



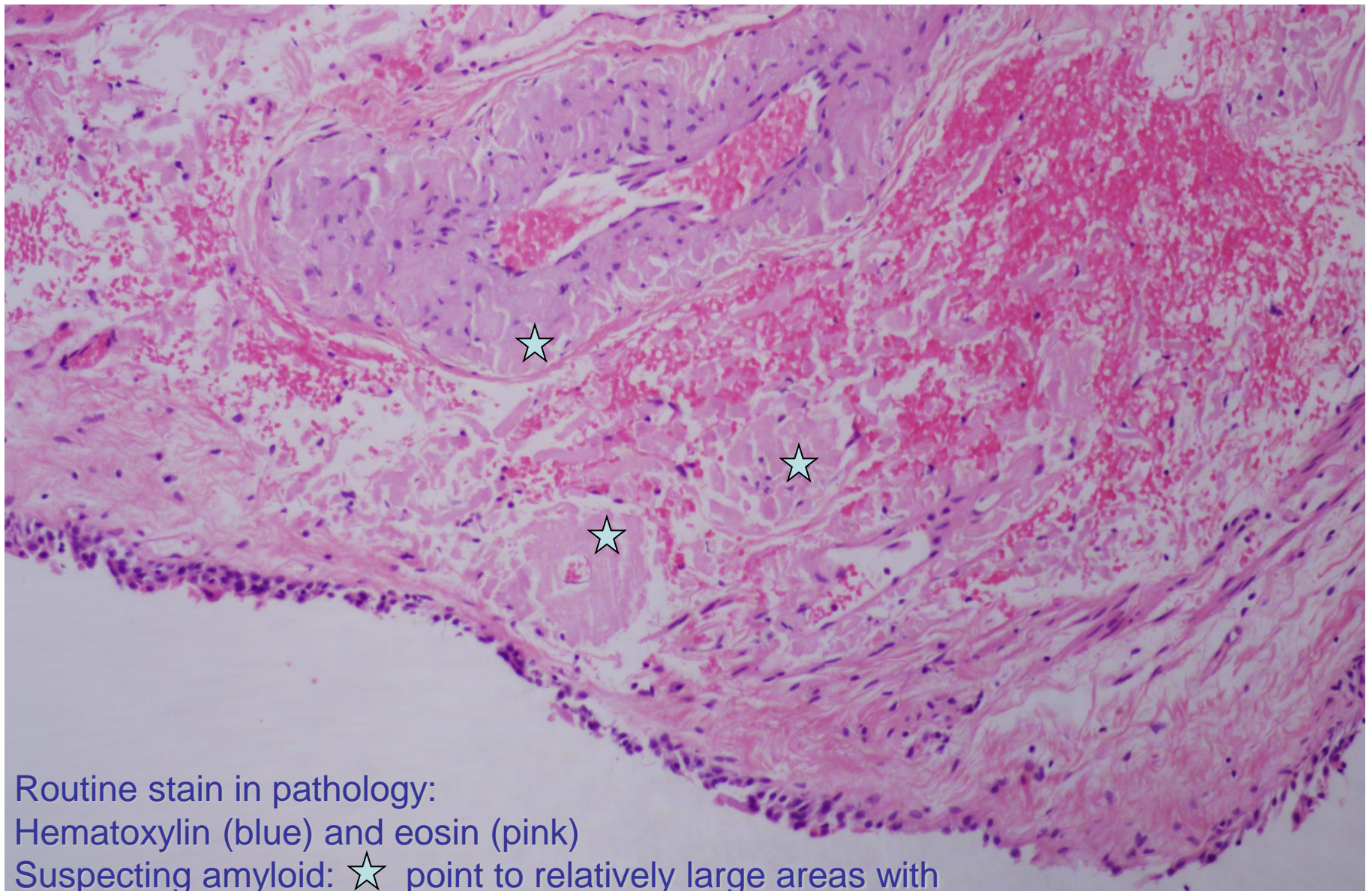
Familial Amyloidosis from the Pathologist's perspective

**Maria M. Picken MD, PhD
Loyola University Medical Center
Chicago**



Outline:

- 1. How amyloid is diagnosed**
- 2. Congo red stain and issues with diagnosis of amyloid**
- 3. Types of biopsies**
- 4. Issues specific to familial amyloidoses**



Routine stain in pathology:

Hematoxylin (blue) and eosin (pink)

Suspecting amyloid: ☆ point to relatively large areas with

homogeneous deposits devoid of cells. Such areas are suspicious for amyloid

Since other pathologies can look similar, Congo red stain is needed to verify the

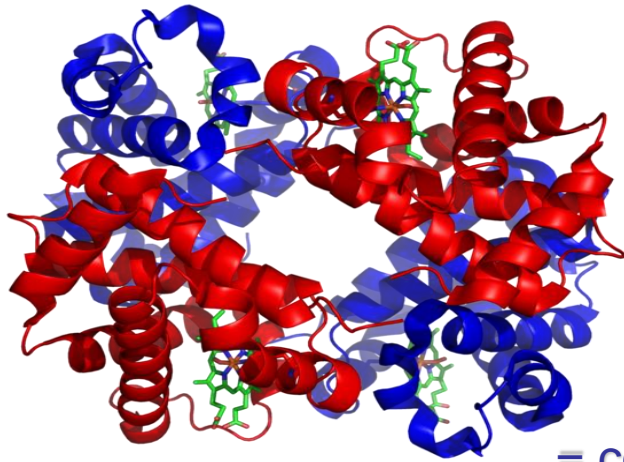
suspicion of amyloid. Caveat: small deposits may not be apparent on a routine stain!

Congo red = bright red color:

- first synthesized in 1883 by Paul Bottiger as a textile dye
- subsequently marketed under the name "Congo red" since at that time Africa and things associated with it were very fashionable
- Since early 1920s used in pathology to stain amyloid

Amyloidoses

Normal proteins: α helix



Amyloid: β pleated sheet

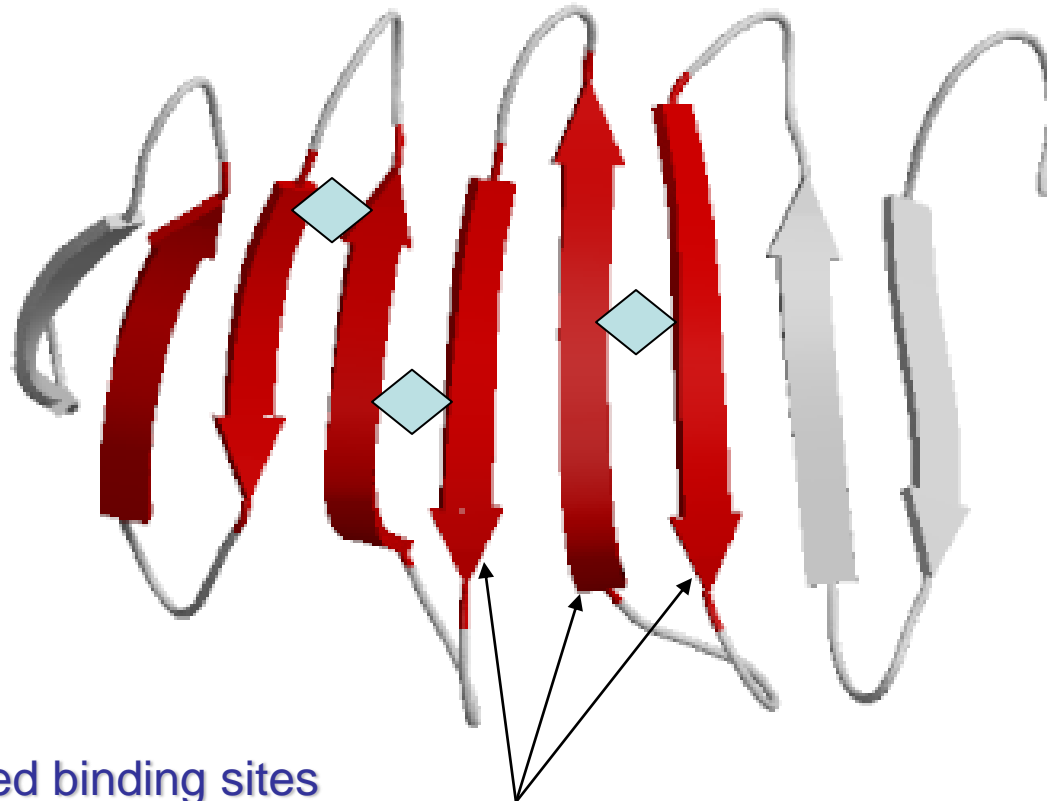


Amyloid formation

= conformational shift to
 β -pleated sheet structure

Why amyloid forms?

- structural abnormalities due to a genetic defect (familial)
- excess production...(see other presentations)

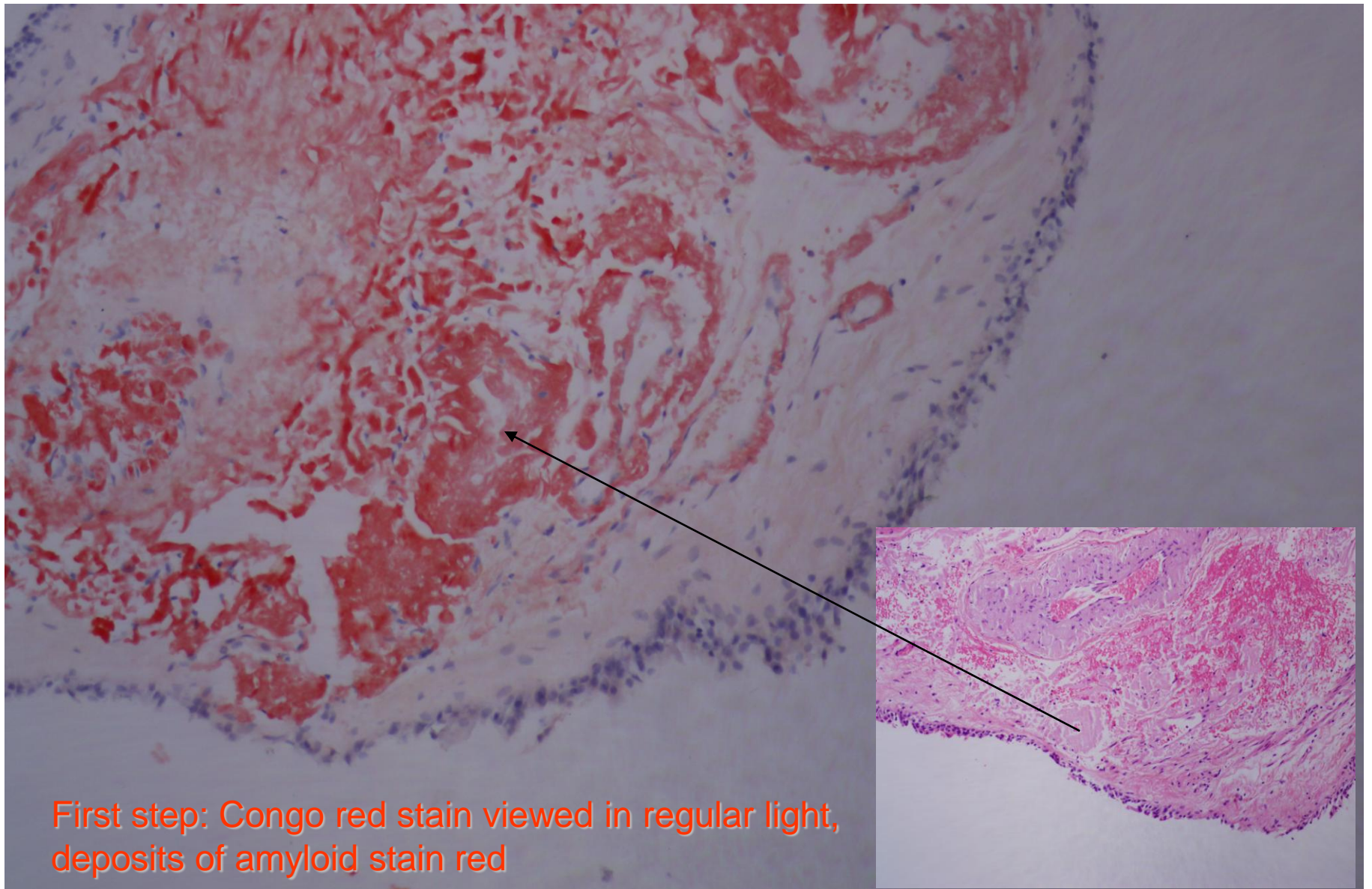


Congo red binding sites

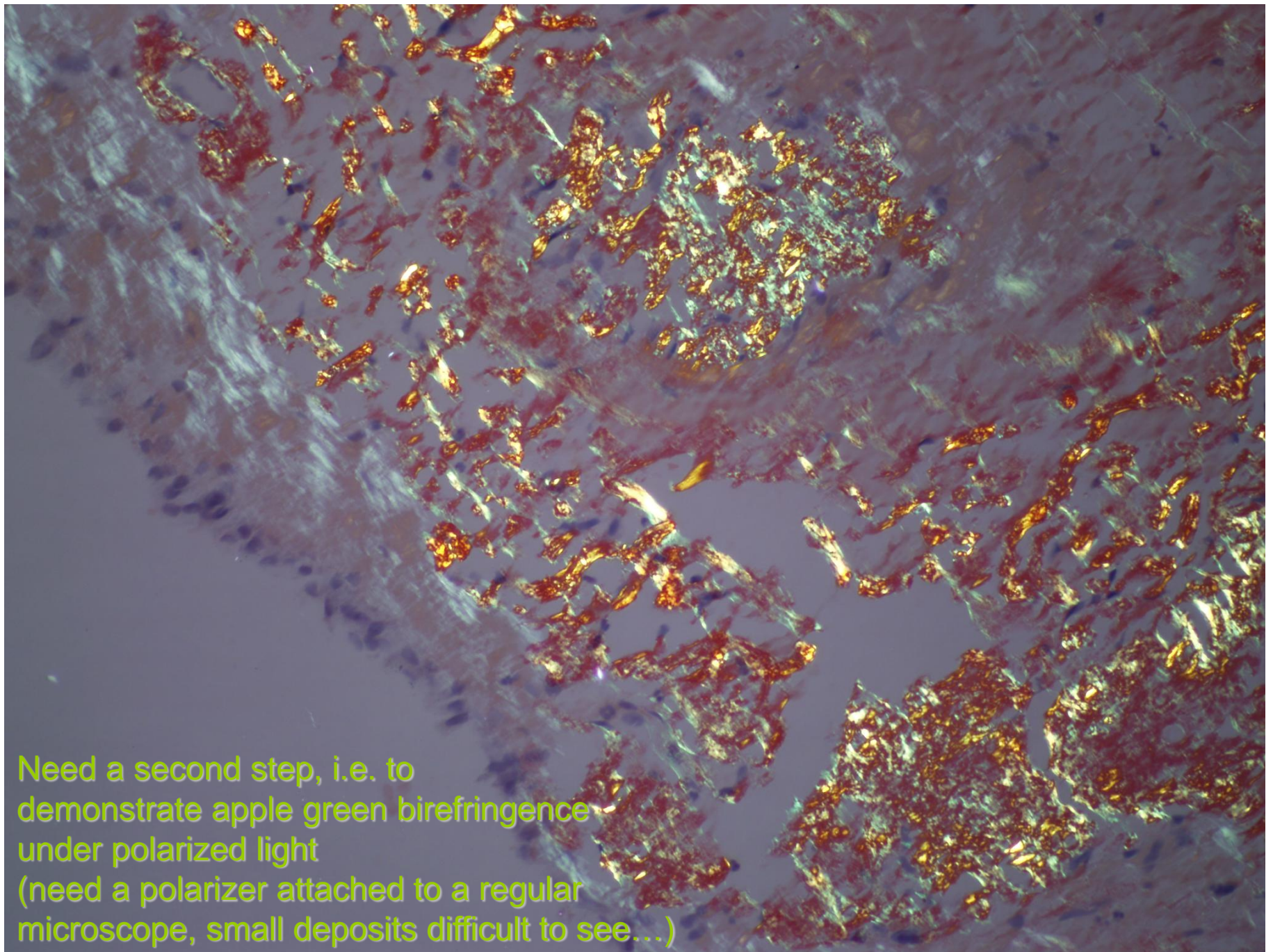
All types of amyloid have β -pleated sheet conformation

All types stain with Congo red

All types are fibrillar under a very high magnification (electron microscope)

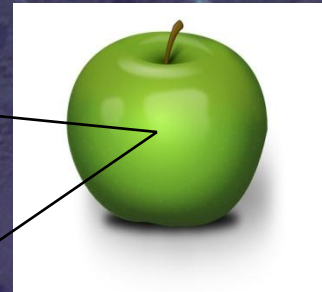


First step: Congo red stain viewed in regular light, deposits of amyloid stain red



Need a second step, i.e. to demonstrate apple green birefringence under polarized light (need a polarizer attached to a regular microscope, small deposits difficult to see...)

Current gold standard



Diagnostic result = apple green birefringence
(deposits are green like a green apple in the insert)
This picture shows a kidney biopsy with amyloid
in the glomerulus seen in the center

Diagnosis of amyloid –

When to do Congo red stain?

- to confirm suspicion of amyloid

(usually larger deposits suspected on a routine stain)

- to **rule out** amyloid

(in early stages when amyloid deposits are small and not apparent on a routine stain)

Kidney biopsy: patients with protein in urine (proteinuria), rarely kidney failure
Since kidney biopsies are routinely examined with additional stains and techniques, amyloid is more often detected than in other tissues

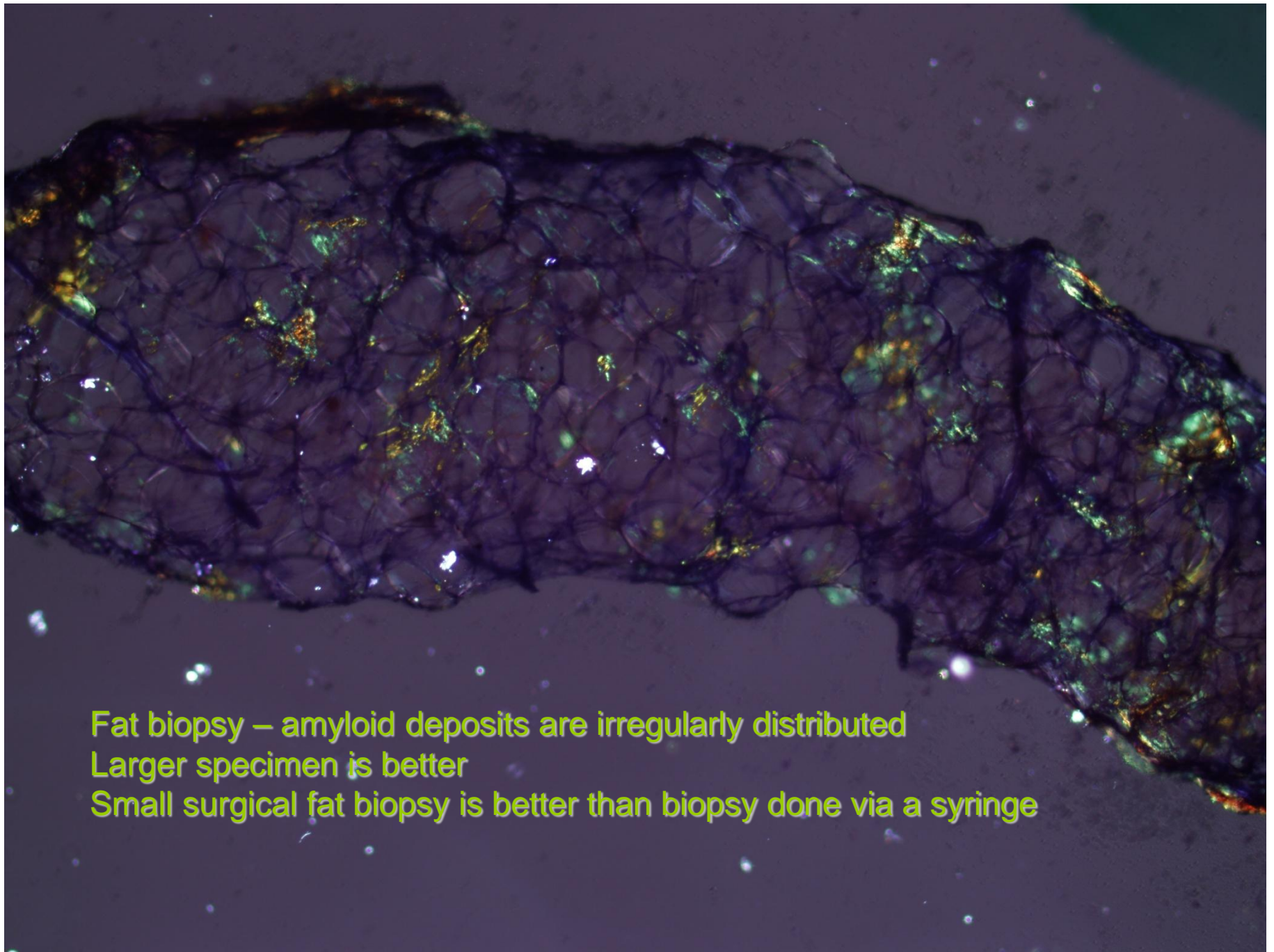
Heart (native) biopsy: routinely, heart failure, orthostatic hypotension

Nerve biopsy: routinely

Gastrointestinal biopsies: many mimickers, many biopsies in daily work, decision which cases should be stained with Congo red is more difficult

Other specimens – similar to above

Also enlarged liver, other glands. In general - unexplained kidney, heart or systemic disease should be suspicious for amyloidosis



Fat biopsy – amyloid deposits are irregularly distributed
Larger specimen is better
Small surgical fat biopsy is better than biopsy done via a syringe

A microscopic image of tissue stained with hematoxylin and eosin (H&E). The image shows several glandular structures, likely from the pancreas, with a characteristic acinar arrangement. The nuclei are stained dark blue, and the cytoplasm and extracellular matrix are stained pink. There are several small, pale, amorphous deposits scattered throughout the tissue, which are characteristic of amyloid. These deposits are most prominent in the interstitial spaces between the glandular units. The overall appearance is that of a pancreatic islet or a similar glandular structure with amyloid deposits.

Detection of early deposits which are small is most challenging
Second opinion if initial pathology reported as negative

Pathology of Familial amyloidoses:

1. Detection of amyloid in the index (first in the family) patient
 - lack of a family history
 - new mutation
2. Examination of family members/known carriers
 - experience from domino liver transplants
3. Staging, definition of organ involvement
4. Education, increased awareness ...