Bronchiectasis, congenital and acquired

Bronchiectasis seems less common in Britain today than 20 years ago—though we have no reliable statistics. Nevertheless, it still occurs often enough for chest physicians to see several new cases each year, and, as whooping cough and tuberculosis have become less frequent, other diseases are being recognised increasingly as playing a part in its cause.

Classically in bronchiectasis there is persistent production of purulent sputum and occasional haemoptysis, usually starting in childhood and preceded by severe pneumonia, whooping cough, or measles. Less commonly, no such initial illness can be implicated, and the disease is thought to be congenital. Pathologists can differentiate the postinfective type, when there is chronic inflammation with some destruction of acinar as well as of bronchial structures, from the congenital one, when in addition to dilatation of the bronchi the acini are maldeveloped.[1] To the clinician, however, the distinction is difficult and unimportant; his task is to recognise the functional effects and to plan treatment.

Two clinical varieties of bronchiectasis are seen frequently in adults. Firstly, that developing after postprimary tuberculosis affects one or both upper lobes. The second type, either congenital or secondary to respiratory infections, affects the lower zones predominantly. The former usually causes no symptoms, though it is often associated with symptoms due to other effects of the tuberculosis. Bronchiectasis affecting the lower zones is the type associated typically with retention of purulent sputum, recurrent infection, and persistent cough. Either variety may cause haemoptysis, occasionally severe, the bleeding being derived from the bronchial arteries which supply the diseased airways. Though bronchiectasis of all types is usually confined to only one or two lobes, it is often associated with generalised airways obstruction. This may sometimes respond to bronchodilators,[2] but pathological changes of chronic bronchitis are commonly found in the airways unaffected by the bronchiectasis. Whether this associated disease is due to the recurrent infections which these patients have or is a less severe effect of the primary disease is not clear, but airways obstruction is important in limiting the applicability and efficacy of surgery.

Fortunately, most patients with bronchiectasis respond satisfactorily to postural drainage and antibiotics early in an infective exacerbation, and surgery needs to be considered only when medical treatment fails to control the production of purulent sputum, or when recurrent haemoptysis presents a risk to life.[3 4] Since most patients have either generalised airways obstruction or bronchiectasis too extensive for resection, surgery is used infrequently in Britain today.

Whatever its cause (be it secondary to childhood infection; bronchial block by tumour, caseous material, or foreign body; cystic fibrosis; or, in proximal bronchi, allergic aspergillosis) the sequence of events leading to acquired bronchiectasis is probably much the same. Blockage in one large or many small airways, together with distal infection, damages the bronchial walls; this weakens their resistance to the tractive force of negative pleural pressure and lung elasticity.[5] Most cases of congenital bronchiectasis are associated with maldevelopment of acini, and again this increases the tractive forces on the bronchi to that region. Recurrent infection—resulting from poor ventilation and clearance of the blind airways—is also presumably important.

In a few patients with congenital bronchiectasis associated with hereditary disease the pathological changes are more like those of the postinfective lesions. The best-known example is Kartagener's syndrome, an association of bronchiectasis, sinusitis, and transposition of the viscera, inherited as an autosomal recessive.[6] Affected men are often infertile, with immobile tails to their spermatozoa. This paralysis is accounted for by absent dynein arms in cross-sections of the tails viewed by the electron microscope.[7] Cilia have the same ultrastructure as spermatozoal tails, and show the same defect, thus explaining these patients' inability to transport bronchial secretions.[8 9] Subsequently another hereditary defect of cilial ultrastructure, lack of radial spokes, has been described in a family with chronic respiratory disease, one member of which also had transposition of the viscera.[10] Such hereditary abnormalities of the cilia are clearly rare, and only occasionally do they cause bronchiectasis. They do, however, explain very nicely the mystery of the associations found in Kartagener's syndrome: the motility of spermatozoa, clearance of bronchial secretions, and rotation of the gut in the fetus all depend on normal function of the cilia.

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Radiation and the embryo

Doctors are well aware that experts may disagree; but they have been slow to appreciate that experts can change their minds. For 40 years or more we have been told that radiographs of the developing embryo should be confined to those that are absolutely essential because of the possible harm they may cause. Strictures on irradiation of the fetus have been placed upon us by national and international bodies and their codes of practice on the grounds that radiation may cause death of the fetus in the early embryonic stage, or the development of a malformed child, or leukaemia or other neoplasia later in childhood.

The hazards of radiography during pregnancy have recently been reviewed by Mole.[1] His extensive and careful analysis of the data available has led him to conclude that the risk per rad to the fetus in diagnostic radiography is probably considerably less than was believed. He concludes that the overall risk of serious radiation-induced harm from diagnostic *x*-rays in the first three months of pregnancy is probably in the range of 0-1 case per thousand receiving one rad tissue dose. The 0-1 cases would usually be cancer in childhood; severe mental retardation would be less common than cancer. This estimate of the hazard of neoplasia is similar to that accepted for some years—that a dose of 3-4 rads doubles the chance of leukaemia or neoplasia, of which the natural incidence is one case per 1200 live births.

Many diagnostic procedures requiring radiography of the pelvis give a uterine dose of 0·5-2·5 rad, and more rarely up to 5 rad. Mole considers that the natural expectation of the

birth of an appreciably handicapped child at the end of a normal pregnancy is about 1 in 30, so that the additional hazard from diagnostic *x*-ray procedures is small compared with the other hazards. Certainly it would not normally justify an abortion.

Nevertheless, while the chances of a developmental abnormality or handicap due to diagnostic radiology are small compared with the natural incidence of these problems, the same is not true of the much rarer cases of leukaemia or neoplasia in childhood. Again the chance that diagnostic radiology will cause these disorders is extremely small, but should they arise the chance that the previous radiography was the cause will vary according to the dose, but will often be as high as 10-50%.

For many years radiologists, radiographers, and clinicians in general have been urged to avoid irradiation during pregnancy in the absence of an overriding medical necessity of proper care for the mother. Women needing routine diagnostic radiographs are scheduled for the first 10 days from the onset of the menstrual period so that the irradiation is given when there is little chance of the patient being pregnant. (The fact that the maturating ovum is also sensitive lessens the value of this procedure: even when the 10-day rule was observed, in theory the patient should perhaps have been advised not to start a pregnancy deliberately until one or two normal periods have occurred.) If, however, the hazard is less than was previously thought and is small compared with all other natural hazards, too much time and effort need not be spent trying to avoid it. On the other hand, women in general have come to believe that there is a hazard from radiation; so it may still be wiser for doctors to take what steps they can to avoid irradiation during pregnancy, since there will then be no worry about what to do or whether the radiography should have been done at all. Caution may avoid the unnecessary tragedy of a woman worrying for 10 or 20 years whether her child might develop leukaemia or neoplasia.

[1] Mole, R H, *British Journal of Radiology*, 1979, **52**, 89.

Neurodevelopmental handicap in very low birth weight infants

Babies weighing less than 1500 g at birth are extremely vulnerable in the perinatal period to respiratory and metabolic disorders, and these account for much of their high mortality rate. The same perinatal problems play an important part in the high incidence of later neurodevelopmental handicap. Better understanding and management of these disorders in specialist centres in Europe and North America have improved neonatal survival and lowered the rates of handicap in these babies of very low birth weight,[1-3] but its incidence is still unacceptably high. When handicap is defined as the presence of major or minor neurological abnormality, a moderate to severe hearing or visual defect, or an intelligence quotient below 70, it is found in between 18% and 44% of babies weighing less than 1500 g.[4] Recent studies have highlighted two neonatal problems which are associated with the later recognition of neurodevelopmental handicap in these small babies: neurological abnormality and intrauterine growth retardation. Better understanding of these problems might help to reduce the incidence of adverse sequelae.

Fitzhardinge and her colleagues in Montreal[5] described the neurodevelopmental state of 149 babies of very low birth weight at roughly 2 years of age. As many as 44 (30%) had major handicaps, at highest risk being those with a history of recurrent neonatal seizures due to intracranial (mainly intraventricular) haemorrhage: neurodevelopmental handicap occurred in 13 out of 15 such babies. Isolated seizures without clinical evidence of intracranial bleeding were not associated with adverse sequelae. At next highest risk were babies with evidence at birth of severe intrauterine growth retardation. Of 40 babies whose birth weights were more than two standard deviations below the expected mean for gestation, 21 were severely handicapped. To determine the effects of intrauterine growth retardation apart from the other complications of preterm delivery 28 such babies of less than 33 weeks' gestation at birth were paired with 28 preterm babies of appropriate weight for gestation and with a similar neonatal course. Twelve of the babies with intrauterine growth retardation were handicapped compared with only three of the others. The affected babies also had significantly lower development scores and were smaller.

Gross and his colleagues[6] reviewed the growth and development at approximately 5 years of age of 118 babies weighing below 2000 g at birth, including 41 of very low birth weight. Particular reference was made to small occipitofrontal head circumference (as a measure of intrauterine growth retardation) and abnormal neonatal neurological behaviour. Major and minor neurological defects, low IQ, sensory abnormalities, and smallness in height, weight, and head circumference were all more frequent in babies whose head circumference was below the tenth centile at birth. Furthermore, 13 of the 118 children who had shown abnormal neurological signs in the neonatal period were later found to have more major abnormalities and smallness of their physical dimensions than those with a normal neonatal history.

The poor prognosis of neonatal neurological abnormality shown in these and other studies[7] is most likely to be due to brain damage from hypoxia originating either in labour or early in postnatal life. The sequelae of severe handicap might be reduced by early recognition of intrapartum asphyxia by fetal monitoring (and prompt intervention); a greater sense of urgency in delivery rooms in establishing respiration in these small infants; and the effective management of hyaline membrane disease and recurrent apnoeic episodes. The poor neurodevelopmental outcome associated with intrauterine growth retardation is harder to explain, though the high incidence reported by Fitzhardinge in poorly grown babies is the highest recorded. Both Fitzhardinge[5] and Gross[6] have suggested that the explanation may lie in interference with brain growth by nutritional or other factors, including congenital virus infections and drugs. This explanation is not in keeping, however, with what is known about the pathological changes in the brain associated with intrauterine growth retardation, which results in widespread distortions and deficits of brain structure (such as smaller brain size, reduced concentration of some myelin lipids, and fewer cells[8-10]) rather than focal structural damage. Since placental lesions are almost universally present in these infants a more realistic explanation may be that poor fetal growth predisposes to intrapartum asphyxia with consequent brain damage. In Gross's[6] study a low occipitofrontal circumference at birth was found to be associated with a low five-minute Apgar score, so giving some support to this hypothesis. On the other hand this explanation seems not