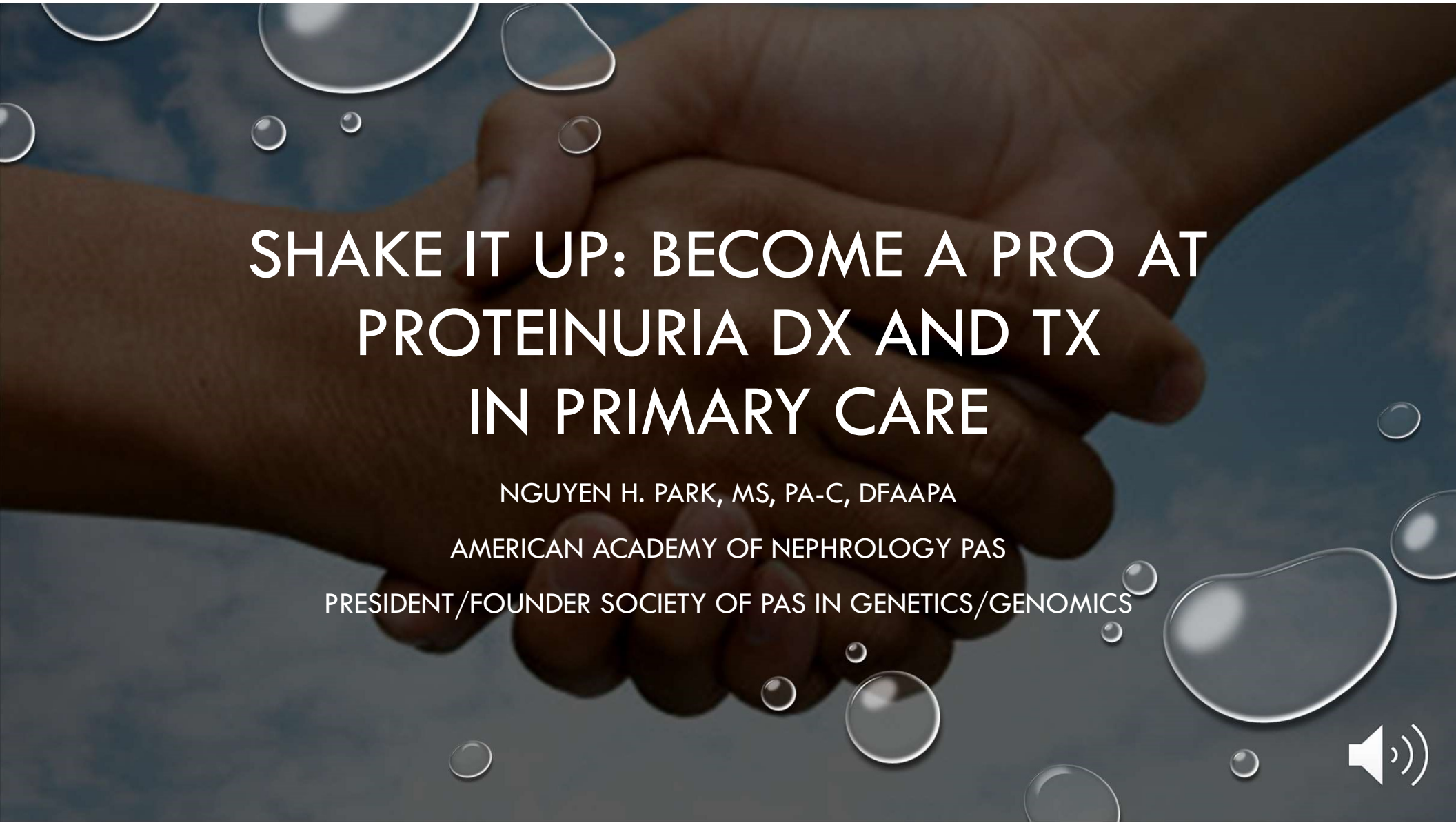

# SHAKE IT UP: BECOME A PRO AT PROTEINURIA DX AND TX IN PRIMARY CARE

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# DISCLOSURES

- MS. PARK HAS NO RELEVANT[S]FINANCIAL RELATIONSHIPS WITH COMMERCIAL INTERESTS TO REPORT.

# OBJECTIVES

1. Recognize the incidence of proteinuria and CKD in the primary care setting.

2. Interpret laboratory findings to differentiate between tubular and glomerular proteinuria to assist in narrowing the differential diagnosis.

3. Describe the optimal management of proteinuria for the prevention of long-term sequelae including hemodialysis and renal transplant.

# WHY BECOME A PROTEINURIA PRO?

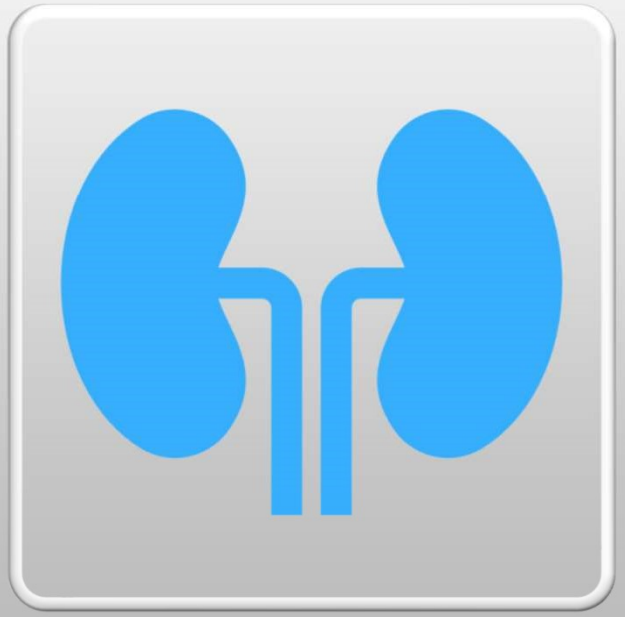
# KIDNEY DISEASE: AKI/CKD

DEFINITION

INCIDENCE

# ACUTE KIDNEY DISEASE (AKD)

- KDIGO DEFINITION:
- AKD, GFR < 60 ML/MIN/1.73 $M^2$, OR MARKERS OF KIDNEY DAMAGE FOR ≤ 3 MONTHS AND >48 HRS



# ACUTE KIDNEY INJURY (AKI)

*SERUM CREATININE (SCR)

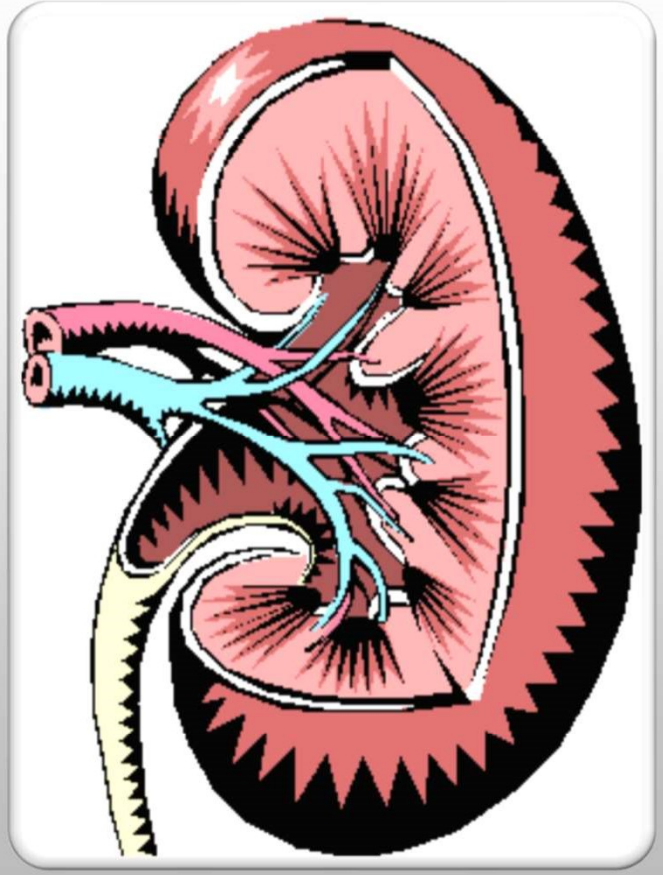
Oliguria for > 6 hours

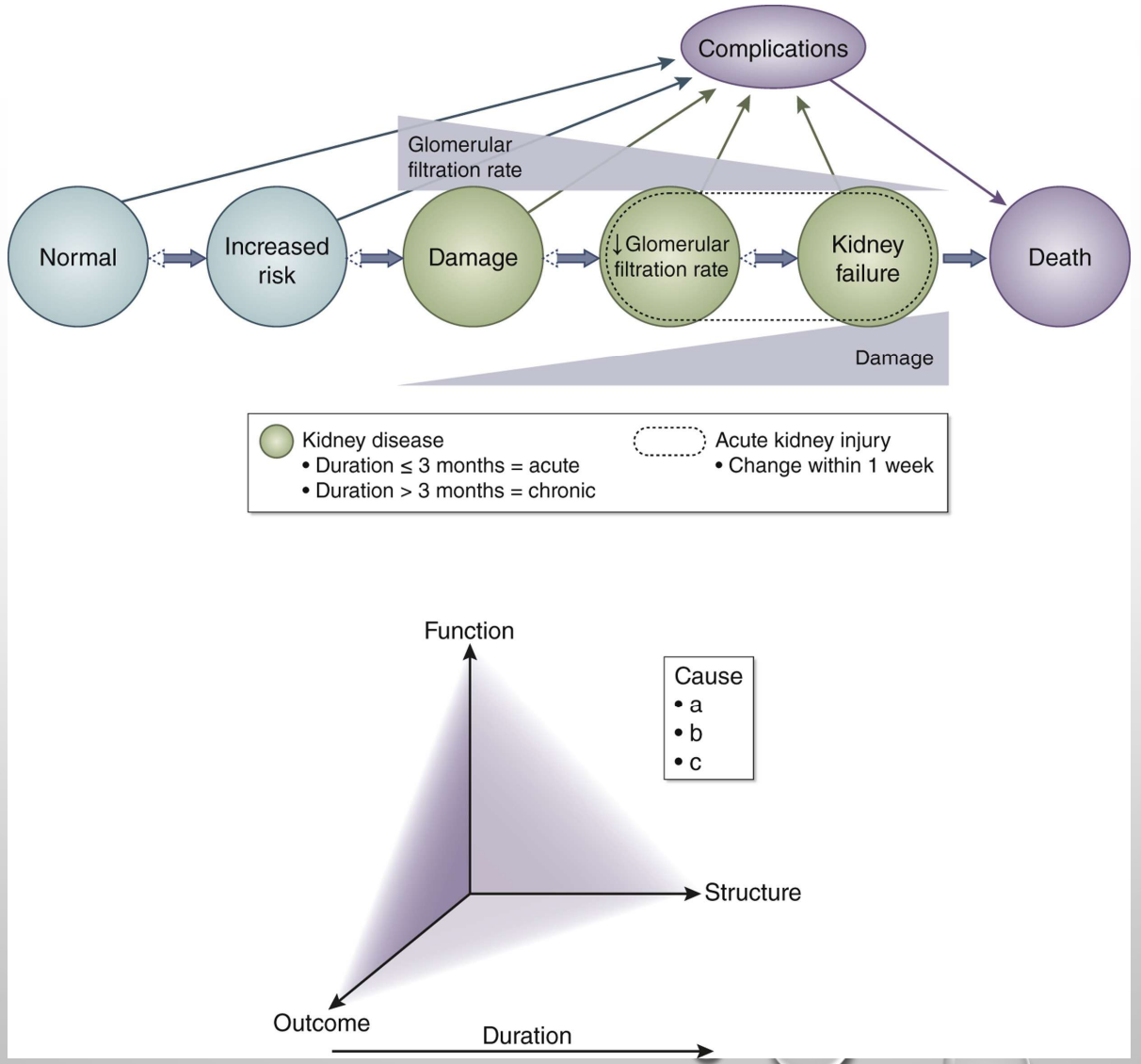
Rise in sCr* by > 0.3 mg/dL in 2 days

Rise in sCr* by > 50% in 1 week

# CKD, DEFINED

BASED ON THE PRESENCE OF EITHER KIDNEY DAMAGE OR DECREASED KIDNEY FUNCTION FOR 3 OR MORE MONTHS, IRRESPECTIVE OF CAUSE.






*Kidney International* DOI: (10.1016/j.kint.2020.02.010)

| Stage | Description | Level of eGFR (mL/minute per 1.73 $m^2$) |
|---|---|---|
| 1 | Kidney damage with normal or high eGFR | ≥90 |
| 2 | Kidney damage with normal or mild decreased eGFR | 60–89 |
| 3 | Moderately to severely decreased eGFR | 30–59 |
| 4 | Severely decreased eGFR | 15–29 |
| 5 | Kidney failure | <15 (or dialysis) |

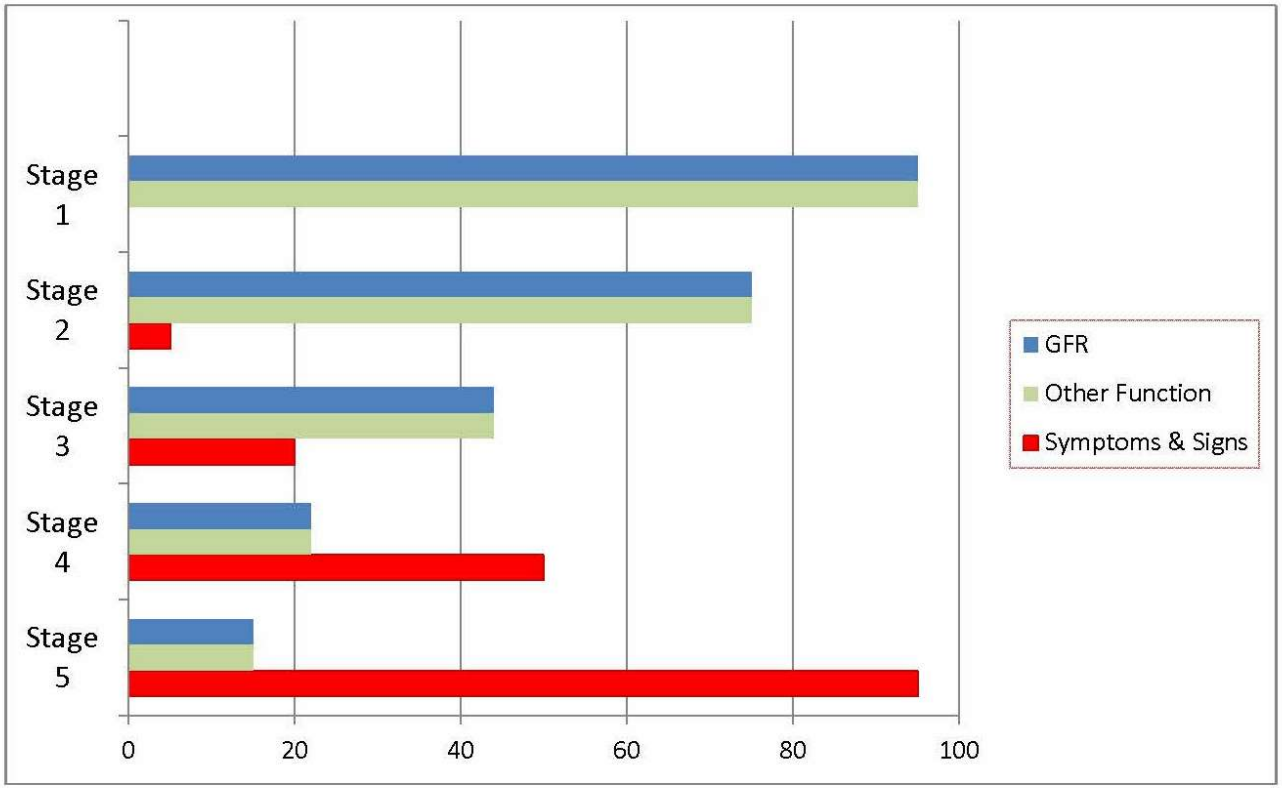
CKD Classification based upon Glomerular Filtration Rate and Albuminuria, revised (KDIGO 2013)

| GFR Stages | GFR (mL/min/1.73 $m^{2)}$ | Terms |
|---|---|---|
| G1 | >/=90 | Normal or high |
| G2 | 60 to 89 | Mildly decreased |
| G3a | 45 to 59 | Mildly to moderately decreased |
| G3b | 30 to 44 | Moderately to severely decreased |
| G4 | 15 to 29 | Severely decreased |
| G5 | <15 | Kidney failure (add D if treated by dialysis |
| **Albuminuria Stage** | **AER (mg/day)** | **Terms** |
| A1 | <30 | Normal to mildly increased (may be subdivided for risk prediction) |
| A2 | 30 to 300 | Moderately increased |
| A3 | >300 | Severely increased (may be subdivided into nephrotic and nonnephrotic for differential diagnosis, mgmt. and risk prediction) |

# PROTEINURIA AND CKD

- THE KIDNEYS PLAY A MAJOR ROLE IN THE RETENTION OF PLASMA PROTEINS, USING RENAL TUBULES TO REABSORB THEM AS THE PROTEINS PASS THROUGH THE GLOMERULAR FILTRATION BARRIER
- KDIGO CLINICAL PRACTICE GUIDELINES INCLUDE PROTEINURIA IN THE STAGING OF CKD.
- LOWERING PROTEINURIA HAS A PROTECTIVE EFFECT AGAINST FURTHER LOSS OF KIDNEY FUNCTION.

# Chronic Kidney Disease Stages, Symptoms, and Signs



# HOW IMPORTANT IS PROTEINURIA?

- INDIVIDUALS WITH A URINE ACR >30 MG/G (OR EQUIVALENT) HAVE A SIGNIFICANTLY INCREASED RISK FOR ALL-CAUSE AND CARDIOVASCULAR MORTALITY, ESRD, AKI AND CKD PROGRESSION COMPARED WITH THOSE WHO HAVE A LOWER ACR **EVEN WHEN EGFR IS NORMAL**
- INDIVIDUALS WITH AN ACR OF 30 TO 299 MG/G (3.4 TO 34 MG/MMOL) OR EQUIVALENT AND AN EGFR OF 90 TO 105 ML/MIN PER 1.73 $M^2$ HAD AN 11-FOLD HIGHER RELATIVE RISK FOR ESRD THAN THOSE WHOSE EGFR WAS SIMILAR BUT WHOSE ACR WAS BELOW 30 MG/G.

# WHAT DO THE NUMBERS TELL US?

- OVERALL PREVALENCE OF CKD IN THE GENERAL POPULATION IS APPROXIMATELY 14 PERCENT.
- MORE THAN 661,000 AMERICANS HAVE KIDNEY FAILURE. OF THESE, 468,000 INDIVIDUALS ARE ON DIALYSIS, AND ROUGHLY 193,000 LIVE WITH A FUNCTIONING KIDNEY TRANSPLANT.
- COMPARED TO CAUCASIANS, ESRD PREVALENCE IS ABOUT 3.7 TIMES GREATER IN AFRICAN AMERICANS, 1.4 TIMES GREATER IN NATIVE AMERICANS, AND 1.5 TIMES GREATER IN ASIAN AMERICANS.
- EACH YEAR, KIDNEY DISEASE KILLS MORE PEOPLE THAN BREAST OR PROSTATE CANCER. IN 2013, MORE THAN 47,000 AMERICANS DIED FROM KIDNEY DISEASE.

# MORBIDITY/MORTALITY ASSOCIATED WITH CKD

- RATES OF READMISSION FOR CKD PTS WERE HIGHER THAN THOSE FOR PTS WITHOUT CKD. IN 2013, 22.3 PERCENT OF PTS WITH CKD WERE READMITTED TO THE HOSPITAL WITHIN 30 DAYS, COMPARED TO ONLY 15.8 PERCENT OF THOSE WITHOUT CKD.
- ADJUSTED MORTALITY RATES REMAINED HIGHER FOR MEDICARE PTS WITH CKD (117.9/1,000) THAN FOR THOSE WITHOUT CKD (47.5/1,000); AND THESE RATES INCREASED WITH CKD SEVERITY, ALTHOUGH THIS GAP NARROWED DURING THE PERIOD 2001 TO 2013.
- CVD CONTRIBUTES TO MORE THAN HALF OF ALL DEATHS AMONG PTS WITH ESRD. ARRHYTHMIAS AND CARDIAC ARREST ALONE WERE RESPONSIBLE FOR > 1/3 (37 PERCENT) OF CVD DEATHS.

# WHAT'S THE COST?

MONEY:

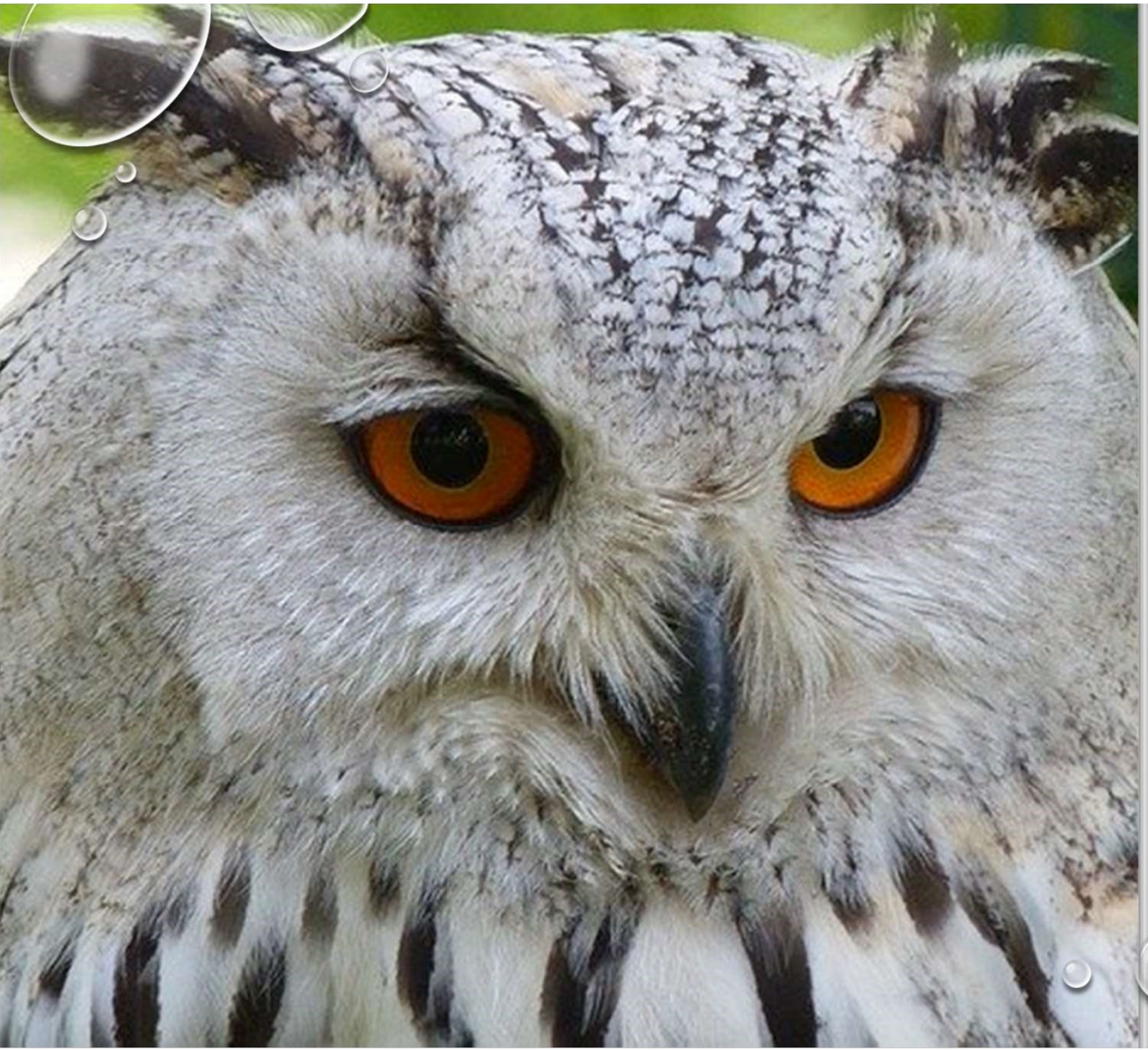
- MEDICARE SPENDING FOR PTS WITH CKD AGES 65 AND OLDER EXCEEDED $50 BILLION IN 2013 AND REPRESENTED 20 % OF ALL MEDICARE SPENDING IN THIS AGE GROUP.
- MORE THAN 70% OF MEDICARE SPENDING FOR CKD PTS AGES 65 AND OLDER WAS INCURRED BY THOSE WHO ALSO HAD DIABETES, CONGESTIVE HEART FAILURE, OR BOTH.

TIME:

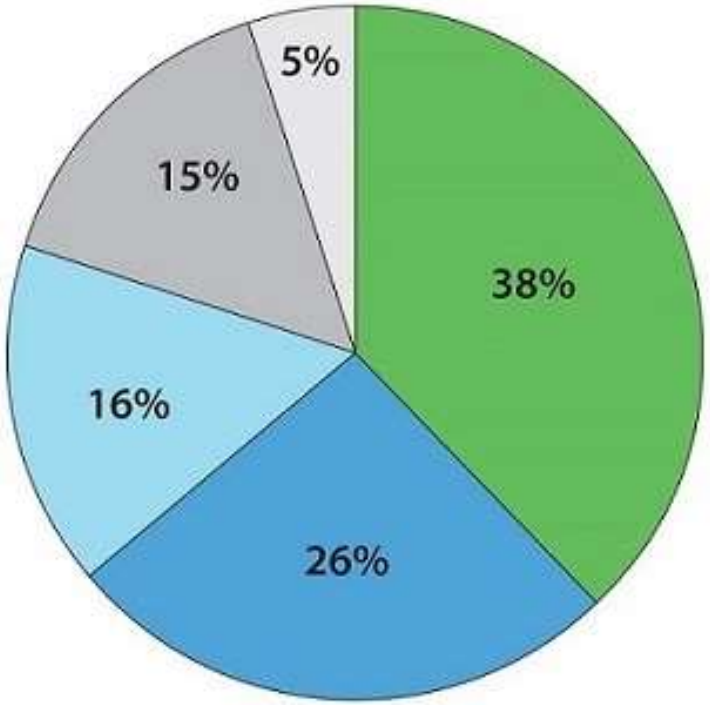
- AMONG CANDIDATES NEWLY WAIT-LISTED FOR EITHER A FIRST-TIME OR REPEAT KIDNEY-ALONE TRANSPLANT IN 2009, THE MEDIAN WAITING TIME TO TRANSPLANT WAS 3.6 YEARS.

# PATIENTS AT RISK

- Who?
- What?
- When?
- Where?
- Why?



WHO DO YOU THINK IS AT RISK?




N=726,331 (all ages, 2016)
Source: US Renal Data System
*Includes polycystic kidney disease, among other causes.

# WHAT?

..IS PROTEINURIA?

..KIND OF PROTEIN CAN BE FOUND?

..DO THESE DIFFERENT TYPES OF PROTEIN AND THEIR LEVELS MEAN?

# WHAT IS NORMAL/ ABNORMAL?

- Normal urinary protein excretion is <150 mg/24 hours and consists mostly of secreted proteins such as Tamm-Horsfall proteins.
- The normal mean albumin excretion rate (AER) is 5-10 mg/day, with an AER of >30 mg/day considered **abnormal.**
- AER btw 30 to 300 mg/day is called moderately increased albuminuria (AKA microalbuminuria).
- Levels > 300 mg/day are called severely increased albuminuria (aka macroalbuminuria).
- Albuminuria that persists for 3 months is considered CKD.

# PROTEINURIA CAN BE DIFFERENTIATED ON THE BASIS OF ANY OF THE FOLLOWING



- AMOUNT OF PROTEIN (NEPHROTIC OR NON-NEPHROTIC)
- TYPE OF PROTEIN (ALBUMINURIA OR LOW MOLECULAR WEIGHT PROTEINURIA)
- UNDERLYING PATHOLOGICAL DAMAGE (GLOMERULAR VS NON-GLOMERULAR).

# AMOUNT OF PROTEIN

- **NEPHROTIC-RANGE PROTEINURIA:**
- > 3.5 G OF PROTEIN EXCRETED IN THE URINE OVER 24 HOURS

- **NON-NEPHROTIC**
- < 3.5 G OF PROTEIN EXCRETED IN THE URINE OVER 24 HOURS

# PROTEINURIA CLASSIFICATIONS

- Tubular
- Overflow
- Glomerular

# TUBULAR PROTEINURIA

- A RESULT OF TUBULOINTERSITIAL DISEASE AFFECTING THE PROXIMAL RENAL TUBULES AND INTERSTITIUM.
- DECREASED PROXIMAL REABSORPTION OF PROTEINS—IN PARTICULAR, LOW MOLECULAR WEIGHT (LMW) PROTEINS (GENERALLY BELOW 25,000 DALTONS) SUCH AS BETA-2 MICROGLOBULIN.
- UNDER NORMAL CONDITIONS THESE PROTEINS ARE COMPLETELY REABSORBED IN THE PROXIMAL TUBULES. THE AMOUNT OF PROTEINURIA IS USUALLY < 2 G/DAY AND DIPSTICK RESULTS MAY BE NEGATIVE.

# CAUSES OF TUBULAR PROTEINURIA

- ACUTE INTERSTITIAL NEPHRITIS
- IMMUNOSUPPRESSIVE AGENTS
- ANALGESICS
- CRYOGLOBULINEMIA
- SJÖGREN SYNDROME

# OVERFLOW PROTEINURIA

- MOST COMMONLY ASSOCIATED WITH INC PRODUCTION OF ABNORMAL LMW PROTEINS THAT EXCEEDS THE REABSORPTION CAPACITY OF THE PROXIMAL TUBULE, LEADING TO SPILLING OF THE PROTEIN INTO THE URINE

- THESE LMW PROTEINS CAN BE TOXIC TO THE TUBULES -→ AKI

# GLOMERULAR PROTEINURIA

Glomerular proteinuria associated with pathological damage to the glomerulus is categorized by protein quantity:

Meaning, the more severe the proteinuria, the more significant the glomerular disease.

The primary protein lost is albumin.

These patients require close follow-up and may need a kidney biopsy if they have abnormal urine microscopy results and/or impairment of kidney function.

# ALBUMINURIA

- ALBUMINURIA REFLECTS INCREASED GLOMERULAR PERMEABILITY TO MACROMOLECULES.
- ALBUMINURIA MAY REFLECT PRIMARY KIDNEY DISEASE OR KIDNEY INVOLVEMENT IN SYSTEMIC DISEASE.
- IN PARTICULAR, ALBUMINURIA MAY REPRESENT WIDESPREAD ENDOTHELIAL DYSFUNCTION, SUCH AS CAN BE SEEN WITH HYPERTENSION, DIABETES, HYPERCHOLESTEROLEMIA, SMOKING, OBESITY, AND OTHER DISORDERS.

# GLOMERULAR PROTEINURIA CLASSIFICATION

- NO PATHOLOGICAL DAMAGE TO THE GLOMERULUS:
  - TRANSIENT AND ORTHOSTATIC PROTEINURIA
- PATHOLOGICAL DAMAGE TO GLOMERULUS, USUALLY SEEN WITH:
  - ACTIVE URINE SEDIMENT - DYSMORPHIC RED BLOOD CELLS AND RED CELL CASTS
  - HYPOALBUMINEMIA
  - LIPIDURIA
  - HYPERLIPIDEMIA
  - EDEMA
  - ABNORMAL RENAL FUNCTION
  - HYPERTENSION

# TRANSIENT & ORTHOSTATIC PROTEINURIA

- TRANSIENT PROTEINURIA OCCURS IN PERSONS WITH NORMAL RENAL FUNCTION, BLAND URINE SEDIMENT, AND NORMAL BLOOD PRESSURE. THE QUANTITATIVE PROTEIN EXCRETION IS LESS THAN 1 G/DAY. THE PROTEINURIA IS NOT INDICATIVE OF SIGNIFICANT UNDERLYING RENAL DISEASE; IT MAY BE PRECIPITATED BY HIGH FEVER OR HEAVY EXERCISE, AND IT DISAPPEARS UPON REPEAT TESTING. EXERCISE-INDUCED PROTEINURIA USUALLY RESOLVES WITHIN 24 HOURS.
- ORTHOSTATIC PROTEINURIA IS DIAGNOSED IF THE PATIENT HAS NO PROTEINURIA IN EARLY MORNING SAMPLES BUT HAS LOW-GRADE PROTEINURIA AT THE END OF THE DAY.

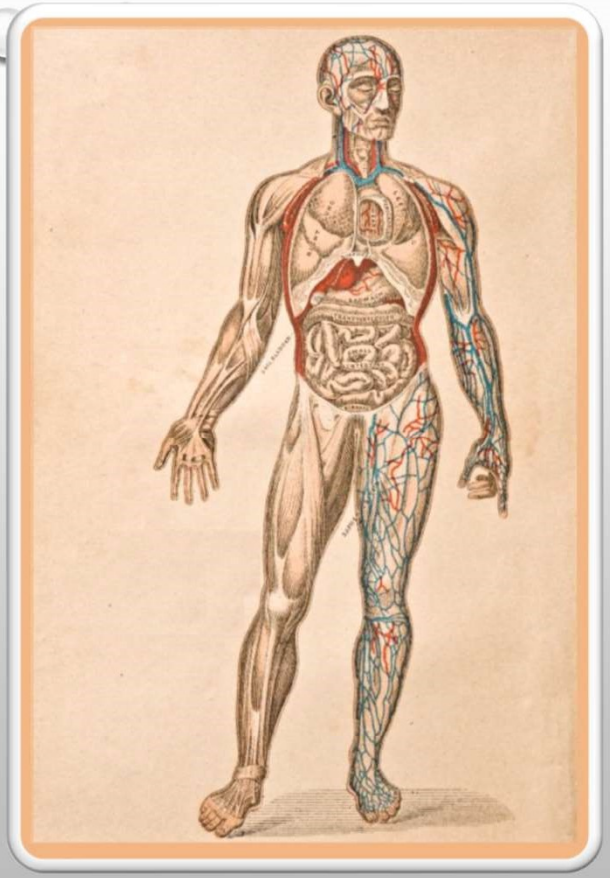


# WHEN IS THE PATIENT AT RISK?

**Table 1. Clinical stages of diabetic nephropathy[3]**

| Stage | GFR | UAE | Blood pressure | Years |
|---|---|---|---|---|
| 1. Hyperfiltration | Super normal | <30 mg/day | Normal | 0 - 5 |
| 2. Microalbuminuria | High normal - normal | 30 - 300 mg/day | Rising | 5 - 15 |
| 3. Overt proteinuria | Normal - decreasing | >300 mg/day | Elevated | 10 - 20 |
| 4. Progressive nephropathy | Decreasing | Increasing | Elevated | 15 - 25 |
| 5. ESKD | <15 mL/min | Massive | Elevated | 20 - 30 |

ESKD = end-stage renal disease; GFR = glomerular filtration rate; UAE = urinary albumin excretion.



# WHERE DO WE START?





# IT'S ELEMENTARY, MY DEARS!

- WHAT CAN WE DO?


# EASY: URINE DIPSTICK

| Dipstick Protein reading | Protein excretion gm/24 hours | Protein excretion mg/dL |
|---|---|---|
| Negative | <0.1 | <10 |
| Trace | 0.1-0.2 | 15 |
| 1+ | 0.2-0.5 | 30 |
| 2+ | 0.5-1.5 | 100 |
| 3+ | 2.0-5.0 | 300 |
| 4+ | >5.0 | >1000 |

# WHAT DOES A URINE DIPSTICK FOR PROTEIN TELL YOU?

Primarily detects albumin

Albuminuria is seen in **glomerular** proteinuria

False-positive results can occur with:

recent exposure to iodinated radiocontrast agents, alkaline urine, and gross hematuria.

# SPOT URINE ALBUMIN/CREATININE RATIO (UACR)

Normal urine ACR in young adults is <10 mg/g.

Albuminuria is a marker of kidney damage → increased glomerular permeability, when urine ACR >30 mg/g (3.4 mg/mmol).

Urine ACR categories 10-29, 30-300 and >300 mg are termed "mildly increased, moderately increased, and severely increased" respectively.

Urine ACR >2200 mg/g accompanied by signs/sx of nephrotic syndrome (low serum albumin, edema and high serum cholesterol).

Threshold value corresponds approximately to urine dipstick values of trace or 1+, depending on urine concentration

High urine ACR can be confirmed by urine albumin excretion in a timed urine collection

# SPOT URINE PROTEIN/CREATININE RATIO (UPCR)

Detects all proteins, not just albumin.

Proteinuria involving non-albumin proteins as well as albumin is seen more in tubular or overflow proteinuria.

# 24-HOUR URINE COLLECTION

The gold standard for quantification of proteinuria

Normal amount of protein in the urine is <150 mg/day.

Results considered reliable based on comparison with the typical amount of creatinine secreted/kilogram of lean body mass.

Gender differences: On average, males secrete 20-25 mg/kg per day and females secrete 15-20 mg/kg.

Age considerations: after the age of 50 years, lean body muscle mass is lost, so these estimates can be inaccurate in older patients.

# HOW DO WE PUT THIS ALL TOGETHER?

# WORKUP TO DETERMINE WHETHER PROTEINURIA MAY BE GLOMERULAR IN ORIGIN

- URINE MICROSCOPY
- URINE COLLECTION (24 H) FOR QUANTIFICATION OF ALBUMIN (OR PROTEIN) EXCRETION AND CREATININE CLEARANCE –SPOT PROTEIN/CREATININE RATIO CAN BE USED FOR SUBSEQUENT ASSESSMENTS
- SERUM CREATININE, ALBUMIN, HDL CHOLESTEROL AND LDL CHOLESTEROL, GLUCOSE, HGB A1C
- AUTOANTIBODY DETERMINATIONS - IF CLINICALLY INDICATED, INCLUDING ANTISTREPTOLYSIN O TITERS, ANTINUCLEAR ANTIBODIES (ANAS), ANTI-DNA ANTIBODIES, COMPLEMENT LEVELS (C3 AND C4), ANTI-PHOSPHOLIPASE A1 RECEPTOR AUTOANTIBODY, AND CRYOGLOBULINS
- HEPATITIS B, HEPATITIS C, AND HIV SEROLOGIES - IF INDICATED
- URINE AND PLASMA PROTEIN ELECTROPHORESIS FOR LIGHT CHAINS - IF INDICATED
- ANTI–GLOMERULAR BASEMENT MEMBRANE (ANTI-GBM) ANTIBODIES AND ANTINEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA)

# TREATMENT OF PROTEINURIA

- #1 TREAT THE UNDERLYING CAUSE:  DM, HTN, SLE, CANCER, MULTIPLE MYELOMA, MEDICATIONS…
- TARGET BP < 125/75 MM HG IN PTS WITH PROTEINURIA OF GREATER THAN 1 G/DAY
- NORMALIZATION OF SYSTEMIC BP IN A PT WITH HTN SHOULD RESULT IN A REDUCTION IN INTRAGLOMERULAR PRESSURE AND A FALL IN ALBUMINURIA.
- HOWEVER: SOME VASODILATORY ANTIHYPERTENSIVES (EG, HYDRALAZINE, NIFEDIPINE) DILATE THE AFFERENT ARTERIOLE, WHICH MAY ATTENUATE THE REDUCTION IN INTRAGLOMERULAR PRESSURE DESPITE THE FALL IN ARTERIAL BP. THUS THESE AGENTS MAY NOT REDUCE PROTEINURIA TO THE SAME DEGREE.

# TX OF HTN: CALCIUM CHANNEL BLOCKERS (CCB)

- NON-DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS (NDCCBS), DILTIAZEM AND VERAPAMIL, DEC PROTEINURIA GREATER THAN DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS (DCCBS).
- THE DIFFERENCE: DCCBS AFFECT ONLY THE AFFERENT ARTERIOLE AND NOT THE EFFERENT, WHEREAS NDCCBS AFFECT BOTH.
- THE EFFECT OF ACTION ON THE AFFERENT ARTERIOLE ONLY: IMPAIRED AUTOREGULATION AND INCREASED INTRAGLOMERULAR PRESSURE, LEADING TO KIDNEY DAMAGE.
- L TYPE CALCIUM CHANNELS ARE FOUND ONLY IN THE PROXIMAL TUBULE AND ARE THE PRIMARY CHANNEL AFFECTED BY DCCBS. HOWEVER, N AND T TYPE CALCIUM CHANNELS ARE FOUND IN BOTH THE AFFERENT AND EFFERENT ARTERIOLE;
- THE NEWER NDCCBS SUCH AS EFONIDIPINE AND BENEDIPINE WORK ON THESE CHANNELS. THE NEWER NDCCBS, USED IN COMBINATION WITH ARBS, HAVE BEEN SHOWN TO REDUCE PROTEINURIA.

# TREATMENT OF PROTEINURIA: RAAS BLOCKADE

- Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) reduce intraglomerular pressure by inhibiting angiotensin II–mediated efferent arteriolar vasoconstriction.
- Proteinuria-reducing effect independent of their antihypertensive effect.
- Add a mineralocorticoid receptor antagonist (MRA) such as eplerenone or spironolactone.
- MRA therapy associated with a 3 - 8x increased risk for hyperkalemia.

# TREATMENT OF PROTEINURIA: DIURETICS

Pts may require increased doses for the drug to be delivered to the renal tubule.

A combination of diuretics acting at different sites of the nephron can be tried.

If the edema is due to marked hypoalbuminemia, aggressive diuresis may put the patient at risk of AKI due to intravascular volume depletion.

Refer to nephrology when in doubt regarding best practices of diuretic therapy

# ANTICOAGULANTS

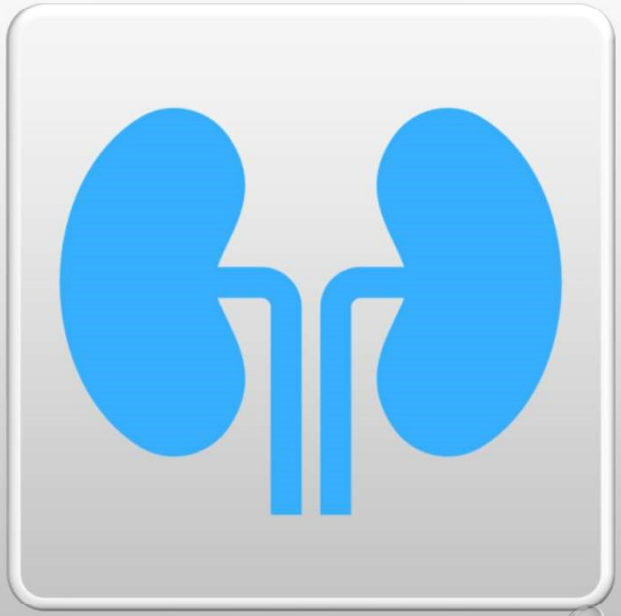
Pts with proteinuria tend to be hypercoagulable due to urinary losses of coagulation inhibitors, such as antithrombin III and protein S and C.

Risk of thrombosis appears to be highest in pts with membranous glomerulonephritis (MGN). Numerous case reports have described renal vein thrombosis (which usu presents as acute onset of gross hematuria and back pain) in pts with MGN.

Guidelines published by KDIGO (2012) recommend tx with warfarin in pts with nephrotic syndrome who have a low serum albumin level (< 2.5 g/dL), especially if the pt has other risk factors for thrombosis.

# IMAGING STUDIES

- RENAL ULTRASONOGRAPHY – IF GLOMERULAR DISEASE IS BEING CONSIDERED, IT IS IMPORTANT TO REVIEW THE SIZE AND ECHOGENICITY OF THE KIDNEYS
- ECHOGENICITY: INC MEANS INC POSS OF UNDERLYING RENAL DISEASE
- SIZE:  KIDNEYS MAY BE TOO SMALL TO SAFELY PERFORM A RENAL BIOPSY



# RENAL BIOPSY

- SHOULD BE CONSIDERED IN ADULT PTS WITH PERSISTENT PROTEINURIA (USUALLY, ABOVE 1 G PER DAY)
- IN CHILDREN, MOST CASES OF NEPHROTIC SYNDROME ARE DUE TO STEROID-SENSITIVE MINIMAL-CHANGE DISEASE.
- IN ADULT PTS WHO HAVE ISOLATED PROTEINURIA OF LESS THAN 1 G/DAY AND NO OTHER INDICATORS OF RENAL DISEASE, MOST NEPHROLOGISTS WOULD PROCEED TO BIOPSY ONLY IF THE DEGREE OF PROTEINURIA INCREASES OR IF THE PT UNDERGOES PROGRESSIVE RENAL DECLINE.

# FREQUENTLY ASKED QUESTIONS

# WHY NOT JUST USE SERUM CREATININE ALONE?

- A RISE IN BLOOD CREATININE LEVELS IS OBSERVED ONLY AFTER SIGNIFICANT LOSS OF FUNCTIONING NEPHRONS.

# CASE EXAMPLE: WHAT DO THESE PTS HAVE IN COMMON?

| | 22 yr old Black male | 58 yr old White male | 80 yr old White female |
|---|---|---|---|
| eGFR (mL/min/1.73 $m^2$) | 98 | 66 | 46 |
| Kidney function | Normal GFR or stage 1 CKD if kidney damage is also present | Stage 2 CKD if kidney damage is also present | Stage 3 CKD |
| Serum creatinine (mg/dL) | **?** | **?** | **?** |

# EXACTLY THE SAME CREATININE LEVELS!

| | 22 yr old Black male | 58 yr old white male | 80 yr old white female |
|---|---|---|---|
| GFR as estimated by the MDRD equation (mL/min/1.73 $m^2$) | 98 | 66 | 46 |
| Kidney function | Normal GFR or stage 1 CKD if kidney damage is also present | Stage 2 CKD if kidney damage is also present | Stage 3 CKD |
| Serum creatinine (mg/dL) | **1.2** | **1.2** | **1.2** |

# WHAT'S THE DIFFERENCE BTW CREATININE CLEARANCE AND GFR?

- GLOMERULAR FILTRATION RATE (GFR) IS GENERALLY CONSIDERED TO BE THE BEST INDEX OF OVERALL KIDNEY FUNCTION, AND DECLINING GFR IS THE HALLMARK OF PROGRESSIVE KIDNEY DISEASE .
- MEASURED GFR VARIES IN NORMAL INDIVIDUALS BY AGE AND SEX, DIETARY PROTEIN INTAKE, AND POSSIBLY BY RACE-ETHNICITY, ALTHOUGH THE MAGNITUDE OF RACIAL VARIATIONS ARE NOT WELL KNOWN.
- CREATININE CLEARANCE (CRCL) IS THE VOLUME OF BLOOD PLASMA CLEARED OF **CREATININE** PER UNIT TIME.
- HOWEVER, CRCL IS SLIGHTLY HIGHER THAN TRUE **GFR** BECAUSE **CREATININE** IS SECRETED BY THE PROXIMAL TUBULE (IN ADDITION TO BEING FILTERED BY THE GLOMERULUS). THE ADDITIONAL PROXIMAL TUBULE SECRETION FALSELY ELEVATES THE CRCL ESTIMATE OF **GFR.**

# WHAT'S THE BEST WAY TO PERFORM A 24-HOUR URINE?

- THE 24-HOUR URINE COLLECTION IS PERFORMED BY VOIDING UPON WAKING AND THEN COLLECTING ALL URINE ON SUBSEQUENT VOIDS UNTIL THE FIRST VOID OF THE NEXT DAY.
- PROVIDE SUFFICIENT NUMBER OF JUGS AND REMIND PTS THEY MUST BE KEPT COOL UNTIL RETURNED TO THE LAB.
- A 24-HOUR URINE COLLECTION SHOWING >3-3.5 G OF PROTEIN IS NEPHROTIC-RANGE PROTEINURIA.

# SHOULD MY PATIENTS WITH PROTEINURIA BE ON A LOW PROTEIN DIET?

- PROTEIN RESTRICTION MAY SLOW THE RATE OF DETERIORATION IN GFR IN PTS WITH GLOMERULAR DISEASES, INCLUDING DIABETIC NEPHROPATHY. THE PRESUMED MECHANISM IS A REDUCTION IN INTRAGLOMERULAR PRESSURE.
- HOWEVER, CONCERN EXISTS THAT PROTEIN-RESTRICTED DIETS MAY INC THE RISK OF PROTEIN MALNUTRITION.
- OTHER METHODS OF REDUCING INTRAGLOMERULAR PRESSURE, SUCH AS THE USE OF ACE INHIBITORS, MAY BE SAFER THAN PROTEIN RESTRICTION.
- MOST NEPHROLOGISTS RECOMMEND NO RESTRICTIONS OR ONLY MILD RESTRICTION IN PROTEIN INTAKE (0.8-1 G/KG DAILY), OR FOLLOWING A PLANT-BASED PROTEIN DIET, THOUGH NO RCT HAVE BEEN PERFORMED STUDYING THIS VS. ANIMAL-BASED PROTEIN.

# WHAT DIET SHOULD MY PATIENTS WITH PROTEINURIA FOLLOW?

As always, the diet to follow is that which allows you to treat the underlying cause of the proteinuria best.

The glomerular capillary pressure can inc in the presence of high sodium intake. For nondiabetic pts with CKD, high dietary salt (>14 g daily) appeared to blunt the antiproteinuric effect of ACE inhibitor therapy and inc the risk for ESRD, independent of BP control.

Pts with nephrotic syndrome &fluid overload should have a salt-restricted diet. A "no-added-salt" diet usually is sufficient, although some patients may need restrictions of as low as 40 mmol/day. Consult a dietician for expert advice.

# WHY ORDER A PROTEIN/CREATININE RATIO (UPCR) OR ALBUMIN/CREATININE RATIO (UACR)?

- THE SPOT ALBUMIN OR PROTEIN–TO-CREATININE RATIO WAS DEVELOPED TO HELP MAKE THE QUANTIFICATION OF PROTEINURIA EASIER AND LESS LABORIOUS.
- HOWEVER, THE RATIO CAN VARY DEPENDING ON THE TIME OF DAY AND THE AMOUNT OF CREATININE EXCRETED.
- A SPOT PROTEIN OR ALBUMIN–TO-CREATININE RATIO OF >3-3.5 MG PROTEIN/MG CREATININE SHOWING >3-3.5 G OF PROTEIN IS NEPHROTIC-RANGE PROTEINURIA.

# WHEN SHOULD I REFER MY PATIENT TO NEPHROLOGY?

Earlier referral is helpful, and preliminary labs/work-up will allow for more efficient diagnosis and start to therapy.

Referral to a nephrologist is indicated for any patient who develops proteinuria, especially those with any adverse prognostic markers (eg, rise in albumin excretion of > 1 g/day), or any worsening in renal function.

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# THANK YOU!

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