INTERSTITIAL LUNG DISEASES
2: MANAGEMENT STRATEGIES

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This is the second part of a two-part unit on interstitial lung diseases (ILDs). Part 1 examined the challenges of diagnosis and the range of investigations. This part explores management strategies for the three most common ILDs.

IDIOPATHIC PULMONARY FIBROSIS (IPF)
IPF is the most common single type of interstitial lung disease that nurses are likely to see. Approximately 4,000 new cases are diagnosed in the UK each year. IPF is one of the idiopathic interstitial pneumonias (IIPs), which give rise to about 40% of all ILDs. It will account for over half of all the IIPs nurses will ever encounter, so it causes a significant burden in both primary and secondary care.

IPF usually presents in people aged over 50, initially as breathlessness on exertion and sometimes with an irritating dry cough. However, if there is a family history of ILD, patients can present much younger.

The cause of IPF remains elusive and there are no proven pharmacological treatments that can reverse its progression. The current life expectancy of a patient diagnosed with IPF is 2–4 years from diagnosis (Wells and DuBois, 1994).

Occasionally clinicians wrongly refer to IPF as usual interstitial pneumonitis (UIP). This can be misleading because UIP is a specific pattern seen on lung biopsy, not a clinical diagnosis. Patients who demonstrate ‘IPF pattern’ on high-resolution computerised tomography and who undergo an open lung biopsy will characteristically show UIP on biopsy. However, UIP on biopsy alone – in the absence of an IPF clinical and radiological pattern – is not diagnostic of IPF. UIP on biopsy can be seen in other ILDs, for example connective tissue diseases, drug-related ILDs, hypersensitivity pneumonitis and sarcoidosis. It is important to remember that the presence of UIP on biopsy in these other diseases does not mean they will not respond to treatment. To make a diagnosis of IPF, all other causes of lung fibrosis need to be excluded.

Traditionally, treatments have been based on the idea that in IPF an unknown alveolar insult has led to lung inflammation. This then leads to injury and subsequent abnormal healing by fibrosis rather than by resolution. There is no good evidence to substantiate the theory that fibrosis can be reversed by treatment (American Thoracic Society, 2000). As a result, most treatments aim to eliminate or suppress the inflammatory component of the disease.

These immunosuppressant treatments are not without substantial side-effects and so their use can be contentious (Egan and Woodcock, 1996). Experimental treatments are now becoming available in clinical trials for IPF. Many of these drugs are designed to prevent lung fibrosis rather than reducing inflammation per se.

Some of the drugs currently or previously used to treat IPF include:

- Corticosteroids;
- Azathioprine;
- Cyclophosphamide;
- Colchicine;
- Penicillamine.

These drugs are used either in combination or alone and require careful monitoring for side-effects.

Newer drugs include the antioxidant N-acetylcysteine (NAC) used in combination with prednisolone and azathioprine (Demedts et al, 2005).

There are several new anti-fibrotic drug treatments that are undergoing clinical study. These include:

- Interferon gamma-1b (the ‘Inspire’ study);
- Pirfenidone (the ‘Capacity’ study);
- Bosentan (the ‘Build 3’ study).

As is the case for patients diagnosed with small-cell lung cancer, it is thought to be in the best interests of patients with IPF to offer them enrolment in current clinical trials. This is because there is a lack of good evidence that the ‘usual’ drug treatments are effective. By contacting a tertiary respiratory centre, nurses can find out where the ongoing clinical trials are taking place.

SARCOIDOSIS
Sarcoidosis is a systemic disease that usually affects younger people between the ages of 20 and 40 years. Its incidence in the UK is 1:10,000 people (Johnston et al, 2006). The cause is not known but it is thought that there is a genetic component. An unidentified environmental agent is thought to trigger the disease in people who are susceptible. Family clustering has been seen in some instances.

The disease process leads to the formation of nodules or granulomas throughout the body that resemble, but are distinct from, those observed in tuberculosis. Sarcoidosis usually predominates in the lung but other organs including the skin, eyes, heart, brain, liver, kidney, spleen and bowels can be affected.

Sarcoidosis can flare up as an acute attack causing fever, malaise, joint pains, skin rashes and enlarged lymph glands. The...
HYPERSENSITIVITY PNEUMONITIS
This is the third most common ILD and is also known as extrinsic allergic alveolitis (EAA). UK physicians often refer to EAA but in the US the term HP is used.

HP is caused by an allergy to something that is inhaled. It is thought that some people may inherit a predisposition to it, as not everyone will develop HP to a specific allergen. Typical allergens include mouldy hay or fungal spores (hence ‘farmer’s lung’), or a reaction to budgerigars, pigeons or cockatiels (known as ‘bird fancier’s lung’). Wood and metal workers may develop HP. Exposure to the allergen is usually prolonged before symptoms develop, so significant irreversible fibrosis has often occurred before HP is diagnosed. In many cases an allergen cannot be identified.

Patients are usually diagnosed on the basis of their medical and occupational history, high-resolution computerised tomography and immunological blood tests. Treatment involves avoiding exposure to the allergen before irreversible lung damage has been caused. Many patients, however, present late when fibrosis is well established. Some may need prednisolone +/- azathioprine or a reaction to budgerigars, pigeons or cockatiels (known as ‘bird fancier’s lung’). Wood and metal workers may develop HP.

‘Burnt out’ or inactive sarcoidosis can flare up after many years. Annual monitoring by a specialist respiratory physician is thus encouraged, even if symptoms settle. It is important to note that ‘burnt out’ does not necessarily mean ‘gone forever’.

LUNG TRANSPANTATION
All patients with progressive ILD, despite optimal medical therapy, should be considered for lung transplantation if they are aged under 65 years and do not have other significant co-morbidities. While most transplant centres do not exclude patients over 60, the evidence suggests that they have a significantly reduced chance of survival (Snell et al, 1993).

There is usually a rigorous assessment process at each centre in order to exclude co-morbidities that would increase the risk of surgery. Absolute contraindications for lung transplantation include:

- Current addiction to tobacco, alcohol or drugs;
- Significant renal or liver dysfunction;
- Malignancy other than basal and squamous cell carcinoma of the skin;
- Active extra-pulmonary infection;
- Progressive neuromuscular disease.

Patients should be instructed that lung transplantation is only considered when all other alternative treatments have been exhausted. It is vital, however, to refer patients with ILD early, particularly those diagnosed with IPF. All those who demonstrate disease progression with a diffusing capacity and/or vital capacity below 50–60% on pulmonary lung function measurements should be considered for lung transplantation.

The transplant assessment process can be lengthy, and transplant units are not immune to the bed pressures and targets present throughout the NHS. It is probably a good rule of thumb to refer all patients who have been diagnosed with IPF to be considered for lung transplantation, provided they are under 65 without other significant co-morbidities. A full discussion can then take place between the transplant team and the patient about preparations for post-operative care and survival figures of lung transplantation.

Most patients with IPF are referred too late for transplantation, which contributes to the high mortality rates on the waiting list (Glanville and Estenne, 2003).