED AND CONTROL GROUPS CONSISTED OF THE 4 DIFFERENT CLASSES IN IDENTICAL PROPORTIONS

	Special distribution	Actual figures
Cases		
Total	16,300	16,313
England	9750	9756
Wales	6550	6557
Treated class	9050	9161
Controls	7250	7152
Deaths	1063	1070
Infant mortality rates		
Treated	59·8	59·6
Controls	72·0	73·2

Ratio of English to Welsh cases as 3 : 2 throughout
Ratio of primiparae to multiparae as 5 : 11 throughout

Table 4 is an amended form of Table 1; it is based on the original data

TABLE 4

INFANT MORTALITY
NEONATAL AND STILLBIRTH RATES COMBINED
A MODIFICATION OF TABLE 1 AS DESCRIBED ON P. 30

Group	Primiparae			Multiparae		
		Deaths			Deaths	
	Number of cases	Number	Rate per mille*	Number of cases	Number	Rate per mille*
England						
Treated with marmite or yeast extract ..	1700	100	58·9	3700	201	54·4
Controls	1350	93	69·3	3000	192	64·0
Wales						
Treated with marmite or yeast extract ..	1150	77	67·1	2500	163	65·1
Controls	900	84	93·5	2000	153	76·3

* Rates derived from Table 2

Group	Number of cases, primiparae and multiparae combined	Deaths		Difference between death rates per mille in favour of treated group	Minimum difference required for statistical significance
		Number	Rate per mille		
England and Wales combined					
Treated with marmite or yeast extract ..	9050	541	59·8	12·2	8·1
Controls ..	7250	522	72·0		

https://doi.org/10.1079/PNS19440002 Published online by Cambridge University Press

as regards the rates of mortality and the total number of cases in England and Wales, but has been freed from any errors due to the combination of the results from the four different groups. The only assumption that has been made is such that, if for example in a certain group it had been possible to observe 50 per cent. more cases, the number of deaths would also have been increased by 50 per cent.

It will be observed that the results shown in this amended table are almost identical with those shown in Tables 1 and 2, and that the effect of considerations (*a*) and (*b*) discussed above is extremely small, the mortality rate of the group receiving marmite or yeast extract (combined figures) remaining practically unchanged and that of the controls decreasing by 1·3 per 1000. The difference between the treated and control groups is of such a magnitude that the possibility of the result being due to chance is 1 in 400.

The mortality rates for the treated and control groups are shown in relation to parity as well as to geographical area in Table 2. Here the groups are necessarily smaller and the difference in favour of the marmite, yeast extract group, though shown by all classes, is not always significant. There are, however, three points of interest. First, the infant mortality is higher in the Welsh than in the English areas for both primiparae and multiparae. Second, the effect of the marmite, yeast extract supplement is greater when the initial mortality is high; this greater improvement in districts having a high mortality is shown also in Table 5. Third, when

TABLE 5

STILLBIRTH AND NEONATAL DEATH RATES COMBINED IN WOMEN ATTENDING ANTENATAL CLINICS

Area	Deaths per mille		Difference
	Control class	Treated class	
Rhondda	96	66	30
Monmouth	84	62	22
Newcastle	71	56	15
Durham (area treated with yeast)	63	55	8

the infant mortality is high, as in the Welsh areas, there is a large difference in the mortality rates of the primiparae and multiparae classes, and this difference is very markedly reduced where the marmite, yeast extract supplement is given, the difference between the classes in the treated groups being only 2 per 1000 whereas in the control groups it is 17·2 per 1000.

Discussion and Summary

The analysis of the records set out in the tables shows that the administration of special food supplements during pregnancy was beneficial to the child. In the marmite, yeast extract group there was a reduction in the neonatal and stillbirth mortality which is statistically significant. These figures are very adequate as the number of cases and deaths observed was large. In the minadex group no significant reduction of the neonatal and stillbirth mortality could be seen, but it is true that the numbers receiving minadex were small. This preparation had been distributed in the first instance in order to establish a second control for

the cases receiving marmite, yeast extract as it was thought possible that the good effect of the supplements might be due to the psychological effect of receiving foods, in which case the areas treated with minadex would have shown the same results.

Similar results, showing the benefit to the child of supplementary feeding, were reported by Ebbs, Tisdall and Scott (1941) in Toronto. These workers, with a series of carefully controlled cases, showed that the infants of women on good diets had a smaller neonatal death rate than those of more poorly fed women. The People's League of Health (1942) also have issued a report on the effect of supplementary feeding in pregnancy which shows that there is a smaller rate of premature births amongst poor women whose diet is supplemented. This is in accordance with an enquiry I made in Bombay when, during a dietetic survey of the city, it was shown that women taking a diet containing wheat or millet, both, like yeast, good sources of the vitamin B complex, had fewer premature infants with a lower neonatal death rate than women whose diet consisted mainly of polished rice (Balfour and Talpade, 1932).

REFERENCES

Balfour, M. I. and Talpade, S. K. (1932). *Indian med. Gaz.* **67**, 601.
Ebbs, J. H., Tisdall, F. F. and Scott, W. A. (1941). *J. Nutrit.* **22**, 515.
People's League of Health (1942). *Lancet*, **243**, 10.

Discussion

Professor J. R. Marrack (Haymeads Emergency Hospital, Bishop's Stortford, Herts.), joint opener: The diets of 25 women at Gateshead who were given supplements by the Birthday Trust have been studied by McCance, Widdowson and Verdon-Roe (1938). Even with the supplements these diets were very poor. The mean intakes of animal protein and of iron were, respectively, 36 g. and 11 mg. daily. On the other hand, in the experiment reported by the People's League of Health (1942) large amounts of iron and of vitamins A, D and C were supplied and moderate amounts of the B group of vitamins while in the Toronto experiment (Ebbs, Tisdall and Scott, 1941; Ebbs, Scott, Tisdall, Moyle and Bell, 1942; Ebbs, Brown, Tisdall, Moyle and Bell, 1942) the diet, as a whole, was brought up to a good standard.

A letter has appeared in the *British Medical Journal* in which the author (Fisher, 1943) has criticized the unsatisfactory nature of some of the evidence in the papers dealing with the Toronto and the People's League of Health experiments, without mentioning the more satisfactory evidence of the effects of improved diet; this included, in the Toronto experiment, the increase in the number of women free from complications, and the reduction of the duration of labour and of the number of babies artificially fed, and, in the experiment of the People's League of Health, the reduction in the number of cases of pre-eclampsia diagnosed on precise signs.

It is desirable that in future experiments either one constituent only of the diet should be raised to a satisfactory level, or the whole diet should be appreciably improved, also that, where possible, attention should be focussed not on occasional incidents, but on some feature present in all cases, such as the rate of growth of the baby.

Professor Huggett seems to have underestimated the quality of the present diet of pregnant women. The average amount of animal protein in the present working class diet, apart from that derived from fresh milk, is about 25 g. per head daily; the pint of milk commonly taken by pregnant women raises the total to 43 g. This is higher than the value found at Gateshead by McCance, Widdowson and Verdon-Roe (1938) in the diet of pregnant women in families with incomes under 16s. per head weekly. With the allowance of cod liver oil and fruit juice and the increased intake of the vitamin B complex due to the use of wheatmeal flour, the present diet of pregnant women must, on the whole, be better than before the war.

Further study is needed of the physiology of pregnancy. Why, for example, do pregnant women need more vitamin A, and excrete less vitamin B_1 and ascorbic acid than non-pregnant women on the same diet?

As pregnancy makes special dietary demands, pregnant women should be suitable subjects for the study of the effect of the present diet on the nutritional state. In particular the incidence of anaemia among them could be used as criterion of the availability of iron. There should be no difficulty in this study as in antenatal clinics blood is frequently taken for the Wasserman reaction.

REFERENCES

Ebbs, J. H., Brown, A., Tisdall, F. F., Moyle, W. J. and Bell, M. (1942). *Canad. med. Ass. J.* **46**, 6.

Ebbs, J. H., Scott, W. A., Tisdall, F. F., Moyle, W. J. and Bell, M. (1942). *Canad. med. Ass. J.* **46**, 1.

Ebbs, J. H., Tisdall, F. F. and Scott, W. A. (1941). *J. Nutrit.* **22**, 515.

Fisher, R. B. (1943). *Brit. med. J.* i, 144.

McCance, R. A., Widdowson, E. M. and Verdon-Roe, C. M. (1938). *J. Hyg., Camb.*, **38**, 597.

People's League of Health (1942). *Lancet*, **243**, 10.

Dr. H. Sinclair (Oxford Nutrition Survey, 10 Parks Road, Oxford), joint opener: Like Professor Huggett, I had the opportunity recently of attending the discussion on this subject held by the Scottish Group, and there seems to be general agreement that giving extra food to pregnant women produces a statistically significant diminution in the hazards of childbirth. The statistical control is particularly important because the incidence of death in mother or child is fortunately very low and, therefore, large numbers must be included in these feeding tests if valid results are to be obtained. Dr. Margaret Balfour in her excellent paper included a statistical analysis of results, but I should like further information about the method of selecting the mothers for the additional food. She said "The women who received the foods were selected by the medical officers in charge of the antenatal clinics", and it was found that the treated and control groups were not comparable in income or in geographical distribution. Her method of selection diminished the chances of obtaining a significant difference in respect of certain factors, but others such as age, parity, attendance at clinics and even unrecognized factors might invalidate the results unless the selection was random so that mothers on the supplemented diet were strictly comparable with the controls.

The last three speakers have all referred to the work of Ebbs and his colleagues in Toronto (Ebbs, Scott, Tisdall, Moyle and Bell, 1942; Ebbs, Brown, Tisdall, Moyle and Bell, 1942; Ebbs, Tisdall and Scott, 1941) and

of the People's League of Health (1942). Professor Marrack referred to the letter from Dr. Fisher in the current number of the *British Medical Journal* which criticizes this experiment on statistical grounds (Fisher, 1943). Dr. Doyne Bell also has criticized these experiments (Bell, 1942). Not only were the numbers very small in the Toronto experiment, but the papers as presented contain contradictions and mistatements, and the incidence of past complications in multiparous patients was so great that it is highly doubtful whether many of the results obtained in the test were significant.

Similarly, certain of the alleged results of the People's League of Health are open to other objections than those mentioned by Dr. Bell. For instance, the mean birth weight of the babies of mothers treated and over the age of 30 was 7·17 ± 0·7 lb. as compared with 6·99 ± 0·07 lb. in the controls; it is stated that the difference, 0·18 lb., "approaches significance"; if the figures are printed correctly, it is quite obvious that there is no significant difference between the two weights.

Though the main drift of such experiments is always the same, it is important to obtain accurate scientific evidence if public health policy is to be based on such results. It is also important to know what factors in the diet are deficient and what nutrients should be increased. The People's League of Health used the method of the dietary questionnaire, which would seem to be too rough for the degree of accuracy of the interpretations; it is stated, for instance, that only 2 per cent. of the women were having a satisfactory iron intake. The most accurate methods of assessing nutritional state are clinical and biochemical, but there are pitfalls in their application to pregnant women. For instance, marginal gingivitis and hypertrophy of the gums are common during pregnancy, but cannot by themselves be taken as a criterion of deficiency of vitamin C or nicotinic acid, because oestrogens produce those conditions (Ziskin, 1938); there are many causes of oedema in pregnancy other than nutritional causes, and oedema is very common in this condition (Weiss, 1940). Some laboratory tests also are untrustworthy; estimation of calcium deficiency by determination of the plasma content of phosphatase is upset because an increased amount of this enzyme is normal in pregnancy. The increase in plasma volume normal in pregnancy must be remembered in interpreting haematological results or results of tests for certain vitamins in whole blood; estimations on plasma or on the leucocyte layer of blood are more valuable.

In fact, the whole question of the effect of diet upon the hazards of pregnancy is a very difficult one, but it is one of the most important that affects the public health. Careful and critical work is needed, and is abundantly worth while.

References

Bell, D. (1942). *Proc. R. Soc. Med.* **36**, 65.
Fisher, R. B. (1943). *Brit. med. J.* i, 144.
Ebbs, J. H., Brown, A., Tisdall, F. F., Moyle, W. J. and Bell, M. (1942). *Canad. med. Ass. J.* **46**, 6.
Ebbs, J. H., Scott, W. A., Tisdall, F. F., Moyle, W. J. and Bell, M. (1942). *Canad. med. Ass. J.* **46**, 1.
Ebbs, J. H., Tisdall, F. F. and Scott, W. A. (1941). *J. Nutrit.* **22**, 515.
People's League of Health (1942). *Lancet*, **243**, 10.
Weiss, S. (1940). *New Engl. J. Med.* **223**, 939.
Ziskin, D. E. (1938). *J. Amer. dent. Ass.* **25**, 422.

Professor O. Kestner (School of Agriculture, Cambridge): In the last war German women got one l. of milk daily with the result that the birth weight of newborn babies was normal.

Dr. T. Moore (Dunn Nutritional Laboratory, Cambridge): Since muscular dystrophy caused by deficiency of vitamin E in experimental animals may fail entirely to respond to treatment with tocopherol it must not be too easily assumed that the failure of human muscular dystrophies to respond to tocopherol rules out the possibility of vitamin E deficiency as an aetiological factor.

Dr. H. Hoch (London Hospital, Whitechapel, London, E.1): The low mean value of 47 I.U. vitamin A per 100 ml. blood plasma found by myself for pregnant women is in agreement with results of earlier authors (Gaehtgens, 1937; de Haas and Meulemans, 1938; Hirst and Shoemaker, 1941). I obtained concentrations of vitamin A below 40 I.U. per 100 ml. also in the plasma or serum of pregnant women or women at parturition whose diets were rich in carotene. In some of the latter the concentration of carotene in serum or plasma was remarkably high. The low values for vitamin A in the plasma of pregnant women may have a different significance from similar values in non-pregnant women but further experiments are needed with controlled diets.

REFERENCES

Gaehtgens, G. (1937). *Klin. Wschr.* **16**, 893.
De Haas, J. H. and Meulemans, O. (1938). *Geneesk. Tijdschr. Ned. Ind.* **78**, 847.
Hirst, J. C. and Shoemaker, R. E. (1941). *Amer. J. Obstet. Gynec.* **42**, 404.

Dr. L. Wills (58 Campden Hill Court, London, W.8): The fall in haemoglobin observed in women of the poorer classes during pregnancy is not due entirely to hydraemia since, when complete counts are done, it is found that the number of red cells has not fallen in proportion to the fall in haemoglobin content; in other words, there is a hypochromic anaemia in these women.

Dr. M. I. Balfour gave the following reply:

To Dr. Sinclair: In the Birthday Trust experiment the cases were selected by medical officers of clinics and the main difference of better financial position was in favour of the controls.

Stillbirth and Neonatal Mortality*

Mr. R. M. Titmuss (5 Beaumont Court, Chiswick, London, W.4)

The Quantitative Problem

During the three years 1936–38 when the infant mortality rate stood at the relatively low figure of 57 per 1000 live births, 103,000 infants died within the first year of life. Just over one-half, 54,000, died within the first month and about one-fifth, 19,500, were dead within the first 24 hours. There were, in addition, during the three years, 75,000 still-births, equivalent to a rate of 39 per 1000 total births. Spontaneous

* Unless otherwise stated, all statistics relate to England and Wales, and include those for both legitimate and illegitimate children. Death rates for illegitimate children are generally higher, but it was not possible in the scope of this paper to separate the two.

abortions have been computed by various authorities to be in the neighbourhood of 20,000 to 30,000 per annum, roughly corresponding to the annual number of stillbirths. In my opinion, however, these estimates are much too low. An analysis of Maternity and Child Welfare Clinic records, the result of which has not yet been published, indicates that the ratio of miscarriages to stillbirths greatly exceeds 1 : 1. If for the time being, however, a figure of 30,000 annually is accepted the total for 1936–38 is 90,000. The number of illegal abortions has been estimated by various authorities but as we are dealing with deaths from natural causes we need not concern ourselves here with this problem.

Apart, therefore, from induced abortion we may say that out of nearly 2,000,000 pregnancies in the three years, over a quarter of a million, or 1 in 8 did not result in a live child aged one year. In comparison the number of maternal deaths appears small. During the three years there were roughly 8250 maternal deaths attributed to, or associated with, pregnancy and childbearing.

Trends in the Stillbirth Rate and Neonatal Mortality

From 1927, when stillbirth registration first became operative in this country, up to 1939 the rate remained practically stationary around 40 per 1000 total births. There has been little change too in the death rate during the first 24 hours. During 1906–10 the rate was 11·5 per 1000 live births and in 1931–35 it stood at 10·7. For the succeeding 6 days the rate has fallen slightly since 1906–10, from 13·0 to 11·2. The second, third and fourth weeks of life show increasingly larger falls since 1906–10. For the second fortnight of life, for instance, the rate has declined by more than half. Neonatal mortality as a whole has fallen by one-quarter from 40 1906–10 to 30 in 1937. But this fall of 25 per cent. is small in comparison with the changes at later ages. Thus the declines amount to 60 per cent. at 1 to 3 months, 62 per cent. at 3 to 6 months, 66 per cent. at 6 to 9 months and 71 per cent. at 9 to 12 months. It is not easy to say how far these striking falls have been brought about by a declining birth rate, and by shifts in birth order, maternal age, birth interval and the narrowing of the class fertility differential. Nevertheless, these changes mean that, whereas neonatal mortality represented one-third of the infant deaths in 1906–10, it now constitutes more than one-half.

Geographical Distribution

The relationship between infant mortality and socio-economic indices is well known. That there exists, however, a similar correspondence between the stillbirth rate and such indices is less generally recognized. For example, the rate in such boroughs as Wigan, Bolton, Merthyr and Oldham exceeds by almost 100 per cent. the rate in Oxford, Croydon, Eastbourne, Canterbury and Bath. But in some socially less favoured boroughs, where the quality and quantity of pre-natal care is good, the rate is nearly as low as that in socially more favoured boroughs such as Oxford and Croydon. Evidently a reduction in stillbirths of at least 25 per cent. over the whole country is possible of achievement.

The variation in the death rate during the first 24 hours in the different boroughs and regions of the country is less pronounced, but during the

remainder of the first month of life the variation steadily increases. It is significant that a low stillbirth rate in a particular area is generally accompanied by a low death rate throughout the first year of life. Thus, if the stillbirth ratio for England and Wales is taken as 100, that for the Home Counties is 85, the ratio for the first day being 88, and for 1 to 7 days, 83, declining subsequently to 61 at 6 to 12 months. On the other hand, the ratio for Lancashire and Cheshire mounts from 116 for stillbirths to one of 129 at 6 to 12 months.

The extent of the differences in mortality during the 2nd, 3rd and 4th weeks of life is much sharper among the 83 county boroughs than between the 28 metropolitan boroughs. Thus, the ratio varies from, for example, 62 in Southend to 232 in Gateshead. On the other hand, in London the lowest ratio, 42, is returned by Chelsea and the highest, 96, by Bermondsey. That climatic conditions do not explain the northern excess is indicated by the fact that in York and Huddersfield, for instance, the ratios are 75 and 78, respectively. It emerges from the examination of such figures, therefore, that, quite apart from social status, the degree and quality of medical and nursing care are important factors in the prevention of avoidable mortality.

Town and Country

Stillbirths are higher in the county boroughs than in the rural districts, but the latter register a rate considerably in excess of that for London. Clearly, the two factors of social environment and medical care have different weights in different areas. Some rural districts with a relatively good social environment but more or less isolated from medical services, such as the East Riding of Yorkshire, and Westmoreland, return a rate as low as county boroughs with highly organized services but a poor environment.

From the first day of life the chance of death for infants in county boroughs on the one hand and rural districts on the other continues to widen, with the remainder of urban districts holding an intermediate position.

As far as trends are concerned, neonatal mortality since 1911–15 has fallen much faster in London, by more than 25 per cent., than in other urban areas or in the rural districts. The explanation of the low rate for London would appear to be that during the puerperium and for a week or two later a large proportion of mothers in the poorest groups enjoy an amount of medical and nursing care that is denied to them at all other times.

Distribution According to Social Class

There are no statistics available of the stillbirth rate among the different social and occupational groups in the community, nor have we any reliable data on the incidence of miscarriages. We have, however, some valuable records of infant mortality by social class and age at death. These show that during 1930–32 the neonatal death rate per 1000 live births was:

Class 1.. ..	22	Class 4.. ..	30
,, 2.. ..	27	,, 5.. ..	33
,, 3.. ..	29	All classes ..	30

https://doi.org/10.1079/PNS19440002 Published online by Cambridge University Press

From these statistics we learn that the rate among the poorest section of the community exceeded that among the rich by 50 per cent. But this difference is small compared with the range at later ages. At 1 to 3 months the excess is 205 per cent., at 3 to 6 months 287 per cent. and at 6 to 12 months it reaches the figure of 439 per cent.

In a recent book I have made an examination of trends in social class mortality since 1911 (Titmuss, 1943). I find that for neonatal deaths the class changes are more or less uniform. Thus Class 1 has fallen to 72 per cent. of its 1911 rate and Class 5 to 76 per cent. When we look at the rate among different occupations we find, for instance, that the death rate among infants of doctors is 20 compared with 33 for Class 5 and 40 for children of miners. But rates considerably lower have been achieved in other parts of the world. Oslo and Amsterdam had, before the war, driven down their neonatal mortality to 16 per 1000 live births and for all Dutch towns with populations exceeding 100,000 the rate was 18 in 1931. This rate, below that for doctors and Class 1 in this country, may be compared with a rate of 34 for all English county boroughs during the same period.

The conclusion to be derived from a study of neonatal statistics drawn from different social groups, cities, regions and countries is that there is considerable scope for a reduction in the rate for England and Wales. It is also important to appreciate that measures taken, whether medical, nutritional, social or economic, which succeed in reducing the rate, will, contemporaneously, drive down the death rate at later ages.

The Classification of Neonatal Mortality

It has long been recognized that the certification of deaths in infancy is faulty and Miller (1942) has warned us to exercise care in interpretation. Nevertheless, it is clear that prematurity is the greatest single factor predisposing to neonatal death. There are considerable variations in the death rate from premature birth in different areas of the country. During 1931–35 the rate for the whole of the country was 18 per 1000 live births; in Greater London it was as low as 14, whereas in South Wales it stood at 21. In New Zealand and Holland the rate from prematurity and debility was, during the same period, 11 and 10, respectively. This latter rate of 10 per 1000 for Holland was the level achieved by Class 1 in this country by 1930–32. In Class 2 it was 14, in Class 3 17, in Class 4 19, and in Class 5 20. With descent in the social scale the amount of prematurity steadily increased. Baird (1941), writing of experience in Aberdeen, states that among the well to do, neonatal mortality due to prematurity is 10 per 1000 live births, which agrees with the Registrar General's rate, as against a rate of 20 for the rest of the city, and finds that among the poor where diet is deficient and adequate rest often impossible, premature labour is much more frequent.

McNeil (1942), Young (1942) and other authorities in this country, and Barnes and Willson (1942) and others in the United States, have concluded that the death rate from prematurity can be reduced. Recent public health work in Chicago and New York and some small scale experiments, such as the Toronto investigation (Ebbs, Tisdall and Scott, 1941) have all shown that the incidence of miscarriage, stillbirth and prematurity can be appreciably lowered.

Birth Rank and Interval, Maternal Age and Plurality

There are at least four biological factors of importance in any consideration of stillbirths and neonatal deaths, namely, the age of the mother, the order of birth, the interval between births, and multiple births. Our knowledge on the influence of these factors is somewhat scanty. There have been a number of private investigations such as that of Burns (1942) in Durham and those of Yerushalmy (1938) and of Woodbury (1926) in America, which have thrown some light on the subject. We now have, however, an excellent report from the Registrar General which should be studied by all those concerned with the problem of stillbirths. This Report (1938 Civil) shows that parity, maternal age and plurality all influence the risk of a child being stillborn. If all first births are taken, the risk of stillbirth increases steadily with advancing age of the mother. For mothers under 20 the risk is less than 3 per cent.; at ages 30 to 35 the risk has doubled, and at 40 and over it has doubled again. The same progression with maternal age is apparent when 2nd, 3rd, 4th and all subsequent birth orders are examined separately. Comparing the stillbirth risk at different birth orders in the same maternal age group we find, for instance, that the rate is higher for all first born at all ages up to 45 than for subsequent children up to at least the 8th child. At ages under 20 the risk is about 30 per cent. lower for second than for first births; at ages 20 to 25 it is 40 per cent. lower, and at ages 25 to 30 the reduction is 45 per cent. At ages 30 to 35 the risk for 4th and 5th children is about 50 per cent. lower than for first born.

As I have already said, between 1927 and 1939 the total stillbirth rate remained constant around 40 per 1000 total births. Since 1939, however, there has been a striking decline in the rate. Part of the explanation is, I suggest, the much higher proportion of first births at ages under 25.

For multiple births the stillbirth rate is twice as high as for all children at single births.

The Registrar General's Report does not provide us with similar data for neonatal mortality. The evidence from various inquiries, such as that of Burns (1942), indicates that the age of the mother exerts some influence on the death rate. The evidence on the effects of birth rank on neonatal mortality is, however, much less conclusive. According to Huntington (1938), Burns (1942) and others, the incidence of miscarriages increases greatly with increasing birth rank.

Not only is very early and very late child bearing dangerous for both mother and child but too rapid breeding is also the cause of some excessive mortality.

Summary

In a very small space it has not been possible to discuss adequately all the factors implicated in the problem of stillbirths and neonatal deaths, nor has it been possible to refer to all the work that has been done on the subject.

Ignoring induced abortion, I have shown that at least one pregnancy in every 8 does not result in a live child aged one year. Neonatal deaths today constitute more than one-half of infant mortality. Contrary to the opinion of those who believe we have practically reached the irreducible minimum I hold the view that there is ample scope for

considerable reduction in the annual incidence of stillbirths and neonatal deaths. This, I think, is abundantly clear from an examination of the statistics according to social class, urban and rural districts, and regional and international areas. The Registrar General in a long series of often neglected reports, unexcelled in many respects by other national vital statistics, has for long drawn attention to the extent of avoidable infant deaths.

I have shown too that there are a number of factors such as maternal age, birth order and rate of breeding, which are not unimportant in any consideration of the problem. These factors are not beyond control. They are essentially social problems. Then there is a multiplicity of factors of which we know little. For instance, that the causative agencies in stillbirths are hard to determine is illustrated by the report of the Registrar General for Scotland for 1937, classifying 37 per cent. of stillbirths as of unknown or ill defined causation. There are, however, other elements, medical, nutritional, economic, educational and genetic, to say nothing of such factors as housing and clothing, which are all of profound importance in deciding the termination of pregnancy. How important these factors are is not, however, my task to discuss in this paper.

REFERENCES

Baird, D. (1941). *Lancet*, **240**, 160.
Barnes, A. C. and Willson, J. R. (1942). *J. Amer. med. Ass.* **119**, 545.
Burns, C. M. (1942). *Infant and Maternal Mortality in Relation to Size of Family and Rapidity of Breeding*. University of Durham.
Ebbs, J. H., Tisdall, F. F. and Scott, F. A. (1941). *J. Nutrit.* **22**, 515.
Huntington, E. (1938). *Season of Birth. Its Relation to Human Activities*. London: Chapman and Hall.
McNeil, C. (1942). *Brit. med. J.* i, 429.
Miller, F. J. W. (1942). *Lancet*, **243**, 269.
Registrar General (England and Wales). *Statistical Reviews*, 1906–38.
Registrar General (England and Wales). *Quarterly Returns*, 1939–42.
Registrar General (England and Wales). *Decennial Supplements* (*Occupational Mortality*) 1911 and 1931.
Registrar General (Scotland). *Annual Report*, 1937.
Titmuss, R. M. (1943). *Birth, Poverty and Wealth*. London: Hamish Hamilton.
Woodbury, R. M. (1926). *Infant Mortality and its Causes*. Baltimore: The Williams and Wilkins Co.
Yerushalmy, J. (1938). *Amer. J. Hyg.* **28**, 244.
Young, J. (1942). *Brit. med. J.* i, 504.

Discussion

Dr. G. Bourne (University Laboratory of Physiology, Oxford), opener: Mr. Titmuss and other speakers have indicated that there are many factors affecting stillbirth and neonatal mortality. It is obvious from what has been said today that one of these factors is certainly nutritional. It is scarcely a coincidence that the best fed countries in the world have low infantile mortality rates. Australia and New Zealand have a rate of less than 40 per thousand. Italy, Spain, Japan and Egypt, in which the diet is much worse have a rate which is three times as high. In Great Britain, the infantile mortality rate in 1936 was about 62 per 1000 live births, a figure which is intermediate between those already mentioned.

Mr. Titmuss has given the stillbirth figures for England and Wales as 39 to 40 per thousand live births. In New Zealand in 1938 it was

26 per thousand. Figures are not available for stillbirths over the whole of Australia because they are not registered in all states, but in New South Wales the figure is very low, reaching only 9·75 per thousand live births. Mr. Titmuss has also given the figure for neonatal deaths in England and Wales for 1937 as 30 per thousand, this being the figure for children dying within the first week. In New Zealand the corresponding figure is 19·41. There is no similar figure available for Australia but that for deaths among children under one month is 26·67.

Thus, we see that, in better fed countries such as Australia and New Zealand, not only is the general infantile mortality rate lower than in England, but the stillbirth and neonatal figures are correspondingly less.

Although Australia and New Zealand are better fed countries we cannot necessarily assume that the more favourable infant mortality rates are due entirely to the better food. Other things may be better too, the medical services and the hospitals. Nevertheless most of the evidence available on this subject points to a high standard of nutrition as being the most important single factor associated with a low infantile mortality rate.

It would be of interest to know how the lowered nutritional state of Europe during the present war has affected the neonatal mortality and stillbirth figures, but it is obviously impossible to obtain such figures. Some figures for infant mortality are available, however, and although not strictly relevant to the discussion they might be of interest.

In Germany the nutritional level has not fallen very much during the war. Special attention has been paid to feeding children, who receive vitamin C tablets and concentrates and vitamin D preparations. The infant mortality rate in Germany for 1938, 1939 and 1940 is given as 60, 61 and 62 per thousand, respectively. The slight rise may be due to the decreased medical services for civilians and to the difficulties of infant care under war time conditions.

In a neighbouring country to Germany, where the nutritional situation is much worse, that is, the Netherlands, infant mortality figures are not available but there is a 31 per cent. increase in deaths of children under four. The cause of this increase is mainly respiratory infections.

In France, where the food situation is also bad, Marseilles doctors claim that there is a 40 per cent. increase in infantile mortality. In Greece, which is in a pitiable nutritional condition, the infant mortality is a national scourge.

Dr. I. Leitch (Rowett Research Institute, Bucksburn, Aberdeen): There is a close parallel between the historical gradient in infant mortality and the social gradient in this and other countries. Where the total infant mortality is high, the difference is mainly due to deaths in the period 1 to 12 months, and the main cause is infective disease, gastro-intestinal and respiratory. The history of the last forty years and the study of social conditions show how the total rate can be reduced by improvement of infant feeding, housing, sanitation and nursing. This part can, in fact, be very rapidly reduced by suitable and vigorously enforced measures as, for instance, in Chicago where the infant mortality rate has been reduced in a few years to a very low level.

When this major part of high mortality rates has been removed, there remains a relatively uniform and less easily reducible part where there

has been little change in the last forty years and where there is little social gradient. This class of mortality includes stillbirths, neonatal deaths, deaths due to congenital debility, prematurity and unknown and ill defined causes; it would include the "lack of vigour" of which Mr. Bourne (1944) spoke. These deaths are, to a large extent, obviously associated with antenatal causes, although unfavourable environment after birth will contribute to the actual death. The antenatal causes may be partly genetic and partly physiological or dietary. There are undoubtedly physiological factors, such as those due to age and parity but, unless the causes are largely genetic, we should expect greater gradients, both historical and social, than actually exist.

It is suggested that the absence of such gradients may be due to the combination of improved obstetrics with improved maternal diet and antenatal care, which might cause a conversion of miscarriages, for which there are no records, into stillbirths or premature births and into death of live born infants from congenital debility, malformations and unknown or ill defined causes. This idea is supported by the fact that recent data from areas where total and neonatal rates are low, that is where the environmental factors are good, show some indication that deaths due to congenital malformations have increased.

REFERENCE

Bourne, A. W. (1944). *Proc. Nutr. Soc.* **2**, 1.

Professor E. J. Bigwood (Belgian Ministry of Finance, 49 Eaton Place, London, S.W.1): The food and health situation in occupied Belgium is extremely serious and the physical condition of expectant and nursing mothers is alarming. There is, for instance, a considerable increase of tuberculosis among them. The physical condition of newborn infants has also seriously deteriorated and already in the first quarter of 1941 the mortality during the first year of life had more than trebled in the main paediatric clinics in Brussels. Premature births also increased threefold during the first 8 months of 1941. Yet it is of interest to note from reports of 4 major university obstetrical departments that the birth weight did not decline appreciably during 1941 in comparison with pre-war figures. This observation is all the more striking as the mothers had during pregnancy a diet supplying only from 1500 to 2000 Calories, including the extra rations to which they were entitled during the last 5 months of pregnancy. Figures for 1942 are not yet available.

Professor A. St. G. Huggett (St. Mary's Hospital Medical School, Praed Street, London, W.2): Mr. Howard Kershner, Director of the American Friends Relief Service, has told me that conditions in Vichy France are bad, the growth rate of children has decreased and it is even believed by the medical officers that the birth weight has been reduced by one-third, though under the conditions of their work this could not be verified by actual weighing.

Mr. A. L. Bacharach (Glaxo Laboratories, Ltd., Greenford, Middlesex): It is possible that the irreducible minimum of neonatal deaths and the increasing social differentiation of death rates with increasing infant age might both be an expression of foetal parasitism. Environment that had acted on the maternal nutritional status would begin to act on the new

born infant with increasing effect as the foetal environment was left behind.

Dr. F. Bergel (Roche Products, Ltd., Welwyn Garden City, Herts.): Vitamin E is recommended for the prevention of miscarriage and for the treatment of muscular dystrophy. Creatinuria occurs in both these conditions and also in pregnancy. Is there any connexion between the role of vitamin E in pregnancy and its effect on creatinuria?

Dr. H. M. Sinclair (Oxford Nutrition Survey, 10 Parks Road, Oxford): I should like to correct Dr. Bergel's statement that the creatinuria of muscular dystrophies is affected in man by vitamin E therapy. Four groups of workers who have employed such therapy (Vivanco, 1940; Ferrebee, Klingman and Frantz, 1941; Fitzgerald and McArdle, 1941; Alpers, Gaskill and Cantarow, 1942) have found no significant effect upon the clinical condition or upon the urinary excretion of creatine.

REFERENCES

Alpers, B. J., Gaskill, H. S. and Cantarow, A. (1942). *J. nerv. ment. Dis.* **96**, 384.
Ferrebee, J. W., Klingman, W. O. and Frantz, A. M. (1941). *J. Amer. med. Ass.* **116**, 1895.
Fitzgerald, G. and McArdle, B. (1941). *Brain*, **64**, 19.
Vivanco, F. (1940). *Rev. clin. esp.* **1**, 336.

Dr. F. Bicknell (79 Wimpole Street, London, W.1): The papers quoted by Dr. Sinclair are valueless as a proof of lack of effect of vitamin E on creatine metabolism in human muscular dystrophy partly because the vitamin was given for too short a time and partly because no information is given about the general condition of the patients. The latter is important since sepsis, for instance, prevents any response to vitamin E therapy.