Condition: α_1-antitrypsin deficiency

Inheritance:
Autosomal recessive.

Genetic etiology:
Mutation in *SERPINA1* gene, which encodes α_1-antitrypsin, a protease inhibitor. Lack of α_1-antitrypsin in the lung leads to pulmonary damage due to inflammation. Alleles that lead to failure of processing of protein in the liver lead, in addition, to cirrhosis.

Frequency:
Approximately 1/5,000 in Caucasians.

Clinical features:
Pulmonary disease consists of chronic lung damage due to unchecked activity of proteases that are part of normal inflammatory mechanisms. Ultimately this leads to chronic emphysema and consequent hypoxia. Specific alleles that lead to abnormal enzyme processing in the liver cause cirrhosis.

Management:
Supportive care, and lung and/or liver transplant for irreversible damage; use of augmentation therapy by infusion of purified a_1-antitrypsin may prevent disease progression; avoidance of exposure to tobacco smoke, both for affected individuals and carriers.

Genetic counseling:
Parents of an affected child face a 25% risk of recurrence. Genetic testing for common mutations is available. Diagnostic testing commonly done by serum protein electrophoresis.

Human Genetics and Genomics, Fourth Edition. Bruce R. Korf and Mira B. Irons.