PRIMEVIEW

PULMONARY ALVEOLAR PROTEINOSIS

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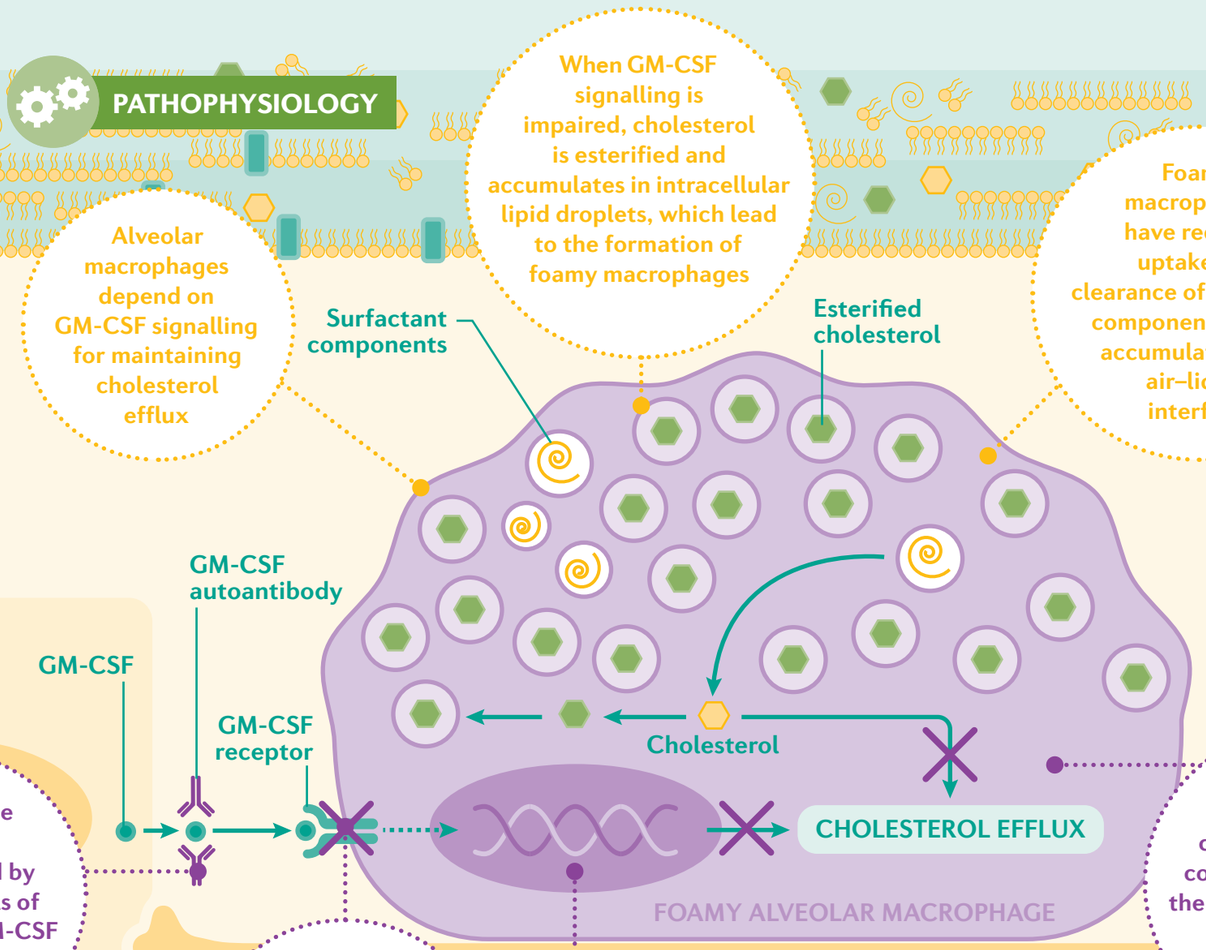
Pulmonary alveolar proteinosis (PAP) is a syndrome characterized by abnormal accumulation of alveolar surfactant in the lungs and dysfunction of the alveolar macrophages. PAP can be classified as primary (autoimmune or hereditary), secondary or congenital, depending on the underlying mechanism.

EPIDEMIOLOGY

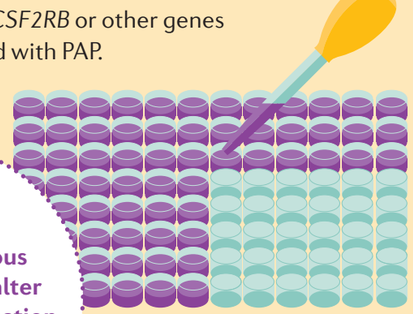
The overall prevalence of PAP has been estimated to be at least 7 per million individuals in the general population in the United States and Japan, where the largest population studies have been conducted. However, the actual prevalence is probably higher, as PAP often remains undiagnosed or misdiagnosed for a long time. Autoimmune PAP accounts for ~90% of all patients.

PATHOPHYSIOLOGY



DIAGNOSIS

PAP should be suspected in individuals with a history of slowly progressive dyspnoea and the characteristic chest CT findings of ground-glass opacities with interlobular septal thickening, often in polygonal shapes. A serum GM-CSF autoantibody test should be the first diagnostic test performed, as it has a 100% specificity and sensitivity for autoimmune PAP. If the test is negative and secondary PAP is ruled out, serum GM-CSF concentration and signalling tests can help to determine whether the patient should receive genetic tests to detect mutations in *CSF2RA*, *CSF2RB* or other genes associated with PAP.



QUALITY OF LIFE

The quality of life varies widely among patients depending on the cause, clinical course and disease severity; most patients have exertional dyspnoea and frequent cough. Granulocyte–macrophage colony-stimulating factor (GM-CSF) augmentation therapy seems to improve quality of life and dyspnoea. Remission has been reported, but it remains unclear whether these instances represent true disease-free remission or simply periods of quiescent subclinical disease.

OUTLOOK

The aetiology of autoimmune PAP remains unclear. Furthermore, the disease-specific mechanisms of the various conditions that cause secondary PAP remain largely unproven, and the mechanisms by which the mutations in genes associated with congenital PAP lead to fibrosis and abnormal surfactant accumulation are poorly understood. Finally, standardized clinical practice guidelines for PAP are needed, as well as objective outcome measures to determine treatment efficacy and disease severity.

MANAGEMENT

The goals of management are to alleviate symptoms and improve oxygenation and quality of life. The current standard of care in primary PAP and some causes of secondary PAP is whole-lung lavage, to physically remove the surfactant sediment by washing it out of the lungs. GM-CSF augmentation therapy can be effective in autoimmune PAP but not hereditary PAP. Emerging pathogenesis-based therapies aim at reducing the abnormal production of GM-CSF autoantibodies (for example, plasmapheresis and B lymphocyte antagonists) or restoring cholesterol homeostasis.

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