## **Difficult Asthma: from Clinical Presentation to the Airways**

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Asthma is an inflammatory disease affecting the whole respiratory system, from central airways to lung parenchyma, with systemic effects. Approximately 5% to 10% of adult patients have "difficult asthma," described as a failure to achieve symptom control despite prescribed treatment at step 4 of the GINA (Global Initiative for Asthma) guidelines. However, the evidence base for the assessment and management of this group of patients is small. Difficult-to-control asthma can be subdivided into several phenotypes: corticosteroid resistant asthma, corticosteroid-dependent asthma, and near-fatal asthma. This sub-group of patients accounts for a disproportionate amount of asthma morbidity and health care costs and are a particular cause for concern because of the potential consequences of uncontrolled disease including fatal or near fatal asthma. Challenged by the high prevalence of asthma and by high asthma-related morbidity, which has a strong socioeconomic impact, various medical societies and organizations have developed protocols and consensuses for a more effective approach to asthma and difficult-to-control asthma.

Neutrophilic asthma is another phenotype of the disease that might not respond adequately to glucocorticoids. In addition, it now becomes important to gain more insight in the risk of small airway disease for asthma outcome, e.g. occurrence of exacerbations and accelerated lung function decline. Future studies are needed to develop tools that help doctors to discriminate between asthma patients with and without small airway disease and to monitor disease with small particle treatment.

The development of protocols for the treatment of difficult-to-control asthma have allowed patients with difficult asthma to be managed more effectively, thus improving their quality of life and possibly reducing morbidity and mortality.