

RENAL FUNCTION TESTS

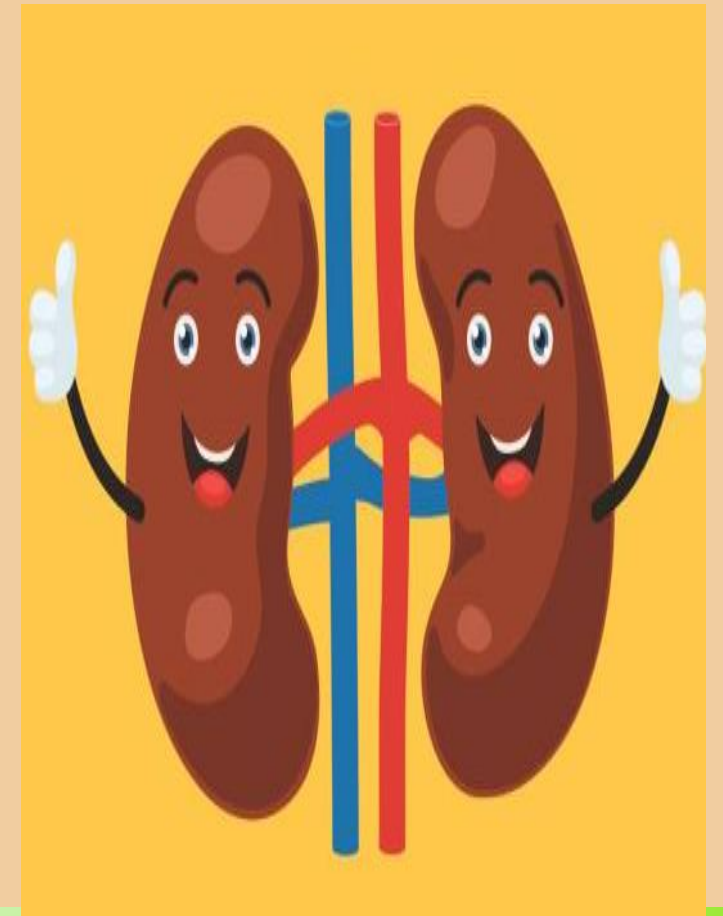


WHY TEST RENAL FUNCTION?

- ▶ *Screening and diagnosing impaired kidney function*
- ▶ *Monitoring the course and management of progressive chronic kidney disease*
- ▶ *Monitor the safe & effective use of drugs which are excreted in urine.*

t of Kidney at **FUNCTIONS OF KIDNEY AT A GLANCE**

1. **Excretion of nitrogenous wastes** like urea, creatinine, uric acid, elimination of toxins, metabolites of drugs
2. Maintaining **water balance**
3. Maintenance of **sodium balance**
4. Maintenance of **potassium balance**
5. **Excretion of hydrogen ions**
6. **Activation of vitamin D**
7. Production of **erythropoietin**
8. **Filtration**
9. **Reabsorption**



CLASSIFICATION OF RENAL FUNCTION TESTS



1. To screen for kidney disease

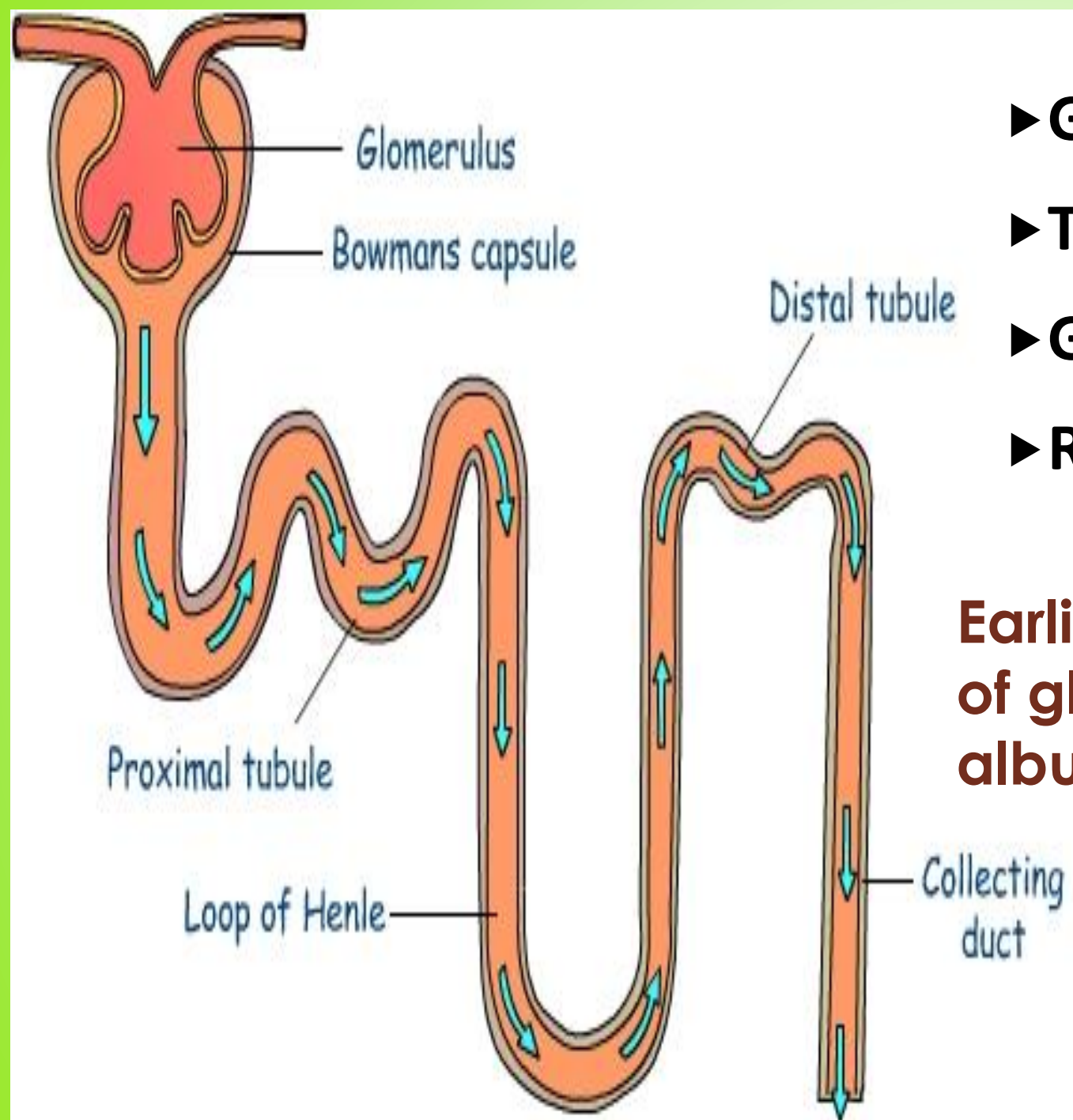
- ❖ *Complete urine analysis*
- ❖ *Plasma urea and creatinine*
- ❖ *Plasma electrolytes*

2. To assess glomerular function

- *Glomerular filtration rate*
- *Clearance tests*
- *Glomerular permeability; Proteinuria*

3. To assess tubular function

- ✓ *Reabsorption studies*
- ✓ *Secretion tests*
- ✓ *Concentration and dilution tests*
- ✓ *Renal acidification*



- **Glomerular function ??**
- **Tubular function ??**
- **Glomerular filtration rate[GFR] ??**
- **Renal Threshold ??**

Earliest manifestation of abnormality of glomeruli - appearance of albumin in urine

Segment	Reabsorption	Secretion
Proximal convoluted tubules	Na, Cl, HCO ₃ glucose, amino acids, water (oblig)	H ⁺ , NH ₄ ⁺
Loop of Henle	Na, Cl, Ca, Mg	
Distal convoluted tubules	Water (facultative)	H ⁺ , K ⁺ , NH ₄ , Uric acid

Renal threshold of a substance-
plasma level above which compound is excreted in urine.

Substance	Threshold value plasma level
Glucose	180 mg/dl
Lactate	60 mg/dl
Bicarbonate	28 mEq/L
Calcium	10 mg/dl

URINE ANALYSIS

PHYSICAL EXAMINATION

- ▶ Appearance – Clear
- ▶ Color – Straw coloured
- ▶ Odour- faintly aromatic
- ▶ Volume
- ▶ – **600-1550ml/day**
- ▶ Specific gravity- 1.015 to 1.025
- ▶ pH – 5.5 to 6.5



CHEMICAL EXAMINATION

1. **PROTEINS**
2. **REDUCING SUGAR**
3. **KETONE BODIES**
4. **BILE SALTS**
5. **BILE PIGMENTS**
6. **UROBILINOGEN**
7. **BLOOD**



Abnormalities Detected in Dipstick

Test and normal range	Interpretations
1. Specific gravity 1.005-1.025	Low SG in renal tubular dysfunction; diabetes insipidus;. High SG in inadequate water intake; volume depletion
2. pH 5.5-6.5	Low pH in high protein diet & acidosis. Recent meal-alkaline tide High pH in low protein diet
3. Blood	Menstruation, traumatic catheterisation, Glomerulo-nephritis, Stones, tumor & trauma of urinary tract. Hemoglobinuria – hemolysis
4. Protein	Fever, exercise, orthostatic proteinuria;glomerulo-nephritis,UTI, tubular diseases
5. Glucose	Diabetes mellitus, Renal glycosuria; Fanconi's
6. Ketone Bodies	Diabetes mellitus Starvation
7. Bilirubin	Hepatitis, obstructive jaundice
8. Urobilinogen	Concentrated urine; hepatitis; intravascular hemolysis; low obst.jaundice
9. Bile salts	Obstructive jaundice
10. Nitrite	UTI
11. Leukocyte esterase	UTI, Fever

TESTS FOR NON PROTEIN NITROGEN

- ▶ **Urea** : depends on protein intake. **[Normal value 20-40mg/dl]**
- ▶ **Creatinine** : specific and sensitive. **[M – 0.7-1.4mg/dl, F – 0.6-1.3mg/dl]**
- ▶ **Uric acid** : represent purine catabolism.
- ▶ **Other minor components** : **Urobilinogen, Indican, Ammonia**
& Amino acids

Blood urea nitrogen – serum urea expressed in terms of its nitrogen
 $BUN \times 2.14 = \text{urea}$

GFR

CLEARANCE MEASURES GFR INDIRECTLY

- Measure of glomerular function
- Affected by age, sex, body size, protein intake
- Cannot be measured directly, Estimated from clearance of a filtration marker

Uses

- Screening renal impairment
- Targeting treatment
- Monitoring progression
- Predicting requirement of renal replacement therapy

► NORMAL GFR

$$= 120 - 130 \text{ ml/min/1.73m}^2$$

[in a person with 70kg body wt]

If a substance is reabsorbed by the tubules –

$$\text{CLEARANCE} < \text{GFR}$$

► If a substance is secreted by the tubules –

$$\text{CLEARANCE} > \text{GFR}$$

TESTS TO ASSESS GLOMERULAR FILTRATION RATE

– CLEARANCE TESTS

CLEARANCE

Defined as the quantity of blood or plasma completely cleared of a substance per unit time.

Expressed as **milli Litre/min.**

$$\text{Clearance} = \frac{\text{mg of substance excreted per min}}{\text{mg of substance per mL of plasma}}$$

$$\text{Clearance} = \frac{U \times V}{P}$$

U = concentration of substance in urine.

V = ml of urine excreted / minute. .[ml/min]

P = concentration of substance in plasma or serum.[mg/dL]

IDEAL FILTRATION MARKER :

Substance should be freely filtered against capillary wall, & neither secreted nor reabsorbed.

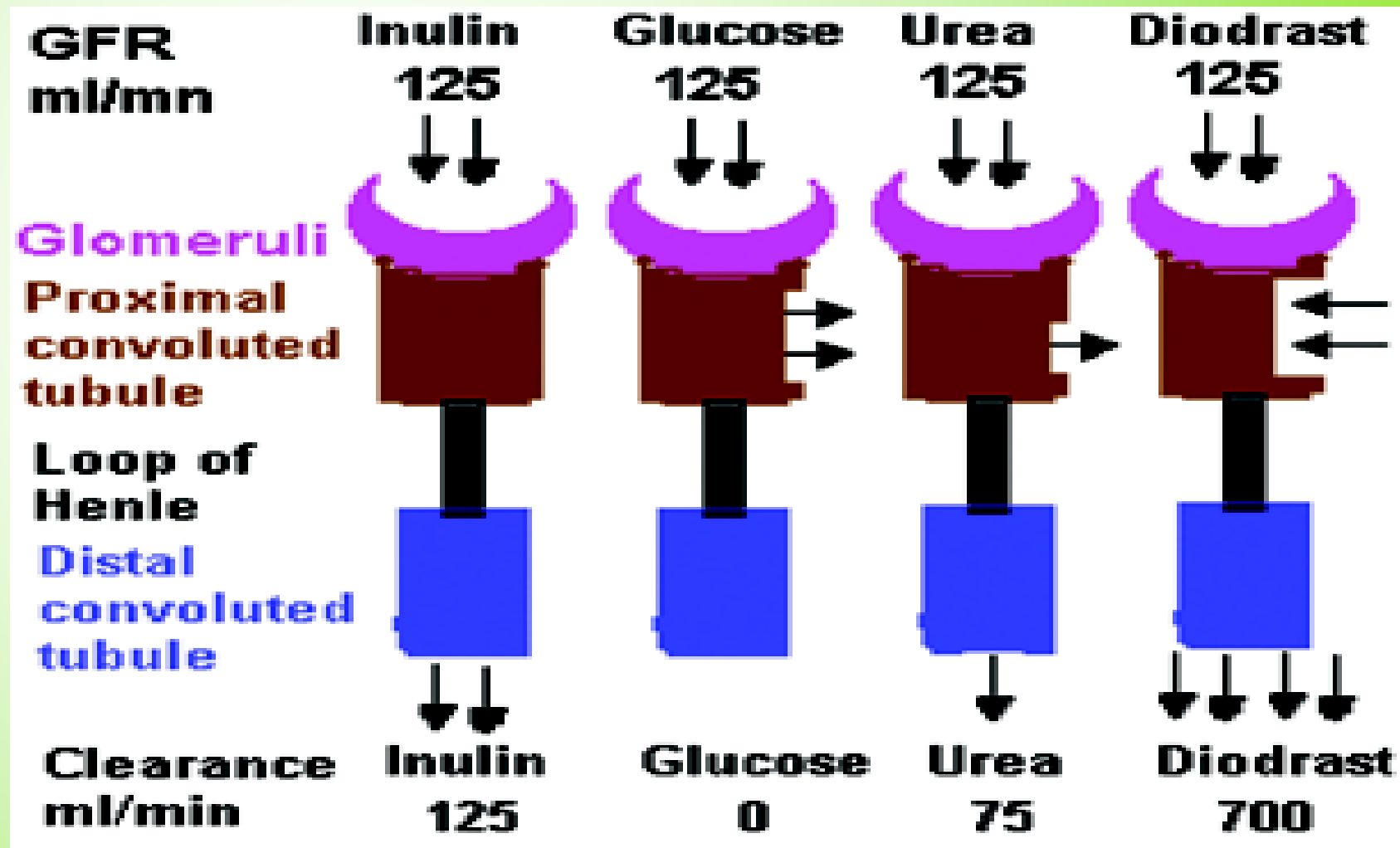
Endogenous markers

- Creatinine , Urea

Exogenous markers

- Inulin, Diodrast

Cr-EDTA



RELATIONSHIP OF GFR WITH CLEARANCE

MECHANISM	RESULT	EXAMPLE
Substance filtered;neither reabsorbed nor excreted	GFR = CLEARANCE	Inulin Creatinine
Substance filtered ; reabsorbed & excreted	GFR $\approx$ CLEARANCE	Uric acid
Substance filtered; partially reabsorbed	CLEARANCE < GFR	Urea
Substance filtered; secreted but not reabsorbed	CLEARANCE > GFR	Diodrast, PAH

CREATININE CLEARANCE

Creatine $\longrightarrow$ Creative phosphate $\longrightarrow$ Creatinine

$$C = UV/P$$

$$\text{Uncorrected clearance} = \frac{U \times V}{P}$$

$$\text{Corrected creatinine clearance ; } C_{cr} = \frac{U \times V \times 1.73}{P \times A}$$

U:urine creatinine concentration [mg/dl]

V:urine flow in ml per min

P:plasma creatinine concentration

NORMAL SERUM CREATININE LEVEL

- Adult males : 0.7-1.4mg/dL
- Adult Females: 0.6-1.3mg/dL
- Children : 0.5-1.2mg/dL

REFERENCE VALUE FOR CREATININE CLEARANCE

Males : 95-115 ml/min.

Females: - 85 - 110ml/min.

- ✓ When corrected for surface area, value become same for male& female
- ✓ Normal value - 100ml/min/1.73m²
- Depends on total muscle mass of the body.
- Low values:females ,children.
- High values: males, old age

SIGNIFICANCE :

- ✓ **Indicator of reduced GFR**
- ✓ 50 % of renal function will be lost before rise in blood creatinine level.
- ✓ Creatinine level $>1.5\text{mg/dl}$ indicate impairment of renal function
- ✓ But clearance estimation helps in early detection.
- ✓ Helpful in long-time monitoring.

ADVANTAGE :

- ▶ Extra renal factors –rarely interfere
- ▶ Conversion of creatine phosphate to creatinine is spontaneous, nonenzymatic
- ▶ Blood level doesn't fluctuate as production is continuous.
- ▶ Not affected by diet/ exercise

DISADVANTAGE

- ▶ Overestimates GFR by 10-20 ml/min.
- ▶ When GFR severely reduced, extrarenal excretion increase.
[via intestinal bacteria]

Estimated GFR (eGFR) ()

A simpler technique of estimating creatinine clearance & thereby GFR is by using serum creatinine level.

This would eliminate the need for timed urine collections.

Cockcroft-Gault equation.

$$Ccr = (140 - \text{age in years}) \times \text{weight in Kg} (0.85 \text{ in females}) / 72 \times Pcr \text{ in mg/dl}$$

MDRD (Modification of Diet in Renal Disease) Equation is more Accurate

UREA CLEARANCE TEST

- ▶ *Number of millilitres of blood which contains urea excreted by kidney in a minute.*
- ▶ Urea clearance $<$ GFR [because urea is partially reabsorbed].
- ▶ $< 75\%$ urea clearance - abnormal
- ▶ $\downarrow$ urea clearance $\propto$ $\uparrow$ renal failure
- ▶ Creatinine clearance preferred over urea clearance - as urea is partially reabsorbed from renal tubules, poor indicator of GFR, levels dependent on non renal factors

▶ Maximum urea clearance :

$$C = UV/P$$

▶ Normal : 75 ml/min

▶ Standard urea clearance :

Clearance value decreased when volume of urine less than 2ml/min.

$$\text{ie, } = [U \cdot V] / P$$

▶ Normal : 54 ml/mt

INULIN CLEARANCE TEST

- ▶ Inulin - polysaccharide of fructose
- ▶ 125 ml/min
- ▶ Freely filtered , neither secreted nor reabsorbed

DIODRAST CLEARANCE

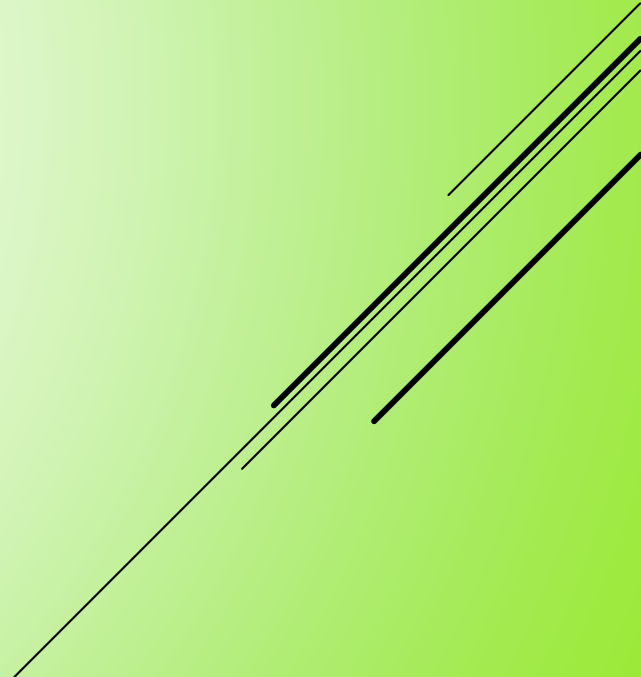
It is a measure of **renal plasma flow**.

CYSTATIN C

- ▶ New superior marker
- ▶ Extracellular cysteine protease
- ▶ Normal blood level – 0.8-1.2mg/l
- ▶ Produced at constant rate, freely filtered
- ▶ No tubular secretion
- ▶ Completely reabsorbed but degraded in tubules
- ▶ Dependent on age, sex
- ▶ Sensitive to changes in creatinine blind area of GFR

MARKERS OF GLOMERULAR PERMEABILITY

PROTEINURIA

- ✓ **Glomerular proteinuria**
 - ✓ **Overflow proteinuria**
 - ✓ **Micro albuminuria**
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Glomerular proteinuria:

- When glomeruli damaged/diseased-more permeable.
- Albuminuria

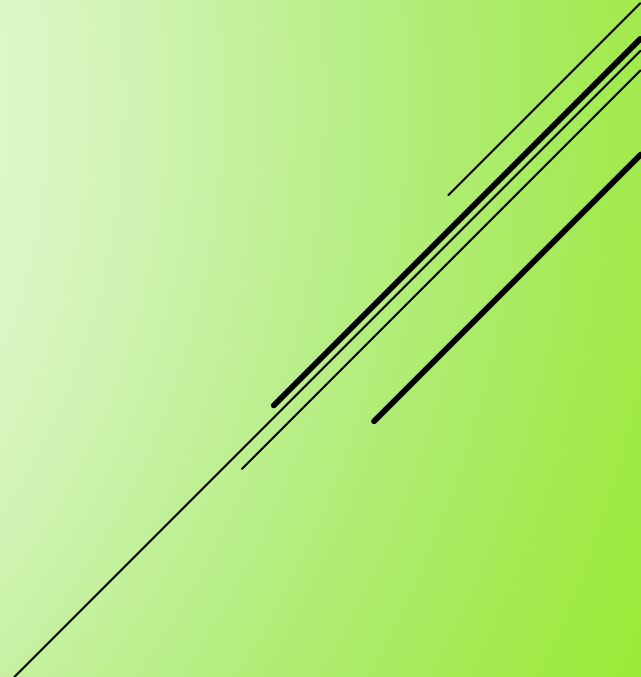
Microalbuminuria:

- ✓ Pauci-albuminuria / minimal albuminuria
- ✓ Excretion of 30 – 300 mg albumin /day
- ✓ Early indicator of nephropathy in DM & HTN
- ✓ Indicator of future renal damage

Overflow proteinuria:

- ▶ When small molecular weight proteins increased in blood,they overflow into urine
- ▶ Hemoglobinuria ,Bence –Jones proteinuria

TESTS FOR TUBULAR FUNCTION

- **Measurement of specific gravity.**
 - **Concentration tests.**
 - **Dilution test.**
 - **Urinary acidification tests**
- 

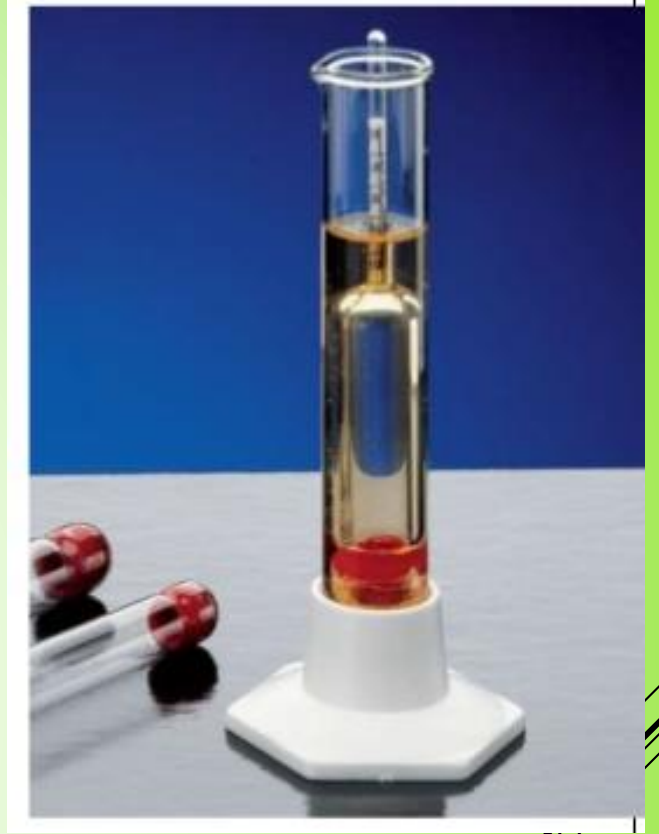
- **Measurement Of Specific Gravity** – Urinometer

- simplest test for tubular function.
- Depends on concentration of solutes
- Normal value:- 1.015 – 1.025

- **Osmolality** : measured by osmometer.

- Depends on number of osmotically active substances

- In Diabetes insipidus – osmolality less



CONCENTRATION TESTS

- Earliest manifestation of renal disease- difficulty In concentrating the urine.
- The patient is allowed No food or water for 12 hours;
then,specific gravity:- > 1.022 .
- **Isosthenuria : specific gravity becomes fixed at 1.010**
[as disease progress,tubular capacity is lost]
- **Nocturia : One of the early symptom of tubular dysfunction**

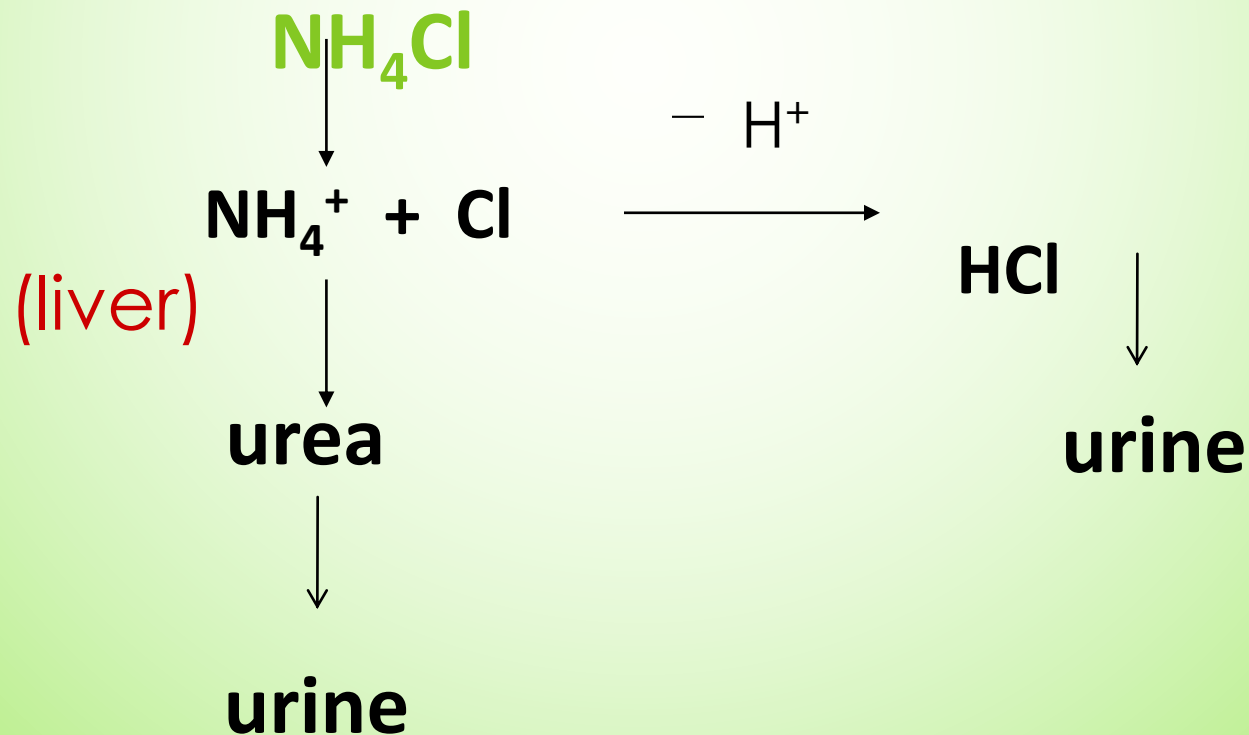
DILUTION TEST

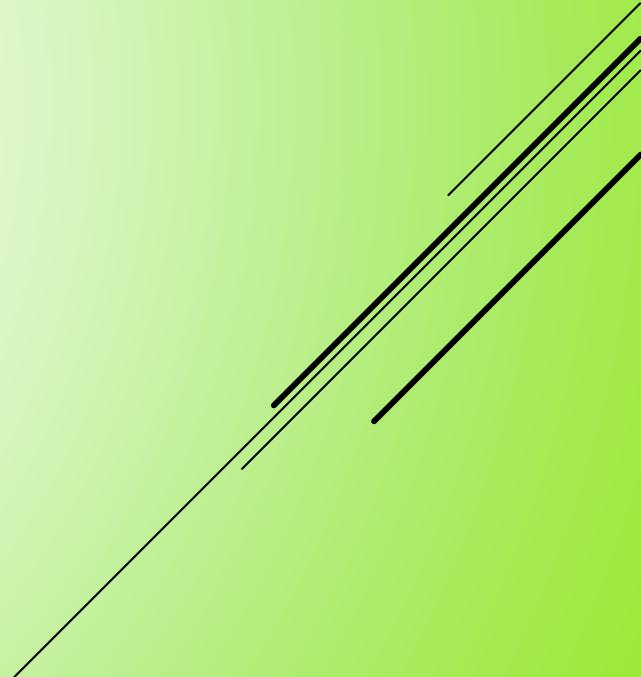
- ▶ More sensitive, less harmful.
- ▶ Bladder emptied at 7am, Water load given : 1200ml in 30 minutes.
- ▶ Hourly urine sample collected for next 4 hours
- ▶ Volume , specific gravity & osmolality of each measured,
- ▶ Normal:- Full excretion within 4 hours
- ▶ **specific gravity:-** of atleast one sample should fall to 1.003

URINARY ACIDIFICATION TEST

Most useful test.

Procedure:- NH_4Cl (0.1 gm/kg body weight)



- Urine is collected hrly from 2-8hrs after ingestion
 - pH and acid excretion of each sample noted
 - pH of atleast one sample ≤ 5.3
 - Ammonia excretion should be – 30-90 mmol/hr.
 - Contraindication:- Liver disease
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Summary of Renal Function Tests

<u>Glomerular dysfunction</u>		<u>Tubular dysfunction</u>	
Serum urea	↑	Urine concentration	↓
Serum creatinine	↑	Dilution test abnormal	
Inulin clearance	↓	Uric acid excretion	↓
Creatinine clearance	↓	Blood uric acid	↑
Urea clearance	↓		
PAH clearance	↓	Acidification of urine	↓
Proteinuria present	↓	Amino aciduria present	
Urine volume	↓	Urine volume	↑
Specific gravity	↑	Specific gravity	↓
Serum phosphate	↑	Serum phosphate	↓

Thank You

