Regular Review

Intrauterine growth retardation

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The recognition that some low birthweight babies (<2500 g) were the victims of intrauterine growth retardation rather than premature birth was a milestone in perinatal medicine.¹⁻³ Up to 10% of all liveborn babies and at least 30% of those of low birth weight suffer from intrauterine growth retardation; their perinatal mortality is four to 10 times higher than that of normally grown babies—both stillbirth and neonatal deaths contributing. Poor growth also exposes the fetus and the newborn to perinatal complications, which leave their scars in the form of later neurodevelopmental disability.⁴

No widely accepted, reliable definition of intrauterine growth retardation is applicable before birth. Instead, those babies who are small for dates—who weigh, for example, less than the 10th centile for their gestational age at birth—have, by inference, suffered intrauterine growth retardation. This approach may cause problems: the precise gestational age may be uncertain, especially in those pregnancies vulnerable to intrauterine growth retardation; the lower limit of normal birth weight for gestational age is variously defined as the 3rd, 5th, 10th, or 25th centile, or less than two standard deviations; intrauterine growth and normal standards of birth weight for gestational age are influenced by ethnic and geographical factors^{5,6}; small for dates babies may be the result of normal genetic constraint rather than pathological growth retardation; and, finally, birth weight is only one index of growth failure, and babies of “normal” weight may none the less have failed to achieve their genetic growth potential.

Causes and patterns of intrauterine growth retardation

The maximum velocity in linear growth occurs at about 20 weeks of gestation, and growth of body weight at about 34 weeks. Towards the end of pregnancy physical constraint within the uterus probably slows fetal growth. Intrauterine growth is partly under fetal control—with genetic⁶⁻⁸ and hormonal^{9,10} determinants—but it also depends on the supply and transfer of energy and nutrients across the placenta.¹¹ Growth retarded fetuses are, therefore, a heterogeneous group with respect to the nature, onset, and duration of the insult restricting growth.

Poor growth in the face of an optimal energy and nutritional supply is commonly the result of genetic factors; indeed, these account for familial smallness and for much of the variation in size at birth between different populations. About 5-15% of fetuses whose growth is retarded have malformations, including dysmorphic syndromes; chromosome abnormalities are observed at birth in 2%.^{12,13} Viral infections, the most common being with cytomegalovirus, probably

account for less than 3% of intrauterine growth retardation.^{14,15} These “intrinsic” causes usually result in symmetrical impairment of growth with reduced birth weight, length, and also head circumference—implying that brain growth is retarded.

Maternal disorders associated with an increased risk of intrauterine growth retardation include pre-eclampsia, recurrent antepartum haemorrhage, hypertension before pregnancy, renal disease, diabetes with microvascular change, sickle cell disease, cyanotic heart disease, malnutrition, and smoking. In the broadest sense they represent causes of impaired supplies of energy and nutrition to the fetus. In many of these conditions—but also in “idiopathic” intrauterine growth retardation, where no maternal risk factors are apparent (which accounts for about 30% of all cases)—uteroplacental vascular insufficiency is thought to play an important part. In contrast with those with symmetrical growth retardation affected fetuses tend to be long and thin (small ponderal index) with loss of subcutaneous fat and a large head. This asymmetrical growth retardation is widely believed to spare brain growth. Although the idea of brain sparing is probably an oversimplification,¹⁶ asymmetrical intrauterine growth retardation does imply a less severe or later onset restriction of growth perhaps confined to the third trimester.

Uteroplacental vascular insufficiency

The placenta is small in most examples of intrauterine growth retardation because it shares with the fetus the same influences limiting growth. The placenta has considerable reserves and may tolerate the loss of up to 30% of its villi without any obvious effect on fetal growth.¹⁷ Placental infarction is not an important cause of intrauterine growth retardation, and primary placental lesions—such as large haemangiomas or circumvallate placentation—probably account for less than 1% of intrauterine growth retardation.

Studies of placental isotope uptake^{18,19} and Doppler ultrasound investigations²⁰⁻²² of the uteroplacental vessels, umbilical vessels, and the descending fetal aorta suggest that in “idiopathic” intrauterine growth retardation and that associated with pre-eclampsia the maternal uteroplacental blood flow is reduced and the vascular resistance in the placental bed is increased. Histological changes may be seen in the spiral arteries within the placental bed in both these conditions,^{17,23} and in a recent morphometric study a reduced number of small arteries in the placental villi was associated with increased placental vascular resistance measured by Doppler ultrasound.²⁴

Investigations in animals have defined many factors which influence uteroplacental vascular reactivity, such as exercise, hyperthermia, oestrogen, prostaglandins, angiotensin, and noradrenaline, but little is known about the control of uteroplacental blood flow in man.²⁵⁻³⁰ In particular, the contribution of the maternal plasma volume needs clarifying. The expansion of the maternal plasma volume in pregnancy correlates positively with birth weight,³¹ and intrauterine growth retardation has been linked to poor expansion of plasma volume in hypertensive women.³² Either relative hypovolaemia compromises the uteroplacental flow or the poorly perfused placenta fails to provide the appropriate hormonal stimulus for hydraemia.

Maternal nutrition, smoking, and alcohol

In developing countries whose populations suffer from chronic dietary deficiency the incidence of low birth weight approaches 25%, and no fewer than 70% of those babies are full term and growth retarded.³³ The diet before conception, nutritional demands made by repeated pregnancies at short intervals, and diet during pregnancy all contribute to poor intrauterine growth. The dominant deficiency in the diet is usually the energy content, and supplementation during pregnancy may increase the mean birth weight by up to 300 g.³⁴ In preindustrialised, underprivileged communities, however, low birth weight at term is not always due to limited maternal energy reserves.³⁵

Severe malnutrition limited to the third trimester in a normally nourished population reduces the mean birth weight by about 200-400 g, as exemplified by the Dutch famine in 1944-5.³⁶ By contrast, in Gambia, when acute food shortage during the wet season was prevented by supplementation, the mean birth weight increased and the incidence of low birthweight babies was reduced from 28% to 5%.³⁷ Maternal dietary deficiency is not an important cause of intrauterine growth retardation in developed countries, but surprisingly little is known about the influence on fetal growth and development of eating habits in deprived mothers from inner city areas in Britain.

Smoking retards growth mainly during the third trimester; this effect is independent of dietary intake and is observed in privileged women³⁸ as well as those who are socioeconomically deprived. The mechanisms proposed include acute³⁹ and chronic⁴⁰ impairment of placental perfusion and increased concentrations of carboxyhaemoglobin in the fetus.⁴¹

A clear association has been shown between heavy consumption of alcohol throughout pregnancy (more than 30 ml absolute alcohol daily) and intrauterine growth retardation, irrespective of the occurrence of the fetal alcohol syndrome^{42,43} and even when allowance is made for confounding variables, such as smoking and nutrition. Heavy drinkers at the start of pregnancy who abstain before the third trimester have normal sized babies, and occasional social drinking does not cause small for dates babies.⁴³ On the other hand, the birth weight of babies born to alcoholic mothers who abstained during pregnancy has been reported as low, implying that more than one mechanism is responsible for the growth retarding effect of alcohol.⁴⁴

Diagnosis and management

Aside from specific maternal medical conditions the risk factors associated with an increased incidence of intrauterine

growth retardation include a history of intrauterine growth retardation, low weight before pregnancy, low weight gain during pregnancy, multiple pregnancy, and smoking. About 30-50% of growth retarded fetuses remain undetected by clinical examination. Abdominal palpation is notoriously unreliable for the assessment of fetal weight, and serial examinations carried out at, say, weekly intervals will detect only the most severe examples of growth retardation.

Serial plotting of the symphysis-fundus height is a useful screening test for intrauterine growth retardation according to some observers,⁴⁵⁻⁴⁷ but not everyone agrees.^{48,49} It is certainly of little value in multiple pregnancy, polyhydramnios, transverse lie, or extreme maternal adiposity. The enthusiasm and experience of the midwife or obstetrician probably influence its reliability, and results from Sweden, where the method is used routinely in most antenatal clinics, are better than elsewhere. In a recent prospective study using symphysis-fundus growth curves almost 80% of small for dates infants were detected with a 92% specificity.⁵⁰ The use of fundal height measurements as a simple way of screening for intrauterine growth retardation in community based antenatal clinics needs examining further.⁵¹

Assays of maternal hormones such as urine or plasma oestriol and of placental lactogen have been used less widely for the diagnosis of intrauterine growth retardation since ultrasonography became available. Factors other than intrauterine growth retardation may lower oestriol production, and in general considerable overlaps are seen in hormone concentrations in growth retarded and normal fetuses.⁵² It has been claimed, however, that small but normal fetuses may be reliably distinguished from those with true growth retardation by measurement of maternal serum concentrations of placental lactogen and Schwangerschaft's protein 1.⁵³

Ultrasound measurements are used singly or in formulations to monitor fetal growth or to predict fetal weight.⁵⁴⁻⁵⁶ Measurement of the biparietal diameter identifies only 50-60% of growth retarded fetuses, while over half of those suspected of being growth retarded prove to be normally grown at birth. Limitations arise because of variations in the shape of the head (from fetal position and compression) and because the size of the head is spared or compromised only late in asymmetrical intrauterine growth retardation. Measurements of the head circumference are less dependent on its shape. The small liver and paucity of subcutaneous fat in the abdominal wall of the fetus whose growth is retarded may be assessed by measuring the trunk or abdominal circumference alone or the head circumference to abdominal circumference ratio; these are better predictors of intrauterine growth retardation than biparietal diameter. Other ultrasound indices used include computations based on trunk area, crown-rump length, and femur length⁵⁷⁻⁵⁹; intrauterine volume⁶⁰; qualitative assessment of oligohydramnios⁶¹; and the echogenicity of placental tissue.⁶²

Assessment of fetal health

The leading cause of stillbirth in non-malformed growth retarded fetuses is intrauterine asphyxia. Not only is placental gaseous exchange compromised but the growth retarded fetus has low reserves of cardiac glycogen, and this makes him intolerant to asphyxia compared with his normally grown counterpart. A growth retarded fetus living on the brink of asphyxia is at special risk during labour, when uteroplacental flow is further restricted. Clearly the control of hypertension and other maternal complications is

important; indeed, prompt delivery may be necessary to protect maternal health. It remains to be proved whether there are practical benefits from enhancing fetal nutrition by amniotic supplementation and from improving uteroplacental flow by bed rest, abdominal decompression, and the use of β sympathomimetics.

The real issue for the obstetrician and paediatrician is to know whether—and, more important, when—to release the fetus from the womb—a procedure which will inevitably expose him to the potential neonatal hazards of prematurity. Although small for dates preterm babies have a lower incidence of hyaline membrane disease than normally grown babies of the same gestational age,⁶³ that should not lead to complacency when elective preterm delivery is contemplated. Even if accelerated surfactant maturation with a negligible risk of hyaline membrane disease is confirmed by prior measurement of the amniotic fluid phospholipids threats are posed by other complications of prematurity such as recurrent apnoea, periventricular brain ischaemia and haemorrhage, necrotising enterocolitis, and sepsis—especially in fetuses of less than 34 weeks' gestation.

Assay of maternal hormone products which reflect placental function is not a reliable basis for judging the timing of elective preterm birth. In chronic asphyxia the transient accelerations in the fetal heart rate usually seen in response to spontaneous fetal movements—biophysical coupling—are absent; this is the basis of the “non-stress test,” in which the fetal heart rate and movements are recorded from the maternal abdominal wall. Periodic changes in the fetal heart rate, particularly late decelerations, in response to induced or spontaneous uterine contractions are other features of chronic asphyxia which form the basis of the “contraction stress test.” Diminished fetal activity may be assessed at home by the mother counting the number of fetal movements over a period of time. Though there is a broad correlation between adverse results of each of these tests and poor fetal outcome, false positive and false negative indications are so common that reliance on a single method of assessment is unhelpful in predicting the need for and, more important, the timing of elective preterm delivery.

One promising development is the use of combined tests to improve diagnostic accuracy—the biophysical profile.^{64 65} Cardiac reactivity, posture, limb movements, and fetal “breathing” movements are evaluated by ultrasound during a single examination together with qualitative assessment of amniotic fluid volume, a reflection of fetal urinary output. Uteroplacental flow measurements might prove to be a useful addition to biophysical assessment.^{66 67}

The choice between elective caesarean section and induction of labour depends on individual circumstances, particularly the past obstetric history and the state of the cervix. Fetuses that have scored badly on antepartum surveillance tests might none the less tolerate labour, provided that intrapartum monitoring is carefully carried out so that delivery can be expedited should that prove necessary.

Neonatal complications and later development

Severe malformations and chromosome defects (often lethal) obviously influence the neonatal course, and some affected babies die soon after birth. Aside from that, the severity and duration of perinatal asphyxia are the main determinants of the baby's condition at birth. Some babies who require resuscitation have a continuing need for ventilatory support because of persistent pulmonary hypertension

or the meconium aspiration syndrome—a disorder associated with meconium plugging of the small airways, air trapping, and pneumothoraces. Other problems which are more common in severely growth retarded babies and are attributable to, or aggravated by, asphyxia include massive pulmonary haemorrhage, hypothermia, polycythaemia (the hyperviscosity syndrome), hypoglycaemia, and hypocalcaemia.

Fetuses with third trimester, asymmetrical growth retardation associated with uteroplacental vascular insufficiency commonly “catch up” in growth by late infancy or early childhood, but this effect is less likely in symmetrically growth retarded babies with an “intrinsic” cause or those with prolonged, severe intrauterine growth retardation. The most important adverse influences on neurodevelopmental outcome in individual babies are malformations (especially chromosome abnormalities and dysmorphic syndromes), low gestational age, and perinatal complications. Probably beyond infancy parental socioeconomic state and education play an increasing part in determining intellectual outcome.^{68 69}

As a group, growth retarded babies who are born at term have only a slightly increased risk of major handicap such as cerebral palsy and mental retardation. Between 10% and 35% of them, however, have minimal cerebral dysfunction in the form of problems with speech and language, attention deficits, learning problems, and minor neurological problems.⁷⁰⁻⁷² Similar abnormalities were recently described in a group of 12-14 year old children in whom intrauterine growth retardation had been diagnosed at birth on the basis of scant subcutaneous fat rather than low birth weight.⁷³

Sharper antepartum surveillance has led to a change in the type of small for dates baby presented to the paediatrician. Badly asphyxiated, severely growth retarded babies born at or past term are now less common. Instead, there is a rising population of preterm babies born electively because of intrauterine growth retardation, particularly in those hospitals where neonatal intensive care facilities are available. At any given birth weight neonatal mortality rises with decreasing gestational age, but we know little about the precise influence of growth retardation on discrete neonatal disorders such as brain haemorrhage and ischaemia, to which preterm babies are prone. Certainly below 34 weeks' gestation it is preterm birth that has a dominant influence on neonatal morbidity rather than any associated intrauterine growth retardation, unless the growth failure is very severe. The reported incidence of major handicap, including cerebral palsy, in preterm small for dates babies followed up for at least two years is much higher than in their term counterparts and ranges from 10% to nearly 50%. Here again it is the degree of prematurity that strongly influences outcome.⁷⁴⁻⁷⁶ Although published data are contradictory, intrauterine growth retardation seems unlikely to pose any substantial additional threat to the neurodevelopmental outcome of preterm babies unless it is associated, firstly, with chromosome abnormalities or dysmorphic syndromes; or, secondly, with perinatal complications related to intrauterine growth retardation, such as severe asphyxia, symptomatic hypoglycaemia, and hyperviscosity syndrome; or, finally, unless the growth retardation is extremely severe.⁷⁴⁻⁷⁷

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- 1 World Health Organisation. *Public health aspects of low birthweight*. Geneva: World Health Organisation, 1961. (Technical Report Series, No 217.)
- 2 Warkany J, Monroe BB, Sutherland BS. Intrauterine growth retardation. *Am J Dis Child* 1961;102:249-79.
- 3 Gruenewald P. Chronic fetal distress and placental insufficiency. *Biol Neonat* 1963;5:215-65.
- 4 Allen MC. Developmental outcome and follow up of the small for gestational age infant. *Semin Perinatol* 1984;8:123-56.
- 5 Simmons K, Savage W, Nicholls B, Rao U. Fetal growth measured by ultrasound in Bengali women. *Journal of Obstetrics and Gynaecology* 1985;5:233-6.
- 6 Ounsted M, Ounsted C. On fetal growth rate. *Clinics in developmental medicine*. No 46. London: William Heinemann, 1973:18-26.
- 7 Polani PE. Chromosomal and other genetic influences on birthweight variation. In: Elliot K, Knight J, eds. *Size at birth*. Amsterdam: Excerpta Medica, 1974:127-64. (Ciba Foundation Symposium 27.)
- 8 Jones OW. Genetic factors in the determination of fetal size. *J Reprod Med* 1978;21:305-13.
- 9 Gluckman PD, Liggins GC. Regulation of fetal growth. In: Beard RW, Nathanielsz PW, eds. *Fetal physiology and medicine*. New York: Marcel Dekker, 1984.
- 10 Hill DJ, Milner RDG. The role of peptide growth factors and hormones in the control of fetal growth. In: Chiswick ML, ed. *Recent advances in perinatal medicine*. No 2. Edinburgh: Churchill Livingstone (in press).
- 11 Battaglia FC, Hay WW. Energy and substrate requirements for fetal and placental growth and metabolism. In: Beard RW, Nathanielsz PW, eds. *Fetal physiology and medicine*. New York: Marcel Dekker, 1984.
- 12 Chen AT, Falek A. Chromosome aberrations in full-term low birthweight neonates. *Hum Genet* 1974;21:13-6.
- 13 Anderson NG. A five year survey of small for dates infants for chromosome abnormalities. *Aust Paediatr J* 1976;12:19-23.
- 14 Andreasson B, Svenningsen NW, Nordenfelt E. Screening for viral infections in infants with poor intrauterine growth. *Acta Paediatr Scand* 1981;70:673-6.
- 15 Primhac RA, Simpson RM. Screening small for gestational age babies for congenital infection. *Clin Pediatr* 1982;21:417-20.
- 16 Brooke OG, Wood C, Butters F. The body proportions for small-for-dates infants. *Early Hum Dev* 1984;10:85-94.
- 17 Fox H. The role of the placenta in perinatal mortality. In: Milunsky A, Friedman EA, Gluck L, eds. *Advances in perinatal medicine*. Vol 2. New York: Plenum Medical Book Company, 1982:203.
- 18 Lunell NO, Sarby B, Lewander R, et al. Comparison of uteroplacental blood flow in normal and in intrauterine growth-retarded pregnancy. *Gynecol Obstet Invest* 1979;10:106-18.
- 19 Nyhult L, Lunell NO, Lewander R, Sarby B. Uteroplacental blood flow index in intrauterine growth retardation of fetal or maternal origin. *Br J Obstet Gynaecol* 1983;90:16-20.
- 20 Trudinger BJ, Giles WB, Cook CM. Uteroplacental blood flow velocity-time waveforms in normal and complicated pregnancy. *Br J Obstet Gynaecol* 1985;92:39-45.
- 21 Trudinger BJ, Giles WB, Cook CM, Bombardieri J, Collins L. Fetal umbilical artery flow velocity waveforms and placental resistance: clinical significance. *Br J Obstet Gynaecol* 1985;92:23-30.
- 22 Rasmussen K, Thorup E, Eriksen PS. Evaluation of the fetal circulation using Doppler ultrasound method in patients with pre-eclampsia and intrauterine growth retardation. *J Perinat Med* 1984;12:257-9.
- 23 Hustin J, Foidart JM, Lambotte R. Maternal vascular lesions in pre-eclampsia and intrauterine growth retardation: light microscopy and immunofluorescence. *Placenta* 1983;4:489-98.
- 24 Giles WB, Trudinger BJ, Baird PJ. Fetal umbilical artery flow velocity waveforms and placental resistance: pathological correlation. *Br J Obstet Gynaecol* 1985;92:31-8.
- 25 Rosenfeld CR. Consideration of the uteroplacental circulation in intrauterine growth. *Semin Perinatol* 1984;8:42-51.
- 26 Clapp JF. Acute exercise stress in the pregnant ewe. *Am J Obstet Gynecol* 1980;136:489-94.
- 27 Oakes GK, Walker AM, Ehrenkranz RA, et al. Uteroplacental blood flow during hyperthermia with and without respiratory alkalosis. *J Appl Physiol* 1976;41:197-201.
- 28 Rosenfeld CR, Morris FM Jr, Battaglia FC, et al. Effect of estradiol-17 β on blood flow to reproductive and nonreproductive tissues in pregnant ewes. *Am J Obstet Gynecol* 1976;124:618-29.
- 29 Parisi VM, Rankin JHG. The effect of prostacyclin on angiotensin II-induced placental vasoconstriction. *Am J Obstet Gynecol* 1985;151:444-9.
- 30 Rosenfeld CR, West J. Circulatory response to systemic infusion of norepinephrine in the pregnant ewe. *Am J Obstet Gynecol* 1977;127:376-83.
- 31 Hytten FE, Paintin DB. Increase in plasma volume during normal pregnancy. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1963;70:402-7.
- 32 Arias F. Expansion of intravascular volume and fetal outcome in patients with chronic hypertension and pregnancy. *Am J Obstet Gynecol* 1975;123:610-6.
- 33 Villar J, Belizan JM. Relative contribution of prematurity and fetal growth retardation to low birthweight in developing and developed societies. *Am J Obstet Gynecol* 1982;143:793-8.
- 34 Lechtig A, Klein RE. Pre-natal nutrition and birthweight: is there a causal association? In: Dobbing J, ed. *Maternal nutrition in pregnancy—eating for two?* London: Academic Press, 1981:131-56.
- 35 Briend A. Do maternal energy reserves limit fetal growth? *Lancet* 1985;i:38-40.
- 36 Stein Z, Susser M. The Dutch famine, 1944/45 and the reproductive process. I: effects on six indices at birth. *Pediatr Res* 1975;9:70-6.
- 37 Prentice AM, Whitehead RG, Watkinson M, Lamb WH, Cole TJ. Prenatal dietary supplementation of African women and birthweight. *Lancet* 1983;i:489-91.
- 38 Ounsted M, Moar VA, Scott A. Risk factors associated with small-for-dates and large for dates infants. *Br J Obstet Gynaecol* 1985;92:226-32.
- 39 Lehtovirta P, Fors M. The acute effect of smoking on intervillous blood flow of the placenta. *Br J Obstet Gynaecol* 1978;85:729-31.
- 40 Anderson KV, Hermann N. Placental flow reduction in pregnant smokers. *Acta Obstet Gynecol Scand* 1984;63:707-9.
- 41 Cole PV, Hawkins LH, Roberts D. Smoking during pregnancy and its effect on the fetus. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1972;79:782-7.
- 42 Ouellette EM, Rosett HL, Rosman NP, et al. The adverse effects of maternal alcohol abuse during pregnancy on offspring. *N Engl J Med* 1977;297:528-30.
- 43 Rosett HL, Weiner L, Lee A, et al. Patterns of alcohol consumption and fetal development. *Obstet Gynecol* 1983;61:539-46.
- 44 Little RE, Streissguth AP, Barr HM, et al. Decreased birthweight in infants of alcoholic women who abstained during pregnancy. *J Pediatr* 1980;96:974-7.
- 45 Belizan JM, Villar J, Nardin JC, Malamud J, de Vicuna LS. Diagnosis of intrauterine growth retardation by a simple clinical method: measurement of uterine height. *Am J Obstet Gynecol* 1978;131:643-6.
- 46 Calvert JP, Crean EE, Newcombe RG, Pearson JF. Antenatal screening by measurement of symphysis-fundus height. *Br Med J* 1982;285:846-9.
- 47 Wallin A, Gyllensward A, Westin B. Symphysis-fundus measurements in prediction of fetal growth disturbances. *Acta Obstet Gynecol Scand* 1981;60:317-23.
- 48 Beazley JM, Underhill RA. Fallacy of the fundal height. *Br Med J* 1970;iv:404-6.
- 49 Rosenberg K, Grant JM, Tweedie I, Aitchison T, Gallagher F. Measurement of fundal height as a screening test for fetal growth retardation. *Br J Obstet Gynaecol* 1982;89:447-50.
- 50 Cnattingius S, Axelsson O, Lindmark G. Symphysis-fundus measurements and intrauterine growth retardation. *Acta Obstet Gynecol Scand* 1984;63:335-40.
- 51 Draper J, Field S, Thomas HA, Hare MJ. Screening for small for date fetuses. *Br Med J* 1985;290:777.
- 52 Creasy RK, Resnik R. Intrauterine fetal growth retardation. In: Milunsky A, Friedman EA, Gluck L, eds. *Advances in perinatal medicine*. Vol 1. New York: Plenum Medical Book Company, 1981:138-9.
- 53 Westergaard JG, Teisner B, Hau J, Grudzinskas JG, Chard T. Placental function studies in low birth weight infants with and without dysmaturity. *Obstet Gynecol* 1985;65:316-8.
- 54 Sabbagha RE, Tamura RK. Diagnosis of fetal abnormality by ultrasound. In: Chiswick ML, ed. *Recent advances in perinatal medicine*. No 1. Edinburgh: Churchill Livingstone, 1983:57-64.
- 55 Hadlock FP, Deter RL, Harrist RB. Sonographic detection of abnormal fetal growth patterns. *Clin Obstet Gynaecol* 1984;27:342-51.
- 56 Seeds JW. Impaired fetal growth. *Obstet Gynecol* 1984;64:577-84.
- 57 Neilson JP, Munjanja SP, Whitfield CR. Screening for small for dates fetuses: a controlled trial. *Br Med J* 1984;289:1179-82.
- 58 Tahilramaney MP, Platt LD, Yeh S-Y. Ultrasonic estimation of weight in the very low-birth weight fetus: a resident versus staff physician comparison. *Am J Obstet Gynecol* 1985;151:90-1.
- 59 Ott WJ. Fetal femur length, neonatal crown-heel length, and screening for intrauterine growth retardation. *Obstet Gynecol* 1985;65:460-4.
- 60 Levine SC, Filly RA, Creasy RK. Identification of fetal growth retardation by ultrasonic estimation of total intrauterine volume. *JCU* 1979;7:21-6.
- 61 Manning FA, Hill LM, Platt LD. Qualitative amniotic fluid volume determination by ultrasound—antepartum detection of intrauterine growth retardation. *Am J Obstet Gynecol* 1981;139:254-8.
- 62 Kazzi GM, Gross TL, Sokol RJ, Kazzi NJ. Detection of intrauterine growth retardation—a new use for sonographic placental grading. *Am J Obstet Gynecol* 1983;145:733-7.
- 63 Procianny RS, Garcia-Prats JA, Adams JM, et al. Hyaline membrane disease and intraventricular haemorrhage in small for gestational age infants. *Arch Dis Child* 1980;55:502-5.
- 64 Manning FA, Platt LD, Sipes L. Antepartum fetal evaluation: development of a fetal biophysical profile score. *Am J Obstet Gynecol* 1980;6:787-95.
- 65 Vintzileos AM, Campbell WA, Ingardia CJ, Nochimson DJ. The fetal biophysical profile and its predictive value. *Obstet Gynecol* 1983;62:271-8.
- 66 Griffin B, Bilardo K, Masini L, et al. Doppler blood flow waveforms in the descending thoracic aorta of the human fetus. *Br J Obstet Gynaecol* 1984;91:997-1006.
- 67 Campbell S, Hernandez CJ, Cohen-Overbeck TA, Pearce JMF. Assessment of fetoplacental and uteroplacental blood flow using duplex pulsed Doppler ultrasound in complicated pregnancies. *J Perinat Med* 1984;12:262-5.
- 68 Eaves LC, Nuttall JC, Klonoff H, et al. Development and psychological test scores in children of low birth weight. *Pediatrics* 1970;45:9-20.
- 69 Parkinson SE, Wallis S, Harvey D, et al. School achievement and behaviour of children who were small-for-dates at birth. *Dev Med Child Neurol* 1981;23:41-50.
- 70 Fitzhardinge PM, Steven EM. The small-for-date infant. II. Neurological and intellectual sequelae. *Pediatrics* 1972;50:50-7.
- 71 Neligan GA, Kolvin I, Scott DM, Garside RF, eds. *Born too soon or born too small. A follow up study to seven years of age*. Philadelphia: Lippincott, 1976. (Clinics in Developmental Medicine, No 61.)
- 72 Rubin RA, Rosenblatt C, Balow B. Psychological and educational sequelae of prematurity. *Pediatrics* 1973;52:352-63.
- 73 Hill RM, Verniaud WM, Deter RL, et al. The effect of intrauterine malnutrition on the term infant. A 14-year progressive study. *Acta Paediatr Scand* 1984;73:482-7.
- 74 Vohr BR, Oh W, Rosenfield AG, et al. The preterm small-for-gestational age infant: a two-year follow-up study. *Am J Obstet Gynecol* 1979;133:425-31.
- 75 Comney JO, Fitzhardinge PM. Handicap in the preterm small-for-gestational age infant. *J Pediatr* 1979;94:779-86.
- 76 Hack M, Fanaroff AA, Merkatz IR. The low-birthweight infant. Evolution of a changing outlook. *N Engl J Med* 1979;301:1162-5.
- 77 Hagberg B. Epidemiological and preventative aspects of cerebral palsy and severe mental retardation in Sweden. *Eur J Pediatr* 1979;130:71-8.