Placental insufficiency—a questionable concept

It has been only during the last 15 years that most of us realized that true prematurity is not the only, and in some populations not even the most frequent, cause of low birthweight. An Expert Committee of the World Health Organization deserves credit for stating in 1961 that the term prematurity should no longer be used to designate all infants with a birthweight of 2 500 g or less. Now that we knew or assumed that many infants were small at birth because they had not grown *in utero* at the normal rate, it was only a short jump to the conclusion that these fetuses had been underfed; since the placenta is their source of nutrition, there had to be placental insufficiency. Leaving aside a sizable minority of these small-for-dates infants who have a reduced growth potential either as part of malformation or because of chronic fetal infection, there is the large group of deprived fetuses, a condition which we should like to prevent or treat. In order to do this, we must know whether it really is the rather inaccessible and intractable placenta which keeps the necessary supplies from the fetus, or perhaps that portion of the supply line which brings materials from the mother to the placenta.

Within the placenta there is a unique and very close approximation of the circulations of mother and fetus. The fixed tissues of the placenta are part of the conceptus, and this includes the villi with their core, fetal capillaries, and trophoblastic lining which is the site of permeability or, more frequently, active transport between mother and fetus. Only a deficiency in these tissues and their function can be true placental insufficiency. Surrounding the villi within the placenta is the intervillous space carrying maternal blood which is under maternal control with regard to both its composition and flow. Any disturbance in this latter system must therefore logically be considered a maternal factor.

By definition, placental insufficiency exists only when the placenta receives supplies from the maternal blood in sufficient quantity and at a sufficient rate, and yet does not transmit them adequately to the fetus. This surely exists in an occasional case, but most of the time it is not so. There are placentas in which premature separation

of some duration, infarcts, haemangiomas, etc., leave only a small portion of the tissue in a functional state, but these are infrequent and except for haemangiomas are generally believed to be secondary to maternal changes. Selective inability of the placenta to transmit essential materials has not been shown, perhaps largely because we do not know what to look for. Maternal factors, on the other hand, which fail to offer the placenta and hence the fetus what is needed, are known to occur. This is true particularly of circulatory factors which prevent adequate circulation in the intervillous space; abnormalities of the composition of maternal blood certainly exist, but our knowledge of these factors, such as 'malnutrition' is vague. The latter always affects multiple substances, and it is not known which basic materials, such as specific amino acids, are essential and thus growth-limiting.

Much has been made of the close correlation of fetal and placental weight, and since the placenta 'nourishes' the fetus it was assumed without evidence that when both are proportionally reduced in size, the small placenta had failed to supply the fetus properly and thus caused its small size. This would presuppose that the placenta is always very near the limit of its functional capacity with regard to its fetus; otherwise a somewhat small placenta could not limit fetal growth. All evidence, circumstantial as it may be, is against that, and it is more likely that the placenta, being part of the conceptus, is regulated in its growth by the same kinds of factors that regulate growth of the entire fetus and its parts. When placental weight is below mean -2 standard deviations for either body weight or gestational age, 8 of 9 fetuses and infants still survive.

What, then, do we know about the relation of the long-term well-being of the fetus to its supply line, consisting of the maternal circulation in the intervillous space, and the placenta proper? It has been mentioned that certain fetuses have a reduced growth potential; their small size is no measure of a defective supply line, and malformed or chronically diseased fetuses should therefore be excluded from studies of prenatal deprivation. Three kinds of maternal factors can interfere with fetal growth:

(1) reduced utero-placental circulation, (2) inadequate ability to satisfy increasing demands, and (3) nutritional and other even less well defined factors such as socioeconomic status.

(1) Reduced blood flow to the uterus and the intervillous space has been shown beyond doubt by several independent investigators and by widely different methods to occur in pre-eclampsia, and this correlates well with the increased incidence of small-for-dates infants. Failure of the mother's heart size to increase during pregnancy (as determined radiologically) has been found by some, but not by others to associate with small fetal size. The same occurs with maternal heart disease, acquired as well as congenital.

(2) Fetal growth decelerates normally before term, at a time depending on other factors to be mentioned below. As a rule, this is the case when fetal weight approaches 3 000 g. The same is true in multiple pregnancy when the combined fetal weights are considered. This cannot be placental insufficiency since twin placentas are, as far as we know, normal and even somewhat larger in relation to fetal weight than in singletons. Here, as well as in prolonged pregnancy when the supplies cannot keep pace with the demands of a very large fetus, maternal limitation must be considered.

(3) Various ill-defined conditions (as far as their mechanism of action is concerned), including nutritional state, altitude, socioeconomic status, etc., affect the fetus via the mother in two ways: during

the current pregnancy they produce a state of deficiency passed on to the fetus, but before this pregnancy they may have affected the mother in such a way that she cannot be an optimal provider for her fetus no matter how well she is taken care of at the moment. Improvement in socioeconomic status could thus have a rapid effect on fetal growth, and subsequently a slow one.

Returning now to 'placental insufficiency', it must be reiterated that only rare cases of primary insufficiency of the placenta are known, and in addition there are a moderate number of instances of secondary destruction of significant portions of the placenta by localized failure of maternal circulation. While it is possible that inability of the placenta to transmit specific substances may one day be found, it appears highly unlikely that true placental insufficiency will ever emerge as a significant factor in fetal deprivation, apart from the few examples already mentioned. This realization is of great medical importance. When we speak thoughtlessly of placental insufficiency, we imply that nothing can be done about it. If, on the other hand, we realize the pre-eminent role of the *maternal* organism, then we enter a wide field of study, treatment, and potential prevention which is worthy of a concerted effort.

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