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Birth weight symposium

Significance of birth weight for the future

C M Law

Correct size at birth is associated with health later in life

“How much did he/she weigh?” is often the first question proud parents are asked after they have announced the sex of their newly delivered progeny. A big baby, according to common knowledge, is a healthy baby. What evidence lies behind this popular assumption?

Paediatricians have long been familiar with the increased risk of mortality and early morbidity of babies born very small or very early. These babies have a greater risk of dying throughout the first year of life.¹ In addition, they are more likely to have a range of morbidities, particularly neurological, respiratory, and gastrointestinal.^{2,3}

In the last 20 years or so, there has been increasing evidence that size at birth is also associated with later health, particularly with the chronic degenerative diseases that are major causes of death in middle and later life. The best documented are the relations between smaller size at birth and higher death rates from coronary heart disease and stroke.⁴⁻⁷ Smaller size at birth is also related to increased levels of cardiovascular risk factors such as hypertension,⁸ type II diabetes mellitus,⁹ and hyperlipidaemia.¹⁰ However, high birth weight is also associated with long term health. People with high birth weight have higher death rates from prostate cancer¹¹ and possibly breast cancer.¹²

“In the last 20 years or so, there has been increasing evidence that size at birth is also associated with later health, particularly with the chronic degenerative diseases that are major causes of death in middle and later life.”

They may also be at risk of obesity¹³ and type II diabetes mellitus.^{14,15}

Although these associations, particularly those of reduced birth weight with increased cardiovascular risk, are now widely recognised, there remains a debate about what they indicate. The most important issue is whether the associations are causal or whether birth weight is simply an indicator of some other factor in prenatal or postnatal life that causes the associations. It seems unlikely that the associations arise simply because of confounding variables in adult life, as they are demonstrable in children (there are over 30 published studies showing an association between lower birth weight and higher childhood blood pressure, for instance) and persist when allowance is made for adult lifestyle factors such as smoking habit or levels of obesity.⁸ The failure to identify genes for

cardiovascular disease and the evidence against the control of fetal growth being primarily genetic argue against pure genetic causes.

PROGRAMMING HYPOTHESIS

The programming hypothesis is a plausible explanation of the associations of birth weight with adult health. Programming occurs when an event in a critical early period of an organism's life permanently changes structure or function, and is well described in experimental biology.¹⁶ Under a programming hypothesis, the fetus, which is highly plastic, adapts to adverse influences, such as undernutrition or hypoxia, in order to ensure its immediate survival. These adaptations are accompanied by reduced fetal growth. However, the adaptations may also lead to detrimental effects in postnatal health. For example, shunting of blood away from the fetal kidney in order to protect the fetal brain may result in a decreased number of nephrons and reduced renal reserve for postnatal challenges.¹⁷ Modification of the structure of the large conduit arteries in order to maintain fetal circulation may lead to blood vessels that are less compliant in adult life.¹⁸ In these scenarios, birth weight is an indicator of the prenatal cause, not the cause itself.

BIRTH WEIGHT AS AN INDICATOR OF RISK

Using birth weight as an indicator of risk at an individual level (for instance, to counsel the parents of a low birth weight baby) has three major problems. Firstly, risk of coronary heart disease, for example, is thought to be related to the extent of the reduction in fetal growth. However, we do not know how much a baby should have weighed, only what it actually weighs. A 3500 g baby who should have weighed 4000 g is just as growth retarded as a 2300 g baby who should

have weighed 2600 g. Furthermore a 3500 g baby may be perfectly grown, growth retarded, or even "overgrown", depending on its genetic potential. Secondly, the differences in risk factor levels between birth weight groups are relatively small—systolic blood pressure may be 1 or 2 mm Hg higher if birth weight is 500 g lower. However, whereas it may make little difference to an individual to reduce his or her blood pressure by such small amounts, if the population mean blood pressure decreased by about 6 mm Hg, then approximately 30% of all strokes would be prevented.¹⁹ Thirdly, parents tend to be interested in risk in terms of longevity or quality of life, whereas the research perspective (and therefore the available evidence) has usually been focused on the prediction of specific diseases or risk factors. This points to the need for "consumers" to be involved in all parts of the research process.^{20, 21}

"Promotion of infant growth and avoidance of childhood obesity are both goals with immediate as well as long term benefits and may be worth emphasising to parents."

Of particular interest to paediatricians are pathologically growth retarded babies. In theory, these infants may be at very high risk of cardiovascular disease in adult life. Currently, empirical evidence is lacking, as the subjects in most cohort studies of very low birthweight survivors have yet to reach adulthood and thus stable indicators of cardiovascular risk. In addition, some of these infants were also born prematurely. Although most studies have indicated that it is growth for gestational age rather than duration of gestation itself that is associated with adult health, few have had the statistical power to look at

the separate effects. In the single study that has, raised blood pressure was associated with both reduced growth for gestational age and reduced gestation. So the highest blood pressures were found in those who grew less well in utero and were delivered early. However, the ranges of gestation studied were only from 35 to 44 weeks.²² Thus the long term health risks of babies born very early or very small remain uncertain.

If part of the risk of adult disease is set before birth, what positive messages can paediatricians give to the parents of neonates who may be at high risk? Recent research has focused on the extent to which postnatal growth can modify or add to the risks established in utero. Both poor infant growth and excessive weight gain in childhood seem to be associated with increased cardiovascular risk.⁴ Promotion of infant growth and avoidance of childhood obesity are both goals with immediate as well as long term benefits and may be worth emphasising to parents.

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