out of control. Breathlessness, coughing, and wheezing are difficult to quantify, and with poor lighting a considerable degree of cyanosis may be missed. Guidelines should instead be based on response to treatment, instructing the parents to seek immediate medical advice if the child fails to obtain satisfactory relief from his beta-2-stimulant treatment, or even if the response to treatment falls off after one or two hours. These recommendations are particularly important if the child has a nebuliser at home or is taking regular systemic steroids, as response to any additional treatment is likely to be slow.

Some children have asthma which is particularly difficult to categorise. The parents may complain bitterly about the child's symptoms which are apparently totally isolating him from his friends and preventing him from attending school, yet on assessment in the clinic he looks remarkably well and has an entirely normal peak flow. A careful history and measurement of peak flow twice daily at home over one to two weeks may show that the child's asthma is, in fact, relatively mild, suggesting other parental anxieties in the home which may need sorting out.

At the other end of the spectrum are the more worrying children who complain little, cope well with school and often games, and yet on examination are obviously undersized with hyperinflated chests—but often with little abnormal heard on auscultation. Their peak flows, however, are strikingly reduced, often to less than one-third of expected. Response to inhaled beta-2-stimulants is usually poor. These children need careful evaluation since they are chronically hypoxic and have very little respiratory reserve. They are particularly likely to die in the night if a further severe attack is superimposed on their chronic state.¹¹ Virtually normal lung function can usually be achieved by giving them a 14-21-day course of prednisolone using 1-2 mg/kg a day.¹² This will confirm the diagnosis of asthma and also reset the child's expectation of life. It will also allow the doctor to reconsider his therapeutic attack.

Undoubtedly the number of deaths from asthma in childhood may be reduced provided the severity of the disease is assessed correctly and appropriate treatment given. A few children, sadly, will die whatever action we take. An example of this is provided by a Nottingham girl who wheezed intermittently up to the age of 12 and was then entirely asymptomatic until the age of 17. Wheezing began again at three o'clock one morning; by 4.30 am she was dead.

A D MILNER

Professor of Paediatric Respiratory Medicine,
University Hospital,
Nottingham NG7 2UH

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Causes of intrauterine growth retardation

When a baby is small for gestational age at birth, a specific cause for the failure of growth can be identified in only a minority of cases. If the baby has a congenital abnormality,¹ or a viral infection such as rubella² or cytomegalovirus,³ these may be recognised as specific causes. In most such cases, however, no single cause can be identified and the failure of growth is due to a number of factors, each making its contribution to the end result. Physiological factors influence fetal growth, and normal genetic influences contribute to birth weight variation.⁴ Boys are bigger than girls, first-born infants are smaller than later born,⁵ and mean birth weights vary among different races. What is important is that every baby should achieve its own optimal potential for intrauterine growth and development.

Because intrauterine growth retardation is a syndrome of starvation and is commoner in lower social-class groups,⁶ maternal malnutrition is often assumed to be an important cause of small size for gestational age. The evidence to support this, however, is unconvincing. Though babies born in Holland under severe famine conditions between 1944 and 1945 were 300-400 g below expected birth weight, the reduction in birth weight was not apparent until maternal food intake fell below 6.3 MJ (1500 kcal) a day. Once energy intakes fell below the threshold level to maintain birth weight the reduction in fetal length was less than the reduction in fetal weight, and the subsequent development of the babies was normal.⁷ This suggested that, though subcutaneous fat was reduced, the development of vital organs had been normal. There have been several trials to investigate the value of prenatal dietary supplements and, though their study designs have been criticised, their results have consistently shown that dietary supplements have only a trivial effect on birth weight.⁸ Indeed, high protein diets may reduce birth weight, possibly by reducing the maternal intake of fat and carbohydrate.⁹ On the other hand, mothers of short stature or low weight before pregnancy, who may have chronic suboptimal nutrition, have an increased risk of a baby small for gestational age.⁶ Possibly to be effective dietary supplementation would be required for months, or even years, before the pregnancy was started.

The ability of the mother to transfer nutrients across the placenta is as important as the concentration of the nutrients in the maternal circulation.¹⁰ Anatomical abnormalities of the placenta are often found in association with small-for-gestational-age pregnancies, but, apart from conditions such as extrachorial placenta or rare vascular tumours, the placental changes are usually secondary to defective uteroplacental blood flow.¹¹ In small-for-gestational-age pregnancies associated with proteinuric pre-eclampsia the uteroplacental vessels are occluded by thrombotic and atheromatous lesions.¹² Similarly,

maternal renal disease, essential hypertension, diabetes, and collagen vascular disease are all causes of fetal growth retardation,¹ and Dawes attributed 35% of growth-retarded pregnancies to maternal vascular disease.¹³ There is increasing agreement that abnormal maternal vasculature is the most important common denominator in intrauterine growth retardation. There is less agreement, however, about the role of vascular disease in growth-retarded pregnancies which occur in the absence of maternal hypertension. Sheppard and Bonnar¹² reported uteroplacental vascular lesions in idiopathic growth retardation similar to those found in pre-eclampsia, but this association was not confirmed by Brosens and his colleagues.¹⁴ Improvements in ultrasound hold out the promise of non-invasive methods of measuring uterine blood flow during pregnancy, and these could greatly add to our understanding of how vascular factors influence birth weight.

Scott *et al*¹⁵ have attempted to measure the relative contributions of different maternal factors to small-for-gestational-age pregnancies and found smoking to be the second most important after hypertension. In their population of Oxford mothers they calculated that if smoking was stopped completely, the number of affected pregnancies would fall by 39%. Those mothers who give up smoking during pregnancy in order to improve their babies' health must receive every encouragement. Cigarette smoke may not be the only noxious factor to influence birth weight; probably both alcohol and drug abuse are also causes of growth-retarded pregnancies.¹

Progress has been slow in the obstetric management of these pregnancies. The diagnosis is difficult,¹⁶ and few therapeutic options are open to the obstetrician. We do not know whether a growth-retarded baby is better remaining in utero for as long as possible or being delivered prematurely for better nourishment in the neonatal unit. An ideal method of treatment would be one which improved intrauterine growth, allowing the pregnancy to continue to term without detriment to the fetus. Progress towards this objective will not be achieved unless methods are developed which will allow the obstetrician to diagnose intrauterine growth retardation at an early stage. Once the underlying pathological processes are well established therapeutic interventions are doomed to failure.

PETER W HOWIE

Professor of Obstetrics and Gynaecology,
Ninewells Hospital and Medical School,
Dundee DD1 9SY

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Osteomalacia in chronic liver disease

For 50 years now, patients with chronic liver disease have been recognised to have bone disorders.¹ Crush fractures of the vertebrae, presenting with pain in the back, are usually due to osteoporosis²⁻⁴ (pathological decrease in the amount of histologically normal bone). Our understanding of this important—and still unsolved—problem may hardly be said to have advanced since the earliest reports. On the other hand, osteomalacia (defective calcification of bone matrix, recognised by diminished calcification fronts histologically) often has more subtle presentations such as diffuse pains and myopathy, and here real advances have been made in recent years.

Osteomalacia was shown to occur in prolonged cholestatic liver disease a quarter of a century ago,⁵ and primary biliary cirrhosis has been the classic example. Osteomalacia may also be seen, however, in patients with other forms of chronic liver disease having prolonged cholestatic features—for example, some patients with chronic active hepatitis,^{6,7} cryptogenic cirrhosis, or alcoholic liver disease.^{6,8}

Advances in our understanding of vitamin D metabolism have brought renewed interest in the osteomalacia associated with chronic liver disease, but at the same time the picture has been confused by the results of research on three aspects. Firstly, one study showed no relation between low plasma concentrations of 25-hydroxy vitamin D (the storage form of the vitamin) and osteomalacia⁸; secondly, osteomalacia was reported in patients taking prophylactic vitamin D supplements⁸⁻¹¹; and, thirdly, vitamin D₂ was reportedly ineffective in patients with liver disease.^{12,13} These findings have been interpreted as showing resistance to vitamin D, and more particularly to vitamin D₂ compounds,^{8,9} either by defective metabolism or by defective responses in the gut or in the bones. One other possibility is that the osteomalacia may have been unrelated to vitamin D.

Vitamin D has to be hydroxylated for its action, and since one of the hydroxylation steps is performed by the liver, an explanation for the osteomalacia of liver disease might be a defect in this step.^{12,13} This attractive possibility has now been effectively disproved.¹⁴ Recent work^{6,15} suggests that the osteomalacia is clearly related to low plasma concentrations of 25-hydroxy vitamin D, and thus defective intake, impaired absorption, or excessive loss must be implicated. Malabsorption of fat and fat-soluble vitamins occurs in liver disease owing to low