



PROTEINURIA

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BUMC INTERNAL MEDICINE RESIDENT LECTURE

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OUTLINE

- IDENTIFICATION
- DEFINITIONS
- CAUSES OF PROTEINURIA
- CLINICAL SIGNIFICANCE
- TREATMENT

IDENTIFICATION

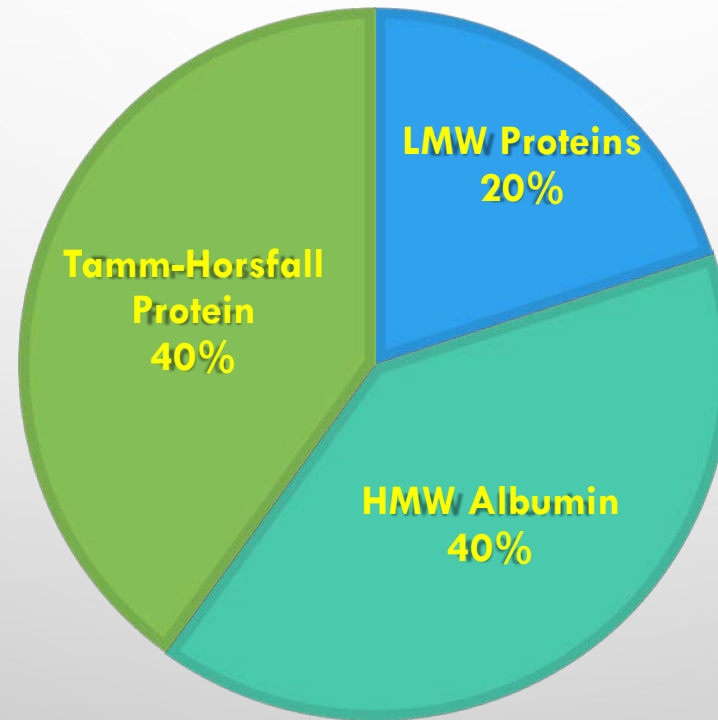
ACTUAL PATIENT QUOTES

- “DOC, I SEE FOAM IN MY URINE”
- “CAN I GET THIS FROM EATING TOO MUCH CHOCOLATE MILK?”
- “I DON’T EVEN DRINK BEER! HOW DID BEER FOAM GET INTO MY URINE?”



WHAT MAKES UP “NORMAL” URINARY PROTEIN?

■ LMW Proteins ■ HMW Albumin ■ Tamm-Horsfall Protein



URINE DIP

Dip detects protein with Bromphenol blue indicator dye - sensitive to albumin and less sensitive to Bence-Jones protein and globulins

TESTS AND READING TIME								
LEU	LEUKOCYTES	Negative		Trace	Small +	Moderate ++	Large +++	
	2 minutes							
NIT	NITRITE	Negative	Positive (any degree of uniform pink color)					
	60 seconds							
URO	UROBILINOGEN	NORMAL mg/dL URINE (1 mg = approx. 1 EU)						
	60 seconds	0.2	1	2	4	8		
PRO	PROTEIN	Negative	Trace	mg/dL	30 +	100 ++	300 +++	2000 or more ++++
	60 seconds							
pH	pH	5.0	6.0	6.5	7.0	7.5	8.0	8.5
	60 seconds							
BLO	BLOOD	Negative	Non-hemolyzed Trace	Hemolyzed Trace	Small +	Moderate ++	Large +++	
	60 seconds							
SG	SPECIFIC GRAVITY	1.000	1.005	1.010	1.015	1.020	1.025	1.030
	45 seconds							
KET	KETONE	Negative	mg/dL	Trace 5	Small 15	Moderate 40	80	Large 160
	40 seconds							
BIL	BILIRUBIN	Negative		Small +	Moderate ++	Large +++		
	30 seconds							
GLU	GLUCOSE	Negative	g/dL (%)	1/10 (ir.)	1/4	1/2	1	2 or more
	30 seconds		mg/dL	100	250	500	1000	2000 or more



Proteinuria threshold detection (+) trace
> 150 mg/24h

PROTEIN URINALYSIS: LIMITATIONS

Factor	False Positive + protein	False Negative - protein
Fluid status	Very concentrated urine	Very dilute urine
Acid/base	Alkaline urine (pH > 7.5)	Acidic urine
Hematuria	Increases	
Infection	+Proteins from organism/bacteria + cellular reactions to infection	
Exercise	Normal increase in urinary albumin excretion	
High fever	Normal increase in urinary albumin excretion	
Vaginal mucus, semen	Non-urinary proteins contaminate specimen	
Non-albumin Urine proteins (BJ proteins/globulins)		Not detected on dip
Drugs	Bleach, acetazolamide, cephalosporins, NaHCO ₃ , PCN, sulfonamides	

URINE DIP & UA PROTEIN QUANTIFICATION

Urine Dipstick Protein Reading	Urinalysis Protein Excretion mg/dL	Protein Excretion mg/ 24 Hours
Negative	< 10	< 100 mg
Trace	15	100 - 300
+1	30	200 – 500
+2	100	500 - 1500
+3	300	2000 - 5000
+4	> 1000	> 5000

PROTEINURIA QUANTIFICATION METHODS

- FOR SPOT URINE, NEED 2 OR MORE SAMPLES 1-2 WEEKS APART TO CONFIRM DX “ PERSISTENT PROTEINURIA”
- UACR: SPOT URINE ALBUMIN / CREATININE RATIO
- UPC OR PCR: SPOT URINE PROTEIN / CREATININE RATIO
- 24 HR URINE COLLECTION
 - ALWAYS GET A URINE CREATININE WHEN YOU ORDER THIS!!!

PROTEINURIA DETECTION METHODS LIMITATIONS

SPOT UACR AND UPC

- LOWER CREATININE IN WOMEN LEADS TO FALSELY HIGHER RATIO
- LOWER CREATININE IN ELDERLY/MALNOURISHED LEADS TO FALSELY HIGHER RATIO
- HIGHER CREATININE IN AA --> UNDERESTIMATES RATIO

24 HR URINE COLLECTION

- CUMBERSOME
- ACCURACY
- VARIATION DURING DAY
- VARIATION WITH RECUMBENCY
- ? NOCTURNAL COLLECTION AS AN ALTERNATIVE

DEFINITIONS

Microalbuminuria

UACR
30 – 300 mg/g



Proteinuria
(sub-nephrotic)
UPC > 300 mg



Nephrotic Proteinuria
UPC > 3 grams
24hr urine > 3.5 grams

NEPHROTIC SYNDROME

- NEPHROTIC-RANGE PROTEINURIA
 - > 3.5 GM / 24 HR URINE
 - > 3 GM ON UPC
- HYPOALBUMINEMIA
- EDEMA
- HYPERLIPIDEMIA
- LIPIDURIA – FATTY CASTS, OVAL FAT BODIES





CAUSES OF PROTEINURIA

- TRANSIENT
 - ORTHOSTATIC
 - GLOMERULAR
 - TUBULOINTERSTITIAL
 - OVERFLOW
- 

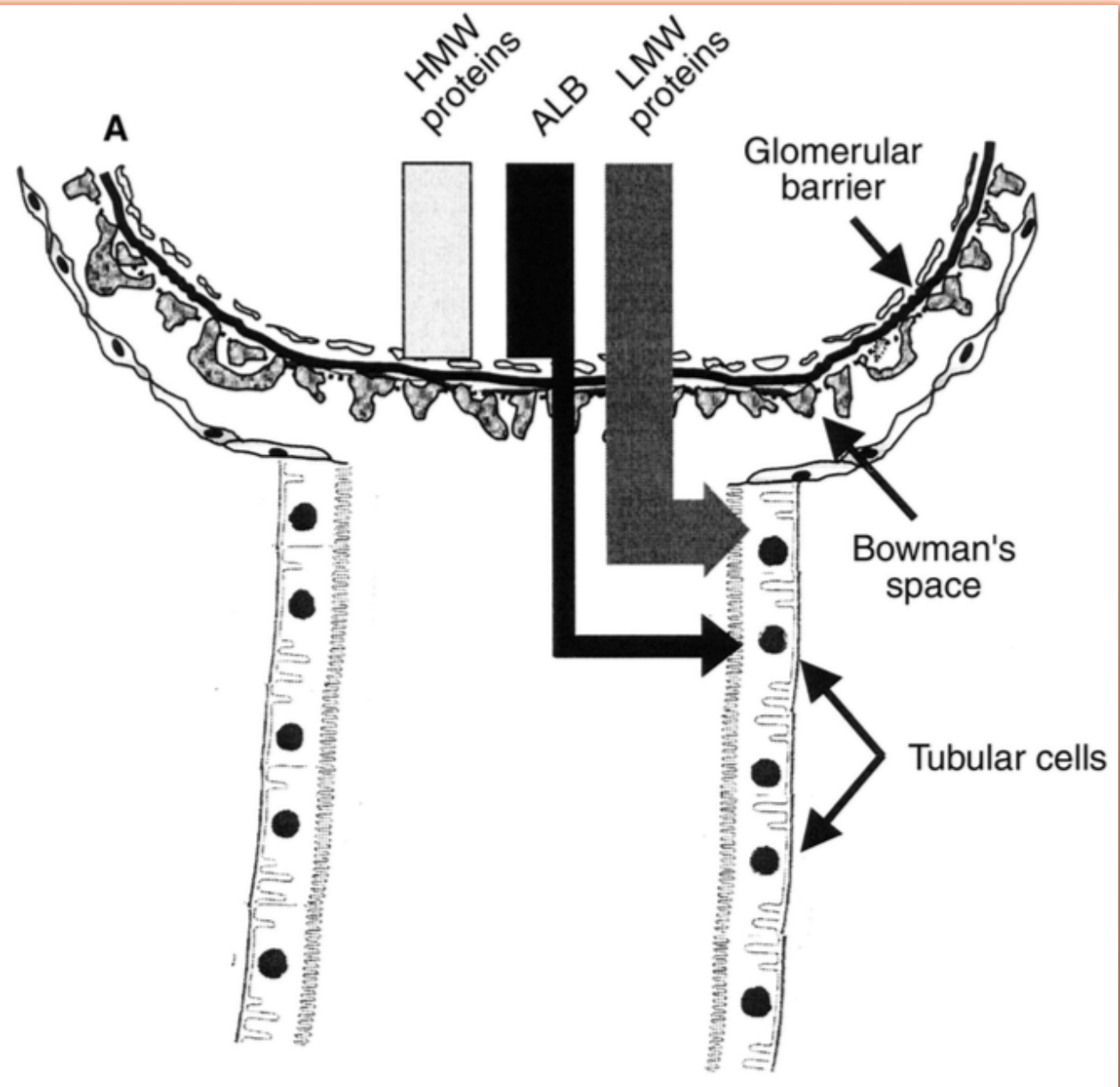
ORTHOSTATIC PROTEINURIA

- PATIENTS < 30 YEARS OLD
- BENIGN CONDITION, 3-5 % OF YOUNG ADULTS
- NORMAL RENAL FUNCTION WITH NO INCREASED RISK CKD
- INACTIVE SEDIMENT ON URINALYSIS
- INCREASED URINARY PROTEIN EXCRETION IN UPRIGHT POSITION **ONLY**
- URINE PROTEIN < 2 GRAMS / 24 HRS
- DX: SPLIT 24 HR URINE
 - DAY 16 HR URINE COLLECTION
 - 8 HOUR NOCTURNAL COLLECTION < 50 MG
 - ALTERNATELY CHECK 1ST AM UPC



GLOMERULAR

- MOST COMMON & IMPORTANT CAUSE
 - SUSPECT IF ACTIVE URINARY SEDIMENT
 - RBCS, CELLULAR CASTS
 - SUSPECT IF $> 1-2$ GRAMS PROTEINURIA
 - SEROLOGICAL WORKUP
 - RENAL BIOPSY FOR DIAGNOSIS
- PATHOPHYSIOLOGY:
 - INCREASED GLOMERULAR CAPILLARY PERMEABILITY TO PROTEIN
 - IMPAIRED PROTEIN REABSORPTION BY EPITHELIAL CELLS OF PROXIMAL TUBULES



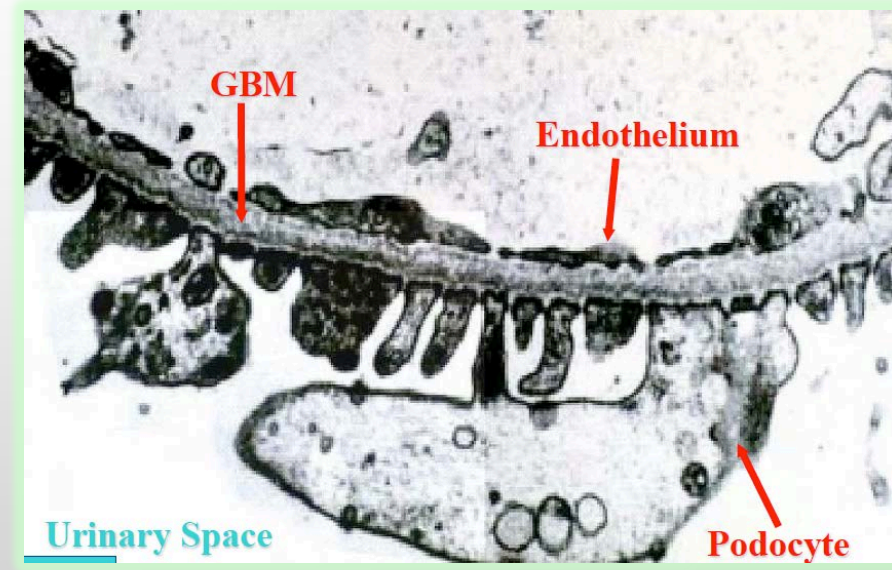
Absence of proteinuria

GLOMERULAR BARRIERS

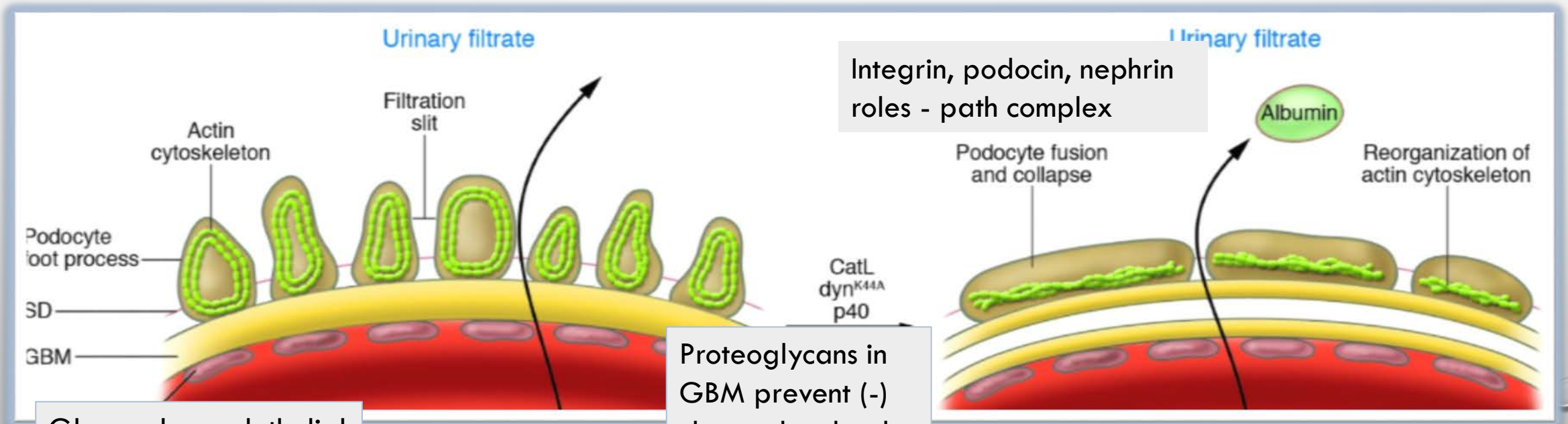


GBM NORMAL BARRIERS

- NORMALLY GBM RESTRICTS PASSAGE INTO BOWMANS SPACE BY:
 - MOLECULAR SIZE
 - ELECTRICAL CHARGE
 - STERICAL CONFIGURATION



PROTEINURIA MECHANISMS



Glomerular endothelial cell: glycocalyx albumin barrier; also requires VEGF to fxn

Proteoglycans in GBM prevent (-) charged molecule passage

TUBULOINTERSTITIAL

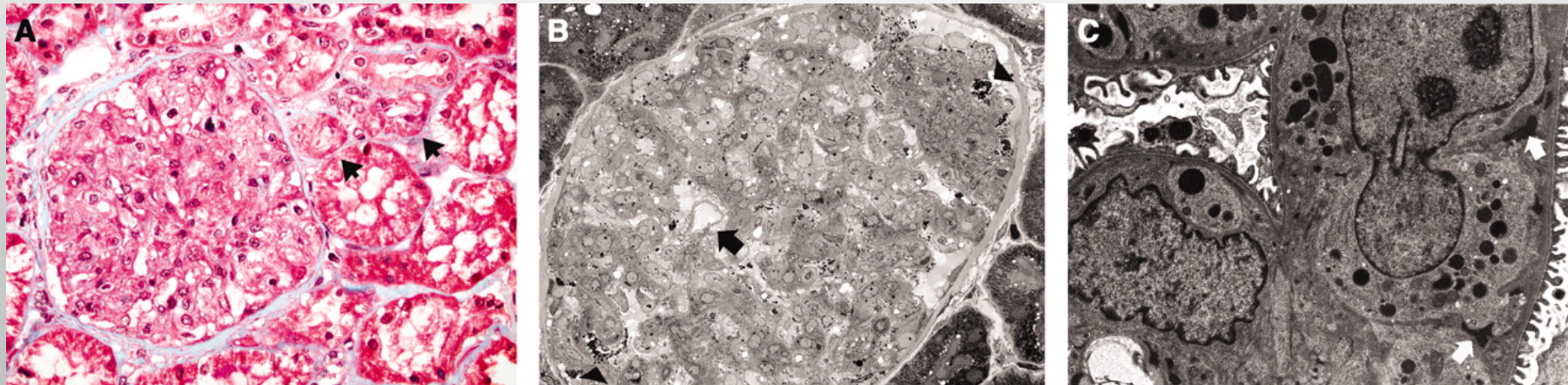
- HYPERTENSIVE ARTERIONEPHROSCLEROSIS
- CHRONIC INTERSTITIAL NEPHRITIS
- FANCONI SYNDROME
- PATH: DECREASED PROXIMAL TUBULE REABSORPTION OF LOW-MOLECULAR-WEIGHT PROTEINS (PART OF NORMAL GLOMERULAR ULTRAFILTRATE)

OVERFLOW

- LOW-MOLECULAR-WEIGHT PROTEINS OVERWHELM THE ABILITY OF THE PROXIMAL TUBULES TO REABSORB FILTERED PROTEINS
- HEMOGLOBINURIA, MYOGLOBINURIA, MYELOMA, AMYLOID, LYMPHOMA

PREECLAMPSIA

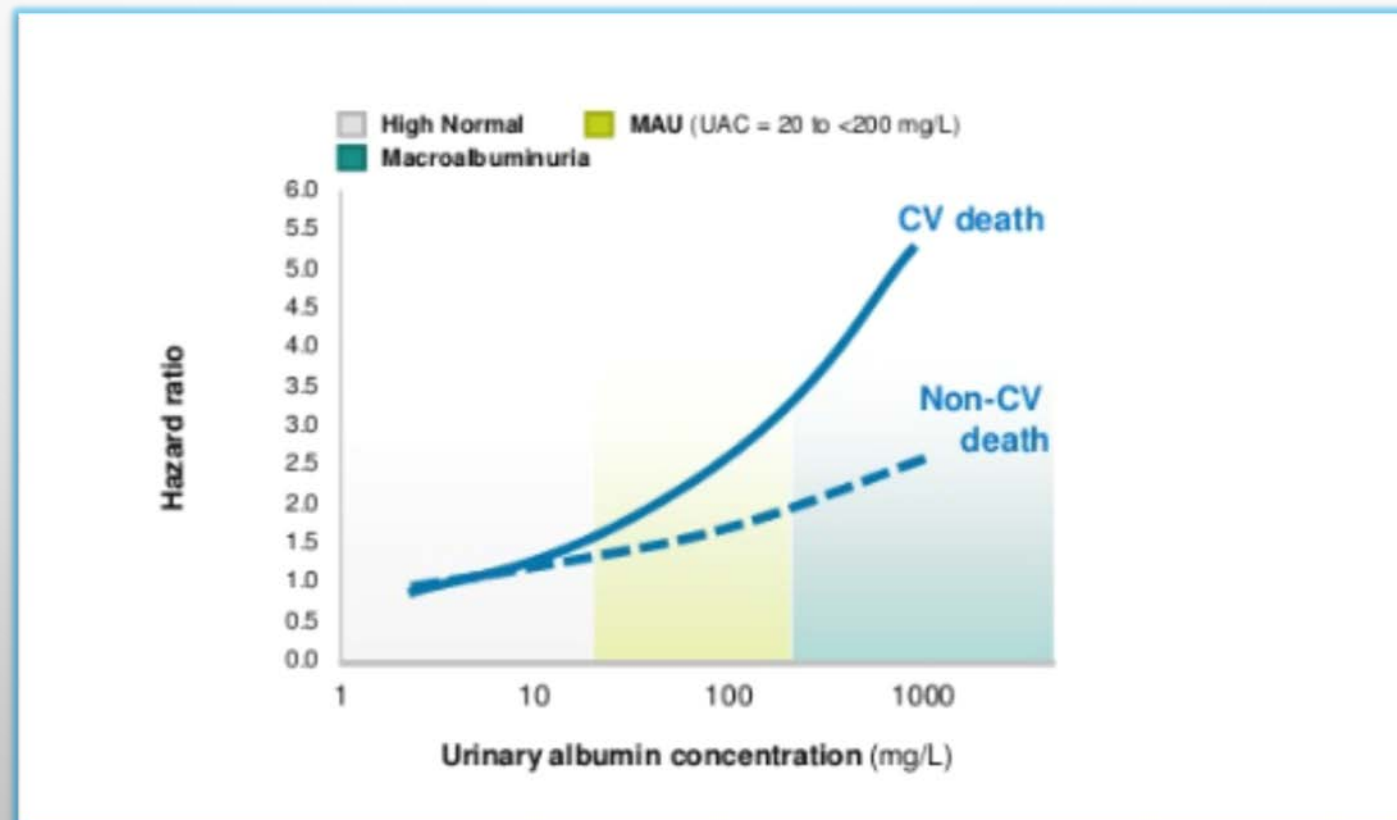
- NEW ONSET HYPERTENSION AND PROTEINURIA > 20 WEEKS GESTATION
- RENAL PATH: GLOMERULAR ENDOTHELIOSIS AND TMA



ALBUMINURIA: CLINICAL SIGNIFICANCE

- INDEPENDENT PREDICTOR OF PROGRESSIVE LOSS OF RENAL FUNCTION
- CV RISK FACTOR
 - INCREASED MORBIDITY AND MORTALITY

URINE ALBUMIN IS A PREDICTOR OF ALL-CAUSE MORTALITY IN GENERAL POPULATION: PREVEND STUDY

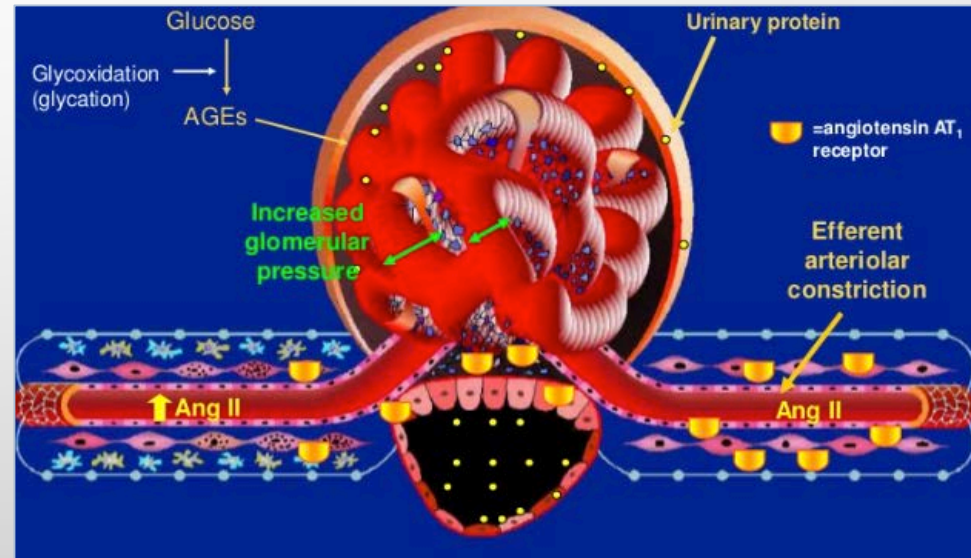


PROTEINURIA SCREENING

- NOT COST-EFFECTIVE OR RECOMMENDED IN GENERAL POPULATION
- SHOULD BE DONE ANNUALLY IN ALL DIABETICS AND CONSIDER IN HIGH-RISK PATIENTS (HTN, SMOKING, OBESITY, OLDER AGE)
- UACR OR URINE MICROALBUMIN/CREATININE IS THE SCREENING TEST OF CHOICE

PROTEINURIA TREATMENT

- RX UNDERLYING PATHOLOGY
- SALT RESTRICTION
- DIURETICS (ESP ALDACTONE R ANTAGONIST)
- RAAS INHIBITORS
- STATINS



The image features a light gray gradient background with several realistic water droplets of various sizes scattered in the corners. The droplets have highlights and shadows, giving them a three-dimensional appearance. The word "QUESTIONS?" is centered in the upper half of the image.

QUESTIONS?

REFERENCES

- VALUATION OF LABORATORY MEASUREMENTS FOR CLINICAL ASSESSMENT OF KIDNEY DISEASE. NKF KDOQI GUIDELINES: PART 5
- DAMICO G AND BAZZI C. PATHOPHYSIOLOGY OF PROTEINURIA. *KIDNEY INTERNATIONAL*, VOL. 63 (2003), PP. 809–825.
- P. MUNDEL AND J. REISER, “PROTEINURIA: AN ENZYMATIC DISEASE OF THE PODOCYTE,” *KIDNEY INTERNATIONAL*, VOL. 77, NO. 7, PP. 571–580, 2010.
- A. K. BELLO, B. HEMMELGARN, A. LLOYD ET AL., “ASSOCIATIONS AMONG ESTIMATED GLOMERULAR FILTRATION RATE, PROTEINURIA, AND ADVERSE CARDIOVASCULAR OUTCOMES,” *CLINICAL JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY*, VOL. 6, NO. 6, PP. 1418–1426, 2011.
- URINARY ALBUMIN EXCRETION PREDICTS CARDIOVASCULAR AND NONCARDIOVASCULAR MORTALITY IN GENERAL POPULATION. *CIRCULATION* 106(14):1777-1782; 2002
- QUANTITATION OF PROTEINURIA BY THE USE OF PROTEIN-TO-CREATININE RATIOS IN SINGLE URINE SAMPLES. SCHWAB S ET AL. *ARCH INTERN MED*. 1987;147(5):943-944.
- STILLMAN I AND KARUMANCHI SA. THE GLOMERULAR INJURY OF PREECLAMPSIA. *JASN* **AUGUST 2007** VOL. 18 NO. 8 **2281-2284**.