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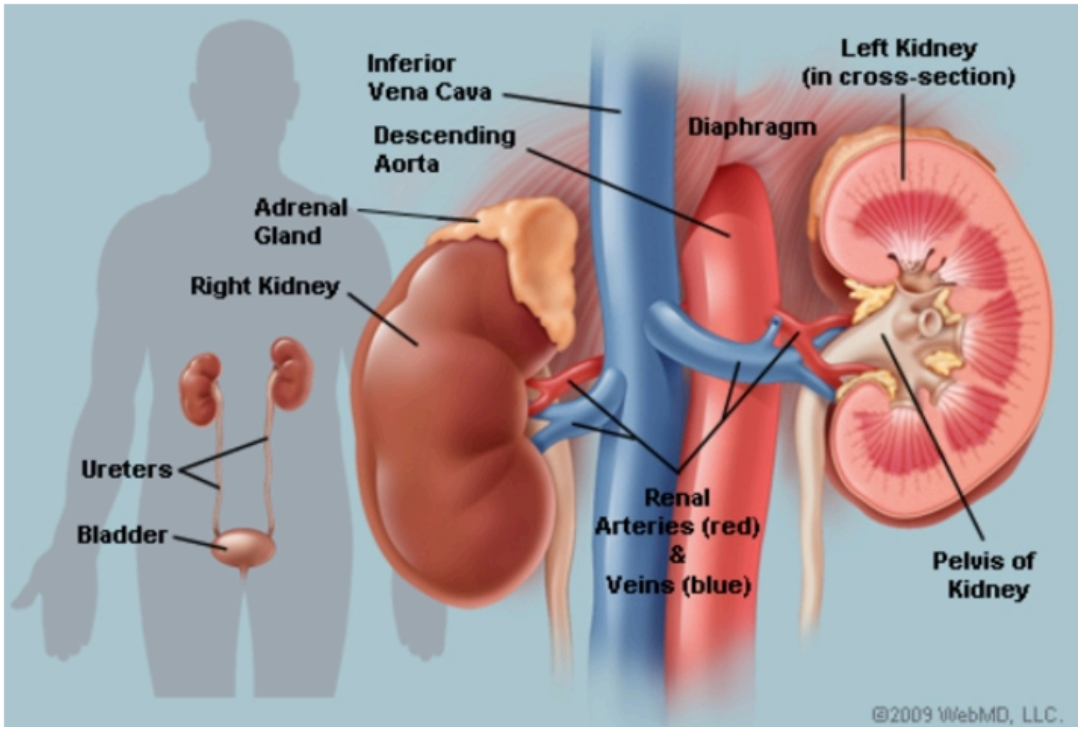
TOPICS TO COVER

- Kidney 101
- How Myeloma can affect the kidneys
- How to follow and interpret kidney labs
- Kidney treatment prognosis
- Prevention & next steps
- Questions and answers

KIDNEY 101



- The kidneys are made up of filters
- Blood passes through the filters
- Waste products are eliminated through the urine and purified blood is returned to the body
- The kidneys regulate levels of minerals and electrolytes in the blood
- The kidneys regulate fluid levels in the body

Poor kidney function leads to

1) Excess buildup of minerals and electrolytes in the blood

2) Fluid excess in the body

Often, people with kidney disease are asymptomatic until the kidney function is less than 15 – 20%

- **Kidney Disease stages are based on the GFR level. The Glomerular Filtration Rate is how much blood passes through the kidney per minute.**

GFR (ml / min)	Chronic Kidney Disease (CKD) Stage
> 90 (+ another kidney abnormality)	CKD I
60 - 89	CKD II
30 - 59	CKD III
15 - 29	CKD IV
< 15	CKD V

HOW BIG IS THE PROBLEM?

- Up to 50% of people with multiple myeloma have some form of injury to their kidneys

- Kidney injury can be treated, especially if it is detected early. Irreversible kidney injury is associated with worse overall outcomes

WHAT ARE SYMPTOMS OF KIDNEY DISEASE DUE TO MULTIPLE MYELOMA?

Patients may not have any symptoms and the kidney disease may only be detectable on blood and urine tests

- Decreased urine output
- Tea-colored urine
- Foamy urine
- Swelling
- Other signs: New high blood pressure

HOW DO WE CHECK FOR KIDNEY DISEASE?

Blood tests

Serum creatinine level (found on the basic metabolic panel)

Serum blood urea nitrogen level

Estimated glomerular filtration rate (GFR)

Urine tests

Blood

Protein

Key point: The urine dipstick only captures albumin protein. In myeloma the kidney may be excreting non-albumin protein, IE light chain proteins.

24-hour collection

Discard the first void and collect the last void! For example, if the collection is from Monday 8am to Tuesday 8am, the patient will pass urine at 8am on Monday and discard it. Then collect all urine until Tuesday at 8am when the patient will void one last time and collect that urine.

Random urine collection

Submit a urine sample around the same time of day for each collection. Heavy exercise or high salt meal can elevate the albumin protein levels in the urine

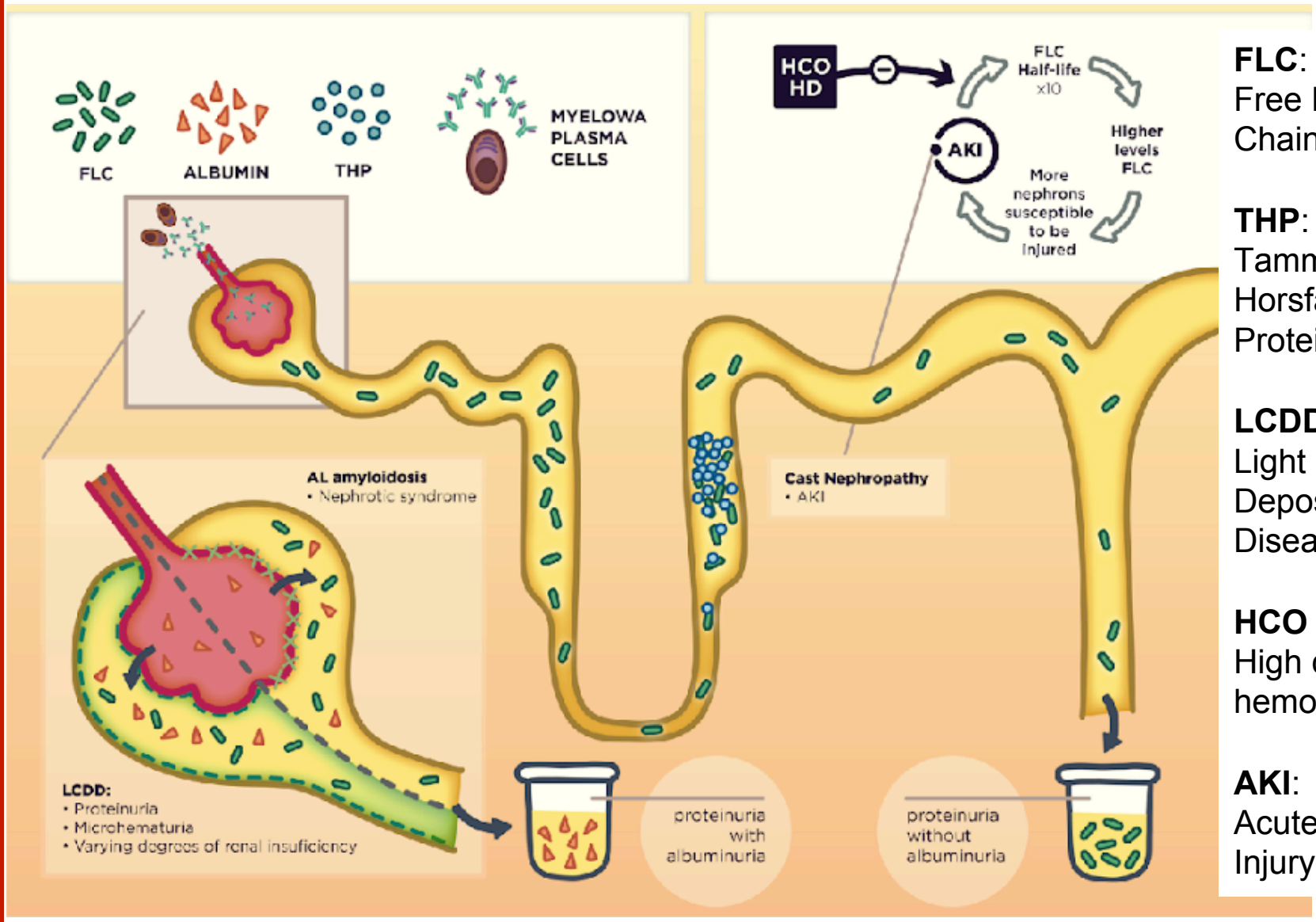
WHAT DO WE DO WITH THE BLOOD AND URINE TEST RESULTS?

Using the blood and urine results we can determine if

1) **Is there kidney injury?**
2) **Is it acute or chronic injury? ****
3) **What part of the kidney is affected?**

****This determination is based on trends in kidney function over time**

WHAT CAUSES KIDNEY INJURY IN MULTIPLE MYELOMA?



FLC: Free Light Chain

THP: Tamm Horsfall Protein

LCDD: Light Chain Deposition Disease

HCO HD: High cut off hemodialysis

AKI: Acute Kidney Injury

Fava et al, Clinical Kidney Journal. December 2018

WHAT KIND OF KIDNEY DISEASE IS ASSOCIATED WITH MULTIPLE MYELOMA?

Kidney disease due to immunoglobulins

1. Cast Nephropathy
2. Monoclonal immunoglobulin deposition disease (MIDD)
3. Light chain amyloidosis
4. Cryoglobulinemic glomerulonephritis
5. Thrombotic microangiopathy
6. Others (rarely membranous or minimal change disease; fibrillary)

WHAT KIND OF KIDNEY DISEASE IS ASSOCIATED WITH MULTIPLE MYELOMA?

Kidney disease due to other myeloma effects

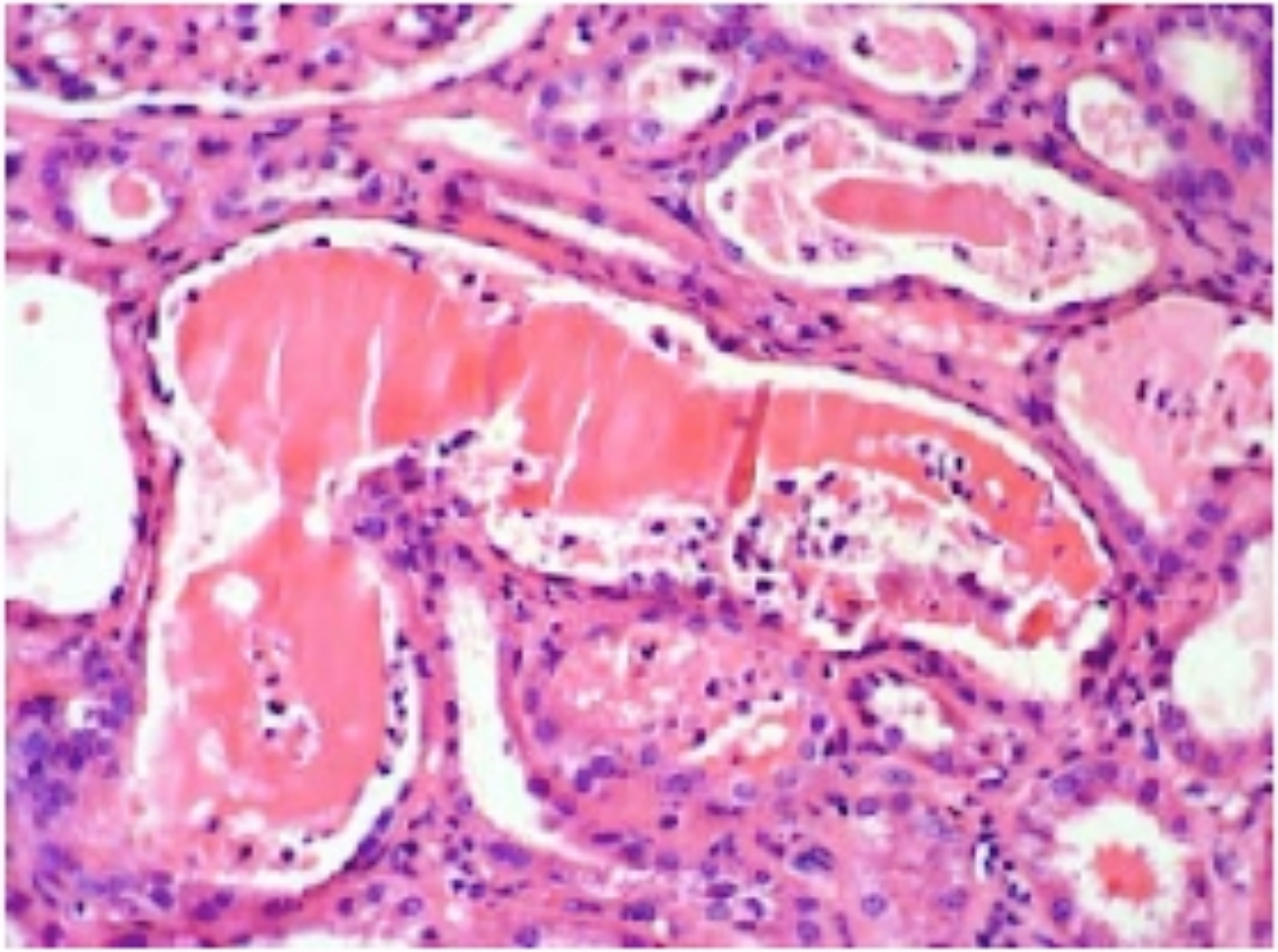
1. High blood calcium levels because myeloma affects the bones
2. Low fluid levels in the body (volume depletion)
3. Tumor cells breaking apart (tumor lysis) and releasing toxic levels of minerals and electrolytes (uric acid, phosphorus)

All patients with monoclonal gammopathy with unclear cause of renal insufficiency

Exceptions

1. Bland urine sediment, Sflc concentration > 1500mg/L, predominance of monoclonal light chains in urine [1] likely cast nephropathy
2. Fanconi syndrome [1] likely proximal tubulopathy
3. Albuminuria and non-renal tissue with al amyloid [1] likely AL amyloidosis

KIDNEY BIOPSY FOR CAST NEPHROPATHY “MYELOMA KIDNEY”



Kidneypathology.com

FOCUS ON CAST NEPHROPATHY

Myeloma Cast Nephropathy, also called light chain cast nephropathy (LCCN) is the most common form of kidney disease in patients with multiple myeloma

High levels of light chains that exceed the kidneys capacity to degrade them, enter the urinary filtrate and join other kidney proteins to form a precipitate or "cast"

Time for a short break for questions…

TREATMENT OF MYELOMA ASSOCIATED KIDNEY DISEASE

- Urgent malignant hematology consult
- Correct hypercalcemia
- Correct volume depletion. Goal UOP > 3L/ day
- High dose Steroids
- Bortezomib-based chemotherapy regimen
- Plasmapheresis?  controversial
- High-cut off dialysis?  controversial, not widely available in US.

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Reduce free light chain burden a quickly as possible

60% free light chain reduction by DAY 21 is associated with kidney recovery in 80% of patients

Tools:

Bortezomib-based therapy; plasma exchange? high cut-off hemodialysis?

TREATMENT OUTCOMES FOR MYELOMA PATIENTS WITH KIDNEY DISEASE THAT REQUIRES DIALYSIS

Bortezomib-based regimens can *reverse dialysis-dependence* in patients who have severe kidney injury from multiple myeloma

Patients who receive bortezomib along with dexamethasone and cyclophosphamide have better kidney outcomes than patients who receive other therapies. This **"triplet" regimen is associated with up to 60% of patients discontinuing dialysis therapy**.

Patients who are able to discontinue dialysis therapy have better overall outcomes

Bridoux et al. MYRE. Blood 2016
Dimopoulos et al. Blood Cancer Journal. 2017