Fetal Growth as an Indicator of Socioeconomic Change

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DIFFERENCES in mean birth weight between population groups have been known for a long time. In some instances it was suspected that racial factors are involved, but there have always also been socioeconomic differences such as, for instance, between whites and Negroes in the United States. The higher incidence of low birth weight in some groups was loosely attributed to "prematurity" because until recently little attention was paid to the fact that not all small neonates are truly premature, that is, born after an abnormally short gestation.

In recent years the appreciation of the relationship of birth weight and gestational age has led to an awareness of the role of fetal growth (as distinct from length of gestation) in determining differences of mean birth weight of populations. Hendricks (*1*) reported that socioeconomic (environmental) differences have a greater effect on fetal growth than do racial (genetic) ones in a hospital population in Cleveland. Also, my co-workers and I noted that the spectacular change in birth weights in Japan during a 20-year period was caused only by better fetal growth and not by an increase in the duration of pregnancy (*2*). It is therefore appropriate to consider fetal growth and methods of studying it with a view to assessing socioeconomic status and its changes.

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There are many reports which, even though they do not contain data sufficient to evaluate fetal growth in detail, testify to the effect of socioeconomic factors. The following are a few examples. Peller (*3*) showed as early as 1924 and earlier in his studies in Vienna that socioeconomic status as well as good care and nutrition in a rest home for several weeks prior to delivery affect birth weight. Venkatachalam (*4*) noted that in three communities in India the mean birth weight in a high socioeconomic group was 372 grams higher than in a low one; the prevalence of low birth weight was twice as high in the latter as in the former. He also observed that at term nearly one-third of the infants of mothers with a poor nutritional status weighed less than 2,500 grams. Baird (*5*), summarizing earlier work in Aberdeen, concluded that social class correlates with maternal height and both correlate with the rate of low birth weight. That rate was twice as high in families of the two lowest social classes as in those of the two highest of five social classes.

The following discussion is limited to birth weight as an indicator of growth since no other parameter has been used to any extent. Only the third trimester of pregnancy is considered because variations in fetal growth of populations arise during this period, as explained later. Whenever populations are compared, it is essential to eliminate differences in the incidence of preterm birth as a cause of variation in weight. This can be done only with a population of known gestational ages, and that is the most severe limitation of the study of fetal growth.

Characteristics of Fetal Growth

It is obviously impossible to study human fetal growth longitudinally, that is, by weighing the same fetus repeatedly during normal intrauterine life. One therefore depends on birth weight curves which are based on the assumption that birth weights after various lengths of gestation are representative of normal fetal weight at those times. Since birth well before term is in itself abnormal, this assumption needs to be examined and justified. Here, as throughout this presentation, certain abnormal groups—infants of diabetic mothers, malformed or chronically diseased infants, and multiple births—are excluded for reasons given later. Apart from these groups, fetal growth early in the third trimester seldom varies abnormally, since the system of feto-maternal exchange has at that time a functional reserve greatly in excess of the need of the fetus except in rare, severely abnormal pregnancies. Thus, so far as we know, fetal growth retardation is unlikely to be responsible for significant proportions of neonates with an abnormal weight early in the third trimester.

Later in the third trimester fetal growth retardation gains in potential significance, but at that time normal birth occurs in the great majority of cases and in numbers sufficiently large to allow confident interpretation. For this reason, birth weight data may be assumed to be reasonably close approximations of normal fetal weights at the respective time in pregnancy. Moreover, this is the only information available.

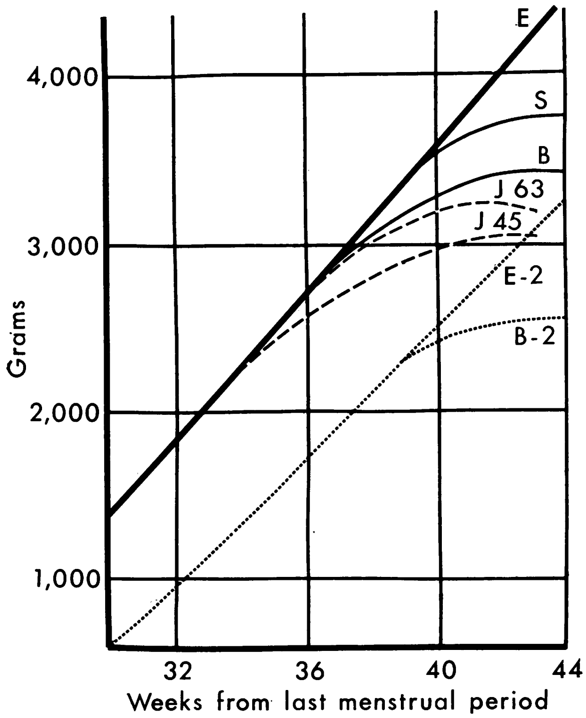
Based on this information, the following hypothesis of fetal growth and its variation has been advanced (*6*). Early in the third trimester, birth weight curves of all populations examined to date follow a similar, linear course if properly corrected. (The distribution of birth weights around the peak is asymmetrical in each week of the first half of the third trimester, with larger numbers on the side of higher weights; sometimes there is a secondary peak. Correction made and justified independently by myself (*6*) and Neligan (*7*) consists of eliminating high-weight births with a presumably understated gestational age to produce a symmetrical Gaussian distribution.) The linear course is indicative of unrestrained growth regulated by the growth potential of the fetus in the presence of an adequate supply line. Since the fetus grows at all times more rapidly than the level of growth support received from the mother via the placenta, a time comes when support is no longer adequate for unrestrained growth. At that time, which in most white populations examined is about 37 weeks or later, the birth weight curve departs from the straight course. The lower the level of growth support, the earlier the departure from the straight-line growth and the lower is the birth weight at term (see chart). In sporadic cases of outright abnormal pregnancy this departure may occur early in the third trimester; this does not concern us here. In multiple pregnancy the earlier departure is the rule since the partners must share the available supply. An abnormal growth potential appears to exist in fetuses of diabetic mothers, who are often abnormally large early in the third trimester, and in malformed or chronically diseased (for instance, rubella-infected) fetuses who as a group show a high incidence of severe growth retardation. This has also been seen in experimental teratology.

Inadequacy of the placenta may be one of the factors limiting growth of the fetus. For some time such limitation was indiscriminately referred to as "placental insufficiency." It is becoming increasingly clear that apart from some of the sporadic, pathological growth retardation just mentioned, the maternal organism is more likely to limit fetal growth than is the placenta (*9*). One exception may be the post term period, perhaps after more than 42 weeks of pregnancy, when placental growth could fall behind sufficiently to produce relative insufficiency. To what extent this is the case, rather than increasing inadequacy of the maternal supply line, has not been determined.

Socioeconomic Factors

The various factors composing or affecting the socioeconomic milieu have escaped definition so far. Nutrition, hygiene, medical care, educa-

Smoothed birth weight curves to illustrate trends in fetal growth. E, extrapolated curve indicating how populations of fetuses would probably grow if they had unlimited supplies; S, Swedish data (*8*); B, Baltimore data (*6*); J 63, Japanese data for 1963–64; J 45, Japanese data for 1945–46 (2); E–2, mean minus 2 standard deviations for the extrapolated curve; B–2, mean minus 2 standard deviations for the Baltimore curve.



tion, living habits, and psychological and other factors enter into complex combinations which defy classification or identification by social parameters such as highest grade of schooling, family income, or others usually evaluated in such studies (*10*). For instance, it is quite obvious even to a casual observer that the somatic sequelae of low socioeconomic status in southern and eastern Europe a generation or two ago were quite different from those apparent in the predominantly Negro slum dwellers in the United States. It is not known to what extent the racial background affects these manifestations, but as more information on the effects of changing circumstances becomes available, the presumable role of racial factors shrinks. (This is not to deny the existence of such factors.) Fetal growth, just like other parameters that may be studied, has so far not helped define the nature of socioeconomic deprivation qualitatively, but it can give an indication of the overall extent of deprivation and it may be a sensitive indicator of change.

The timing of the effects of change needs to be considered. As the results of the study in Japan (*2*) suggest, dramatic changes in living conditions may have demonstrable effects on fetal growth in a few years. On the other hand, socioeconomic deprivation has permanent effects on physical development; the shorter height of women in the lower social classes is well known, and these short and otherwise not optimally developed women are not optimal reproducers so far as the support of fetal growth is concerned (*5*). There are, in other words, immediate effects in response to circumstances affecting the mother at the time of her current pregnancy and delayed ones which influenced her years ago during her own development and permanently reduced her functional efficiency during pregnancies. This strongly suggests that the full manifestation of socioeconomic improvement may take two or three generations. One may suspect that such differences among populations of mothers contributed to the differences of the effects of the "hunger winter" in the Netherlands (*11*) where reduction in average birth weight was 200 grams, and the siege of Leningrad (*12*) where the reduction was 500 grams.

Standards of Fetal Growth

In any consideration of growth the time factor, which is gestational age here, is an essential parameter. As is general custom in medical practice, the date of onset of the last normal menstrual period is used as the starting point, which is about 2 weeks earlier than conception. If this date is carefully elicited at the first prenatal visit and not changed as a result of examination later in pregnancy, it is remarkably valuable even though occasional errors do occur. Unless one wishes to indicate gestational age in days, which is cumbersome and to most readers does not give immediately intelligible values, there are two methods of counting weeks: the nearest week (week ±3 days) and completed weeks (week +0 to 6 days). The *n*th week (week −6 to 0 days) is seldom used.

The first two methods differ by about ½ week, and it is therefore necessary to indicate which one is used in a particular study and make appropriate corrections when comparison with other studies is undertaken. In this presentation the nearest week is used.

If the hypothesis of fetal growth as outlined is accepted, fetal growth data for the early part of the third trimester up to about 34 weeks should be universally valid. This relieves investigators of the need to acquire baseline data of their own, which are difficult to obtain because of the small numbers of births in that period and the possible need for correction.

Normal growth may be defined in two ways. If normal is used in the statistical sense and therefore represented by the usual, prevailing standards, empirical data based on the population in question or one assumed to be similar to it should be used. If, on the other hand, normal is taken to mean optimally healthy, then extrapolated standards are in order since they indicate, if the present hypothesis is correct, how any population of fetuses would grow if it were optimally supplied. The table gives smoothed values for an example of local standards, empirically derived from the mixed white and Negro population of the Sinai Hospital of Baltimore, and extrapolated standards, with standard deviations for both. The chart shows mean and mean minus 2 standard deviations for these two sets of standards.

Beyond 34 weeks the selection of standards depends upon the problem under study. If different segments of a population are to be compared or the immediate effect of the introduction of a particular change studied, then empirical standards may be used. If, on the other hand, populations in various parts of the world are to be compared, then extrapolated standards (corresponding to line E in the chart) are recommended. A minor disadvantage in using extrapolated standards is that no known population corresponds entirely to them, although Lindell's (*8*) Swedish data differ only past term. By 44 weeks the Baltimore mean is below mean minus 1 standard deviation by extrapolated standards. Yet it is particularly in the study of prolonged pregnancy that extrapolated standards are valuable because of the considerable degree of growth inhibition built into empirical post term standards as "normal" (*13*).

Empirical and extrapolated birth weight standards

Gestational age [1]	Smoothed empirical standards [2]	Extrapolated standards [3]
28	1, 050±350	
29	1, 200±350	
30	1, 380±370	
31	1, 560±360	
32	1, 750±400	
33	1, 950±420	
34	2, 170±440	
35	2, 390±440	
36	2, 610±440	
37	2, 830±430	
38	3, 050±430	
39	3, 210±430	3, 270±440
40	3, 280±440	3, 490±470
41	3, 350±450	3, 710±500
42	3, 400±460	3, 930±530
43	3, 410±490	4, 150±550
44	3, 420±520	4, 370±580

[1] Nearest week from last menstrual period.
[2] Sinai Hospital of Baltimore, Inc.
[3] These are arbitrary figures corresponding to an extension of the straight portion of the empirical curve. Depending on slight changes in the slope of the straight portion, one may arrive at different values diverging with increasing gestational age. The standard deviation was set arbitrarily in proportion to the empirical level at 39–42 weeks, at about 1 per 7.5 of body weight.

Fetal growth retardation of pathological degrees, originating when growth support has been below requirements of normal growth for weeks, is judged by the degree of deviation from normal for the respective week of gestation. The two most frequently used arbitrary borderlines are the 10th percentile and 2 standard deviations below the mean. The former includes more than three times as many cases as the latter.

The following groups of births may be excluded when comparing new birth weight curves of populations with either empirical or extrapolated standards: pregnancies lasting less than 35 weeks, of which only small numbers of cases are usually available, and, for the reasons given, infants of diabetic mothers, infants with serious malformations, and multiple births. The last three groups, however, are numerically small and failure to exclude them may not be a serious defect.

It is desirable to group birth weights in 100-gram to 250-gram groups and gestational ages in 1-week periods; 500-gram groups and 2-

week periods are the bare minimum of discrimination. The Program Area Committee on Child Health of the American Public Health Association (*14*) has recently proposed requirements for data on perinatal mortality. As far as these requirements do not pertain directly to circumstances of death, they apply to the study of populations as suggested previously. Since it has been shown in at least one instance (*2*) that differences in mean birth weight in the same area at different times are due entirely to the rate of fetal growth, the question may arise as to why data should be broken down by gestational age which may be difficult to ascertain. The main reason is that early birth, the other principal cause of low birth weight, is governed by factors which differ from those affecting fetal growth and it is likely that the share of each of these two in affecting mean birth weight varies from group to group. It has been attempted to arrive at significant data on fetal growth by eliminating preterm births and combining all others, but when information on gestational age is adequate to do this, a complete study of birth weight by week of gestation should also be feasible.

It may also be of interest to examine the incidence of pathological or borderline growth retardation in a population defined by geographic, ethnic, social, or medical criteria, using definitions based on standard deviations or percentiles for the respective week of gestation. It is important, of course, to use the same set of standards for all groups to be compared, either derived empirically from one population or extrapolated.

Discussion

It is not surprising that pregnancy, which taxes the maternal organism so heavily, should be a sensitive indicator of the mother's functional state even in the absence of disease in the usual sense. The efficiency with which the maternal organism satisfies the needs of pregnancy can be judged by fetal growth.

Compared with simple consideration of mean birth weights, the study of fetal growth adds the possibility of separating differences of fetal growth rates of populations from variations in the incidence of preterm birth. Both these factors should be examined and both reflect socioeconomic status, but in different ways. Another aspect which is pertinent here is perinatal mortality. This is related to both fetal growth and duration of gestation and perhaps to other factors influenced by socioeconomic status as well. The high mortality of infants born immature is well known, but poor fetal growth also carries its share. Among infants born at 33 to 40 weeks of gestation, those with a weight below mean minus 2 standard deviations have eight times the mortality of the total infant population born after the same length of gestation (*15*). In fact, Butler and Bonham (*16*) noted that among infants weighing 1,500–2,000 grams, those with a gestational age of 38 weeks or more have a higher perinatal mortality than those of shorter gestational ages. Thus, investigations of fetal growth, preterm birth, and perinatal mortality complement each other.

The scientific and medical usefulness of studying fetal growth transcends the crude evaluation of socioeconomic status. From the point of view of fetal physiology it will be necessary to refine the definition of poor fetal growth by studying indexes other than birth weight. It is unlikely that, for instance, all fetuses weighing 2,900 grams at the end of a 40-week pregnancy have been subjected to the same kind of moderate deprivation and have reacted to it in the same manner. Likewise, a more sophisticated analysis of fetal growth may make it possible in the future to pinpoint certain specific factors in the socioeconomic environment of the mother either at the time of pregnancy or during her development.

In this connection it must be remembered that linear growth by the same amount each week represents a declining growth rate. Also, growth is never uniform and affects various components of the body in different proportions. It is therefore remarkable, but perhaps fortuitous, that such uniform weekly increments prevail during much of the third trimester of pregnancy.

Other known factors such as maternal age, parity, interval between pregnancies, and family planning may affect birth weight. Some of these might be properly considered as part of the socioeconomic status. For instance, the decline of family size which frequently accompanies improved socioeconomic conditions results in a higher proportion of primiparity with lower birth weight. This particular factor actually tends to counteract the trend toward larger average weights.

The question arises as to whether bigger babies are necessarily better. They are in the sense that they indicate a better socioeconomic environment. Excluding the possibility of dystocia, it is not known whether infants, having grown to an as yet undetermined minimal respectable size, benefit by growing bigger. It may be stated confidently that continued improvement of living conditions will not lead to an indefinitely continuing increase in fetal size. Bakwin and McLaughlin (*17*), in a study of postnatal growth, concluded that the end is in sight; the same is to be expected of fetal growth. According to the hypothesis of fetal growth followed in this presentation, the extrapolated growth curve in the chart indicates full realization of the growth potential even in the presence of more than the needed support. This should therefore be the maximum attainable up to shortly after term. Beyond that time the placenta may well be one of the limiting factors and may prevent post term growth from even reaching the extrapolated values in populations, but not in some individuals.

Summary

Fetal growth may be studied in populations by means of birth weight curves, relating weight to gestational age. Comparison of data obtained in different groups or at different times is a useful indicator of socioeconomic differences or changes. Theoretical considerations of fetal growth during the third trimester indicate that in most instances data on pregnancies lasting less than 35 weeks from the last menstrual period, which are difficult to obtain in significant numbers, need not be considered.

Sample standards, based on a voluntary hospital in Baltimore, are given as well as extrapolated standards indicating how a population of fetuses would presumably grow if optimally supplied. The extrapolated standards should be useful in comparing populations from different parts of the world. Studies of fetal growth may help in the future to pinpoint significant factors within the broad spectrum of socioeconomic conditions.

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