**Information for patients**

**Interstitial Lung Diseases**

Interstitial Lung Disease is a term that comprises a broad collection of more than 200 disorders of the lung. These diseases are classified together because they all affect the tissue around the alveoli which is called the pulmonary interstitium. Depending on the particular disease, other compartments of the lung such as the alveoli bronchi, bronchiole (small bronchi), blood vessels and the pleura may also be affected. In general, interstitial lung diseases are characterized by the following manifestations: Unproductive cough, shortness of breath at exertion characteristic abnormalities in chest x-ray or computer tomography, defects in pulmonary function and microscopic patterns of inflammation and fibrosis.

**What do we know about these disorders?**

Varying degrees of fibrosis and inflammation can be found in microscopic investigations of specimen of affected lungs. Fibrosis is characterized by increased amounts of connective tissue and inflammation by an excessive influx of white blood cells. Patterns with predominance of fibrosis indicate advanced disease and those with a predominance of inflammation an early stage which in many cases responds to treatment. Interstitial lung diseases are rare disorders, however, all these disorders together total in a high number which poses a tremendous burden. Estimates of prevalence of specific interstitial lung diseases are given in table I. In addition, over the last decades the incidence of interstitial lung diseases and their death toll have doubled.

Interstitial lung diseases are disorders of any age although they also occur in children. Certain interstitial diseases such as sarcoidosis, autoimmune disease-associated lung disorders and Langerhans cell histiocytosis tend to develop in young adults, whereas idiopathic pulmonary fibrosis (IPF) most often occurs between the ages of fifty and seventy. In some cases of IPF a familiar predisposition can be observed and in those families the disease onset seems to appear earlier.

There are numerous causes of interstitial lung diseases: Diseases associated with systemic disorders (for example autoimmune or collagen-vascular diseases), diseases associated with an exposure to an agent known to injure the lung (for example occupational exposures such as asbestos, silica or beryllium; medications such as bleomycin, biological agents from the environment such as bird droppings causing hypersensitivity) and diseases associated with known genetic abnormalities (lymphangioleiomyomatosis, tuberous sclerosis). However, most frequent interstitial lung diseases are idiopathic.

The following table lists the prevalence of specific interstitial lung diseases.

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| **Interstitial Lung Diseases** | **Prevalence / 100.000 population** |
| Idiopathic pulmonary fibrosis | 18 |
| Other fibrosing lung diseases  | 10 |
| Interstitial pneumonitis  | 2 |
| Occupationonal disorders  | 21 |
| Sarcoidosis | 42 |
| Connective tissue diseases  | 8 |
| Drug, radiation diseases  | 2 |
| Pulmonary hemorrhage | 1 |
| Other  | 11 |
| Total | 115 |

Inflammation is an immediate response to injury, noxious or infectious agents. Subsequent fibrosis is a part of the human response. In the case that the organism is not able to stop the process of wound healing, fibrosis develops which destroys the microarchitecture of the lung causing pulmonary function defects. When the injurious agent is known exposure has to be stopped and lung function may stabilize.

Interstitial lung diseases caused by occupational exposure are well studied. It appears that minerals such as asbestos and silica directly injure the lung but other agents such as beryllium cause a specific immune response resulting in inflammation. Inhaled biological agents causing farmer’s or pidgeons breeders’ lung induce immunulogic responses which cause scaring when exposure is not stopped. Unfortunately, for most of the interstitial lung diseases such causes are not known and they have to be called idiopathic. Viruses might be an infectious trigger but this has not yet been proven.

**Prevention, treatment and prognosis**

When the course of the disease is known, the injuries agent needs to be avoided. Other disorders causing pulmonary harm need to be treated. The most important is gastroesophageal reflux. There is ample evidence that inflammation proceeds fibrosis and, therefore, the therapeutic regimen for interstitial lung diseases include corticosteroids (prednisolone), immunosuppressive agents such as azathioprine or cyclophosphamide and biological drugs such as rituximab. In particular these drugs are helpful in connective tissue disease-associated interstitial lung disease. Recently, two drugs (Pirfenidone and Nintedanib) have been approved for idiopathic pulmonary fibrosis (IPF) which dampen fibrotic mechanism but do not eliminate the causing agent. Without therapy the median survival from diagnosis on is 3 to 4 years. The usefulness of the new drugs in everyday practice still needs to be established.

In cases of advanced interstitial lung disease, especially IPF, lung transplantation is the only option. Of note, 5-year survival rate is approximately 60 % and in elderly patients complications are more frequent. Of those patients with IPF who are waiting to receive a transplant, more than 30 % die before receiving one. This highlights the urgent need for effective medical therapies for IPF and other progressive interstitial lung diseases.

Interstitial lung diseases have varying prognoses. Sarcoidosis usually has a good prognosis with reversal of disease in about two thirds of cases. Although, we have new drugs for IPF it is still a complex disorder difficult to treat.

**Perspective**

Recent immunobiological studies furthered the understanding of high relevance for inflammatory and fibrotic processes which can be used as pharmacological intervention points for future pharmacological trials. Studies of the genetics of patients with interstitial lung diseases show that alterations in specific genes may dispose individuals to IPF.

Moreover, in sarcoidosis and berylliosis numerous gene variations have been identified and the corresponding genes play pivotal roles in the immunopathogenesis of these disorders. Unfortunately it is too early to predict individual prognosis on the basis of genetic tests.

The better understanding of the inflammatory processes allows the development of markers which can be used in clinical trials for the development of new drugs.

Links to further information material on IPF can be found at our webpage.