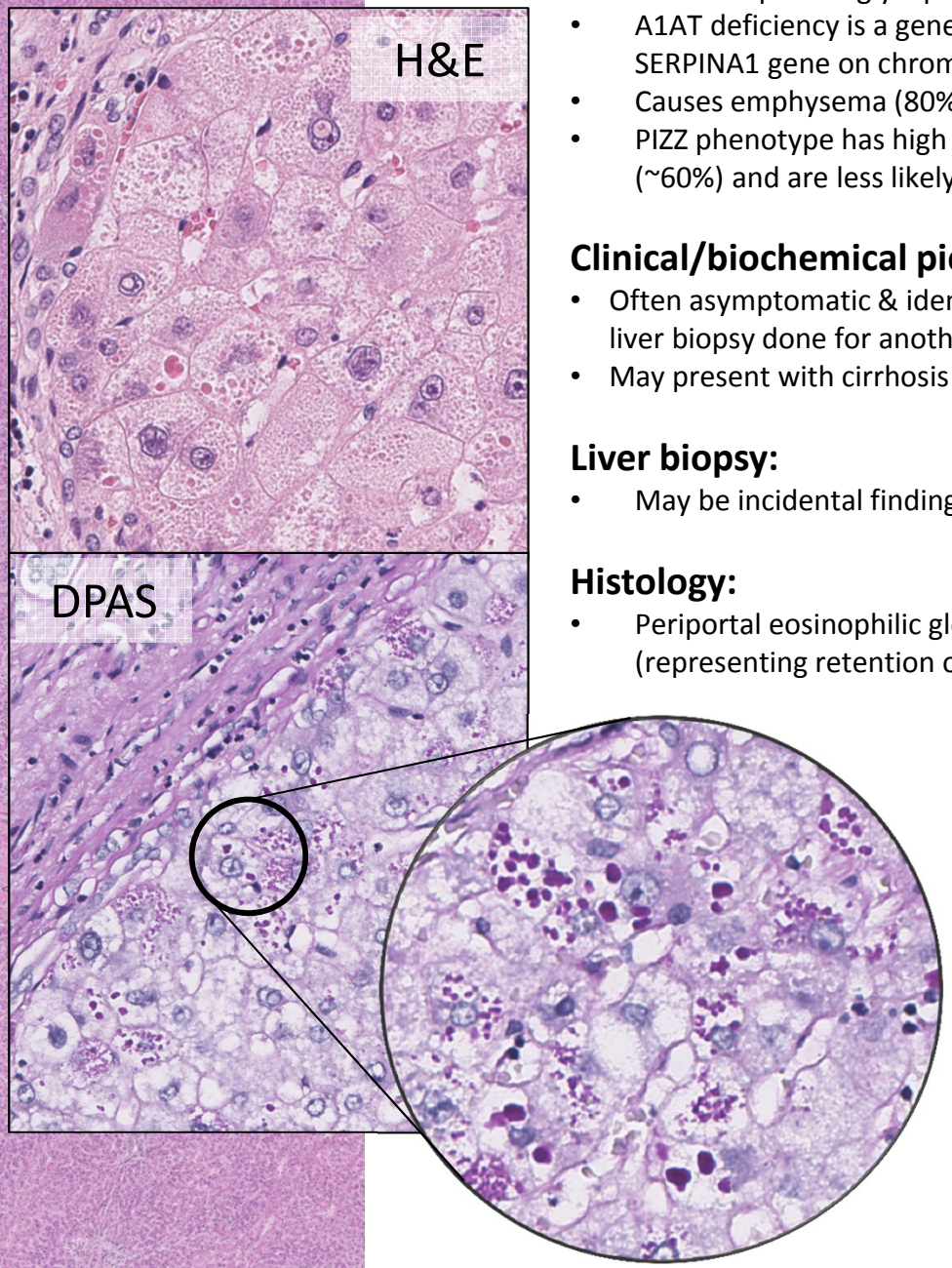
Alpha-1 Antitrypsin (A1AT)



Aetiology:

- A1AT is a plasma glycoprotein synthesised by hepatocytes.
- A1AT deficiency is a genetic autosomal co-dominant disease, causing a mutation in SERPINA1 gene on chromosome 14.
- Causes emphysema (80%, usually aged 20-40) and liver disease.
- PIZZ phenotype has high risk of clinical disease. PIMZ have intermediate levels of A1AT (~60%) and are less likely to develop liver disease.

Clinical/biochemical picture:

- Often asymptomatic & identified incidentally on liver screen with low A1AT blood test or liver biopsy done for another reason.
- May present with cirrhosis & end stage liver failure.

Liver biopsy:

- May be incidental finding.

Histology:

- Periportal eosinophilic globules of both small and large calibre seen within hepatocytes (representing retention of polymers on endoplasmic reticulum).
  - Can be highlighted on a DPAS stain, or by using the A1AT immunohistochemical stain.
  - NOTE: Similar globules can be seen in the periportal location in patients with alcoholic liver disease and some chronic inflammatory conditions (e.g. rheumatoid), and within zone three in congestive hepatopathy (also stain with the IHC), so clinical and biochemical correlation is required.

Clinical Course:

- Management is generally supportive. Some drugs currently in clinical trials, but not in general use.
- With time become increasingly fibrotic and cirrhotic. Ultimately if severe, often require transplantation.