childhood or early adult life and does not resolve. Though four fifths of patients survive for at least 10 years, progression to end stage renal failure continues, so that only half of patients are alive with functioning kidneys at 20 years.[16] Fifteen of our 19 patients who developed end stage renal failure had impaired renal function at presentation and progressed to renal failure over a median period of only 2·5 years. In 58 of our patients who deteriorated, however, the calculated time for progression to renal failure ranged from five to 25 (median 17·2) years.

Just over a quarter of patients followed up for at least a year had deterioration in renal function but other studies have shown that when followed up for 10 years or more half deteriorate.[16] The long term prognosis may, however, be excellent, some patients showing no functional or histological deterioration over 20 years. (At the other end of the spectrum, a small group of patients show rapid deterioration.[26,27])

The results of treatment have been disappointing. In patients with disease running a rapidly progressive course steroids, cyclophosphamide, and plasma exchange have been tried with some anecdotal accounts of improvement. We have found that, although renal function improves during plasma exchange, it deteriorates abruptly when plasma exchange is stopped.[26] Tonsillectomy and phenytoin may produce some benefit, and of particular interest is phenytoin because it significantly lowers the serum IgA concentration.[28,29] Although Clarkson *et al* did not show any benefit from phenytoin,[30] a recent controlled trial from Spain showed a clear cut reduction in episodes of macroscopic haematuria and urinary erythrocyte counts.[31] Our data suggest that such a reduction reflects a reduction in the number of glomerular crescents.[18] Circulating IgA immune complexes are also reduced by phenytoin and these almost certainly have a role in the progression of IgA nephropathy.[13] In a controlled study we observed reduction in the urinary erythrocyte count in the group treated with doxycycline 100 mg daily for 12 months.[32] Recently a report from Japan has documented a study in two groups of patients with impaired renal function in a trial of eicosapentaenoic acid.[33] Significant benefit was reported in the treated group, and the simplicity of using fish oil rather than immunosuppressive drugs to treat glomerulonephritis has great appeal.

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Lung biopsy

Samples of lung tissue may be obtained through the bronchoscope—transbronchial lung biopsy, brush biopsy, and bronchoalveolar lavage; through the skin—needle aspiration, screw needle biopsy, cutting needle biopsy, and high speed trephine biopsy; through the thoracoscope; and by open lung biopsy.

Transbronchial biopsy is commonly used to investigate diffuse lung shadowing. Initial enthusiasm for the technique has been tempered by disappointing results in some conditions, such as fibrosing alveolitis, where recognising the pattern of lung inflammation is so important.[1,2] The overall diagnostic rate is 38-64%,[1-4] but it is higher in conditions with specific histological features such as sarcoidosis (67-88% positive[1,2,5]), diffuse malignancy (67-80% positive[1,2]), opportunistic infection,[1,6,7] and alveolar proteinosis. Other useful techniques that may be employed at bronchoscopy include bronchial biopsy (often giving positive results in sarcoidosis and diffuse malignancy), brush biopsy,[6,8] needle aspiration,[9] and bronchoalveolar lavage.[1,10,11] The last may be particularly helpful in diagnosing opportunistic infection. In one study 15 of 16 episodes of infection in immunosuppressed patients were correctly diagnosed with lavage.[10] Complications of transbronchial biopsy are uncommon but include the hazards of bronchoscopy.[12] Pneumothorax occurs in 3-5% of patients; it is more common in those with pulmonary fibrosis.[1,4,5,8] Clinically important haemoptysis is uncommon except in uraemic patients.[6,8] Postbronchoscopy pneumonia and fever are occasionally reported,[5] and patients at risk of endocarditis should receive antibiotic prophylaxis. The mortality has been estimated as 0·2%.[2]

A percutaneous method is preferable to transbronchial biopsy for investigating pulmonary nodules not seen bronchoscopically. With percutaneous needle aspiration adequate samples for cytological and microbiological exami-

nation may nearly always be obtained and a positive diagnosis (usually of malignancy) made in 80-90%.[13-17] False positive findings are rare, but the tumour cell type identified may be inaccurate in one quarter to one third of cases.[15 17] The false negative rate is between 5% and 16%, and at least three separate samples should be taken before considering a lesion benign.[15] A highly experienced cytohistologist is essential. A screw stylet increases sensitivity and specificity, and disposable screw biopsy needles are now widely used.[13 17]

Percutaneous needle aspiration has been used successfully to investigate lung infection but is less helpful in other forms of diffuse lung shadowing.[15 17 18] The main complication of needle aspiration is pneumothorax, which occurs in a quarter to one third of patients with 1-10% needing drainage.[13 14 17] Clinically important bleeding, air embolism, and tumour seeding are rare.[15] The mortality is less than 0·1%.[15 18] Complications increase with the depth of biopsy, emphysema, and age[15 19] and are reduced with experience[13] or by using ultrathin needles.[17] These are difficult to guide accurately, however, and give less good results for small nodules.[15]

A recent study has reported the usefulness of percutaneous (Tru-Cut) cutting needle biopsy of lung nodules.[19] A specimen giving helpful and accurate histological information was obtained from over 90% of 89 consecutive adults. No false negative samples were identified. Complications were not appreciably greater than with needle aspiration, except that one patient developed a haemothorax and tumour seedlings developed at the biopsy site in two others—a complication reported before with cutting needle biopsy.[20] Cutting needle biopsy is rarely used now in diffuse lung disease because of complications.[16 19] A safer approach is with trephine biopsy needle driven by a high speed air drill. Generous samples, up to 2 mm diameter, allow accurate histological diagnosis in 70-90% of cases.[21 22] Pneumothoraces occur in a quarter to a third of patients, however; 7% require tube drainage; 2% have substantial blood loss; and occasional deaths are reported. Cover by a thoracic surgeon is recommended whenever a cutting biopsy is being performed with a needle or trephine.[19 20] Neither trephine biopsy nor perthoracoscopic lung biopsy is widely used in Britain.[21]

The advantage of open lung biopsy is that the surgeon can inspect the lung and take representative samples for histological and microbiological study. The most diseased areas and the tip of the lingula and middle lobe should be avoided as they may show only non-specific or end stage changes.[21] In immunosuppressed patients with acute lung shadowing open lung biopsy gives a specific diagnosis (usually of infection) in 50-80%.[23-26] The diagnostic rate in adults with chronic lung shadowing is over 90%.[2 3] The operative mortality is 0·3-1·0%, and minor complications occur in only 7-11% of patients.[21] The value and safety of open lung biopsy were shown in a prospective study of 53 adults with chronic interstitial lung disease.[2] Transbronchial biopsy specimens were diagnostic in only 20. A specific diagnosis was made in 30 of the other 33 by open lung biopsy. In another study 20 adults with diffuse lung shadowing had a percutaneous needle aspiration biopsy, cutting needle biopsy, and a transbronchial biopsy all performed at the time of open lung biopsy.[3] The respective diagnostic yields for each technique were 29%, 53%, 59%, and 94%.

How a lung shadow is investigated will depend, then, not only on the condition of the patient and the urgency of the need for information but also on what skills are available locally to take the biopsy specimen and examine it. Absolute contraindications to closed lung biopsy include an uncooperative patient, pulmonary hypertension, uncorrectable bleeding disorders, and inability to withstand a pneumothorax.

Most peripheral lung nodules considered for biopsy turn out to be malignant, and direct referral for thoracotomy is often reasonable. In those patients with questionable fitness for thoractomy a positive diagnosis of a malignancy by percutaneous screw needle biopsy may strengthen the decision to operate. A negative biopsy specimen is more difficult to interpret and should be repeated.

In the patient not fit for thoracotomy the decision whether to biopsy an asymptomatic peripheral nodule or to await events is difficult. For adults with diffuse lung shadowing transbronchial biopsy with bronchial biopsy, brush biopsy, and bronchoalveolar lavage are safe initial investigations, particularly if the diagnosis suspected is active sarcoidosis, diffuse malignancy, infection, or alveolar proteinosis. If the result is unhelpful and further histological information is needed then open lung biopsy should be considered. In some centres a percutaneous trephine biopsy is an alternative. With rapidly progressive lung shadowing open lung biopsy should be considered early—even as the first biopsy procedure—especially in immunosuppressed children, who are likely to be intolerant of other procedures. The chances of obtaining a result that will alter treatment or dramatically improve chances of survival, however, should not be overestimated in such circumstances.[21 23 24]

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