

Solutions to [CASTS – A Diagnostic Clue](#)

1. Hyaline Casts

These casts are comprised of uniform eosinophilic material with sharp edges, typically within the distal nephron. By electron microscopy, they are composed of granular, electron-dense material. Admixed fibers with an appearance similar to amyloid may be seen. They likely represent Tamm-Horsfall (uromodulin) protein, the “framework” upon which this and other casts can form. Uromodulin is responsible for the strong PAS positivity seen in these casts. In contrast, the casts in myeloma cast nephropathy are often PAS negative. Similarly, trichrome usually stains these casts blue, as opposed to the red of myeloma casts. Readers of eAJKD may recall that uromodulin is NOT required for the formation of casts (see [prior quiz](#)). Hyaline casts are the most common type of cast, and may be seen in association with any type of kidney disease. They may be less common in the setting of proliferative or necrotizing glomerulonephritis.

False statement: *A. Diagnostic of amyloid when positive for Congo Red with apple-green birefringence under polarized light.*

Casts like these have been known to show false Congo Red positivity. A definitive diagnosis of amyloid should be made on deposition within tissue only.

2. Bile Casts

Pigmented casts fall in to two major categories. Brownish casts are usually due to the presence of myoglobin or hemoglobin. Hemoglobinuria may result from acute hemolysis (eg, transfusion reaction, malaria, quinine, or paroxysmal hemoglobinuria). Myoglobinuria is usually seen in association with skeletal muscle injury. Differentiation of myoglobinuric versus hemoglobinuric casts may be accomplished by immunohistochemistry and through examination of blood and urine. However, in this example, the pigmented casts are greenish, and thus represent the second and less common category of pigmented tubular

casts—bile casts. Patients with markedly elevated bilirubin levels may develop so-called bile nephrosis. These casts may also be seen in the context of hepatorenal syndrome. Typically, tubular injury does not develop until bilirubin levels are greater than 20 mg/dL. These casts usually have a more green hue than myoglobin casts, and will be positive by the infrequently available Hall stain. Prior to formalin fixation, they are typically more yellowish. They often show marked retraction artifact, and do not fill the tubular lumen on histologic section.

False statement: *B. Positive for myoglobin by immunohistochemistry.*

Bile stained casts will be positive by Hall stain and will be negative for myoglobin by immunohistochemistry. Myoglobin positive casts are seen in association with rhabdomyolysis.

3. Red Blood Cell Casts

These casts are seen in association with glomerular bleeding due to capillary wall disruption, and are especially present when bleeding is brisk. Accordingly, they are most commonly seen in association with IgA nephropathy or ANCA associated pauci-immune crescentic glomerulonephritis. The erythrocytes seen in these casts can show dysmorphic features and various stages of degeneration and compaction, appearing as “ghosts” or fragments, often in association with proteinaceous debris. Unlike hemoglobin casts, the outlines of the red blood cells are plentiful.

False statement: *C. These casts are usually positive for IgA.*

While red blood cell casts are often seen in association with IgA nephropathy, the casts themselves, in contrast to hyaline or granular casts, are typically IgA negative.

4. White Blood Cell Casts

These casts are formed by migration of white blood cells across the tubular wall and may be associated with intraepithelial inflammatory cells (“tubulitis”) as well as intraluminal apoptotic cells, cellular debris, and/or bacteria. This non-specific inflammatory response can be seen in a wide variety of situations, but is usually indicative of acute kidney injury. These casts can be seen in the context of an active glomerulonephritis, and in these cases are attributed to it, rather than a second process. Prominent neutrophils present within the epithelium (“tagging” along the tubular basement membranes) and in the lumen (“pus casts”), and associated with microabscesses, are characteristic of an infectious acute pyelonephritis. Special stains for microorganisms have a very low sensitivity as organisms are usually quite sparse. Scattered “pus casts” may be present in “acute tubular necrosis”, drug associated acute interstitial nephritis, and occasionally in end-stage kidneys without particular diagnostic significance. In acute cellular rejection, WBC casts are typically composed of T-cells and macrophages, but neutrophils, eosinophils, and plasma cells may be prominent, particularly in “late” rejection. Interstitial infiltrates in rejection typically resolve before the tubulitis/casts.

False statement: *D. Not seen in myeloma cast nephropathy.*

Myeloma cast nephropathy is identified by its distinctive casts, that are often surrounded by reactive tubular cells and multi-nucleated giant cells of macrophage origin. These casts, however, may be infrequent. In other areas, prominent “non-specific” mononuclear or neutrophilic WBC casts may be present.