that cannot be proved or disproved by any of the studies so far cited—it might eventually produce groups of women with perhaps a one-in-five chance of developing breast cancer in their lifetimes.[7]

Attempting to offer recommendations on the basis of these data is an awesome responsibility. An excessively alarmist response could result in an epidemic of unplanned pregnancies, with all the attendant social and medical consequences they entail; yet to provide blanket reassurance might prove to be irresponsible. The "worst-case" conclusion is that young girls should avoid prolonged use of the pill before their first pregnancy, especially if they have a history of benign breast disease. Alternatively, girls starting the pill in their teens might be included among the "at-risk" population offered screening, which on present evidence can be recommended only for women over the age of 50.[8]

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Non-rheumatic mitral regurgitation

The mitral valve has a complex functional anatomy. Its competence depends on the left atrial wall, mitral annulus, valve leaflets, chordae tendineae, papillary muscles, and left ventricle.[1] Mitral regurgitation may result from disease of any of these structures, but moderate to severe regurgitation usually results from disease of the valve leaflets or subvalvar apparatus, classically caused by chronic rheumatic heart disease. Yet now that acute rheumatic fever has become rare in Britain new cases of mitral regurgitation continue to present.

Non-rheumatic mitral regurgitation is a useful term, which may include causes such as infective endocarditis, myocardial infarction with papillary muscle necrosis and avulsion of the chordae, and the "floppy" mitral valve. This last category is now recognised as being a common cause of isolated mitral regurgitation, and may be differentiated from rheumatic disease not just by the pathological appearances but also by echocardiography. The rheumatic valve is thickened and relatively immobile, whereas the floppy valve is thin, abnormally mobile, and may prolapse into the left atrium during systole. The floppy valve may be associated with rupture of the chordae tendineae, which will precipitate sudden severe mitral regurgitation and pulmonary oedema.

Acute mitral regurgitation carries a poor prognosis, and surgical treatment should be recommended. The survival of patients with chronic mitral regurgitation is better and nearly 60% are alive 10 years later.[2] Some patients, however, will become disabled by exertional dyspnoea and palpitation, and in this group again surgical treatment should be considered. The results of cardiac surgery are largely determined by the state of the heart muscle, which will gradually deteriorate if subjected to chronic overloading, as in mitral regurgitation. When the myocardium remains healthy but while the patient has few symptoms, early operation gives good results; when the patient has severe symptoms with irreversible left ventricular dilatation and fibrosis, surgery gives poor results. Somehow a compromise must be achieved so that surgery may be recommended before the left ventricle becomes too badly damaged.

Left ventricular performance can be assessed by measurements of pressure, volume, and flow. Measures of left ventricular volume may be derived from angiography, and the ejection fraction (the stroke volume divided by the end-diastolic volume) has proved most helpful in predicting the outcome of surgical treatment.[3] Usually a low ejection fraction indicates poor left ventricular function and a smaller chance of recovery after surgery. In mitral regurgitation, however, the left ventricular blood can leak back into the left atrium and this low pressure outlet allows the ejection fraction to remain normal even when the myocardium is severely damaged. Two recent papers have suggested that the left ventricular end-systolic[4] or diastolic volume[5] may be a better predictor of the ventricular performance after valve replacement in patients with mitral regurgitation—though a low ejection fraction is uniformly associated with a poor outcome. A simple predictor of a good result is a history of symptoms that is less than one year.

Left ventricular angiography requires left heart catheterisation (though this may change with the development of nuclear angiography). In contrast, echocardiography allows one dimension of the left ventricle to be studied repeatedly without harm or discomfort to the patient. Left ventricular end-systolic and diastolic shortening of the echocardiographic dimension reflects the ejection fraction. In patients with mitral regurgitation who remain well all these indices of left ventricular performance are increased, but as the left ventricle fails the fractional shortening falls to normal again.[6 7] Thus the echocardiogram can both help the cardiologist make the diagnosis of non-rheumatic mitral regurgitation and give him an indication of left ventricular performance which may serve as a guide to the timing of surgery. Schuler and his colleagues[8] have shown that patients with end-systolic and diastolic dimensions of greater than 5·0 and 7·0 cm respectively, coupled with a low normal or depressed ejection fraction, continue to have impaired left ventricular function after surgery, with the implication that these patients have a poor prognosis.

The other important factor that influences the results of surgery in patients with mitral regurgitation is the nature of the operation. The alternatives are repairing the valve or replacing it with a prosthesis or biological valve. Reconstructive surgery has its advocates,[9] but most British surgeons prefer to replace the valve. Prosthetic valves, though imperfect, are well tried, and the Björk valve may be preferable to the Starr.[5] They require long-term anticoagulant treatment and if this is contraindicated then a porcine heterograft may be the better option.[10]

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Pulmonary problems of the immunocompromised patient

The protective cuticle surrounding the body is deficient from mouth to anus. The lungs present an area of naked mucous membrane almost the size of a football pitch, making it scarcely surprising that they are the most common site of entry for pathogens. The chances of infection are narrowed by a field of defences set in readiness. IgA-laden mucus at the bronchi and IgG in the alveoli are both dependent on normal function of the thymic-independent, B-cell lymphocytes. Alveolar macrophages, regarded by some as the linchpin of pulmonary defence, depend on normal function of the thymic-dependent, T-cell lymphocytes and their free-ranging lymphokines.[1]

Understanding of these mechanisms has become more important in recent years as patients have their defences suppressed, either as an unwanted side effect of cancer chemotherapy or deliberately in an effort to induce the host to accept transplanted foreign tissue. In such patients the physician should expect an increased chance of infection with common bacterial pathogens, but these can usually be identified either in sputum or in blood and controlled with broad-spectrum antibiotics. The more difficult problems are caused by the truly "opportunistic" agents—those organisms which infect only immunosuppressed patients, which are often difficult or impossible to isolate and which may fail to respond to conventional treatment. In practical terms the worried physician needs to know when to suspect opportunistic lung infection, how to isolate the organism responsible, and how to treat the patient.

The clinical setting is one of fever, shortness of breath, and unproductive cough in a patient with a pulmonary infiltrate in the chest radiograph. The shadowing produced is in no way characteristic but may provide a clue to the causative agent in a few instances.[2] In immunosuppressed patients with tissue transplants the diagnosis may be clear cut, but the picture is more complicated in patients receiving treatment for tumours, especially leukaemia, because the primary disease itself may be responsible for lung changes. Tenholder and Hooper[3] suggest that an opportunistic infection is more likely if the pulmonary infiltrate is diffuse and does not occur within three days of a pulse of cytotoxic treatment.

Opportunistic organisms cause great difficulties for microbiologists. They often demand the most bizarre nutritional requirements, and on many occasions more than one pathogen may be present. In a prospective study by Singer *et al*[4] of 80 patients with lung infiltrates, many of whom had leukaemia, the most extensive laboratory investigations identified a cause in only a third. When open-lung biopsy was added to the investigations the success rate was improved to two-fifths. Nevertheless, in a little over a fifth of the cases no infecting agent was found either on open-lung biopsy or at necropsy.

Heading the list of opportunists is *Pneumocystis carinii*, accounting for 38% of lung infiltrates in the series reported by Singer *et al*[4] and 33% in Tenholder and Hooper's study.[3] The incidence among patients with transplants is lower, reported at 12% in one series of renal transplant recipients, probably because of their lower degree of immunosuppression.[5] Running *Pneumocystis* a close second are fungal infections, especially with *Candida* spp and *Aspergillus fumigatus*, and viruses such as cytomegalovirus and herpes simplex. With improved diagnostic techniques an increasing number of exotic and unusual diseases are being unearthed. Recently a hitherto unknown organism, similar in staining properties to the tubercle bacillus, has been identified by open-lung biopsy and subsequently dubbed the "Pittsburgh pneumonia agent," after the city in which it was first isolated.[6 7]

Open-lung biopsy is a major procedure for any seriously ill patient who already has diseased lungs, and many British physicians are reluctant to pursue investigations to that extent. Having excluded infection with common bacterial pathogens these pragmatists will give high doses of co-trimoxazole on the assumption that the infection is due to *Pneumocystis*. Scientific purists may object to this "cook-book" approach, but such pragmatism often pays off.

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Hazards of biliary tract surgery

Operating on the biliary tract of patients with obstructive jaundice is hazardous; the immediate mortality is broadly correlated with the depth of jaundice. Factors which may increase the risks of operation include cholangitis and predisposition to septicaemia,[1] impaired renal function with a low glomerular filtration rate,[2] malnutrition with hypoalbuminaemia, failure of hepatic reticuloendothelial cells to remove endotoxin from the portal venous blood,[3] and depres-