Renal Function Tests

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Lec. 3

Markers of Glomerular Filtration Rate

- Clearance Tests: is defined as the volume of blood or plasma completely cleared of a substance per unit time.
- It is expressed as milliliter of plasma per minute.
- Clearance = mg of substance excreted per minute/ mg of substance per mL of plasma
- $C = U \times V / P$
- U = concentration of the substance in urine;
- P= concentration of the substance in plasma or serum

V = the mL of urine excreted per minute.

The value is expressed as mL/minute.

Markers of Glomerular Filtration Rate

If the substance is freely filtered across the capillary wall, and neither secreted nor reabsorbed,

then its clearance is equal to GFR.

A substance which meets these requirements is an ideal filtration marker.

Clearance Tests

- Measurement of glomerular filtration rate (GFR) provides the most useful general index for the assessment of the severity of renal damage.
- A decrease in the renal function is due to the loss of functional nephrons, rather than a decrease in the function of individual nephron.
- Normal GFR for young adults is 120–130 mL/ min/1.73M$_2$.
- Clearance decline with age < 25% in people older at 70y may have a GFR less than 60 mL/min.

Creatinine Clearance Test

- *Importance of Creatinine Clearance:*
- Creatinine is a waste product, formed from creatine phosphate.
- This conversion is **spontaneous, non-enzymatic,** and is dependent on total muscle mass of the body. It is not affected by diet, age or exercise.
- Women and children excrete less creatinine than men, because of their smaller muscle mass.
- About 98% of creatine pool is in muscle. Since
- the production is continuous, the blood level **will not**
- **fluctuate** much, making creatinine an ideal substance
- for clearance test.

- *Reference Values of Creatinine*

- Adult males, 0.7 – 1.4 mg/dL
- Adult females, 0.6 – 1.3 mg/dL
- Children, 0.4 – 1.2 mg/dL.
- The kidney reserve is such that about 50% kidney
- function must be lost before creatinine level in blood
- is raised. Serum level usually parallels the severity of
- the disease.
- *Creatinine level more than 1.5 mg/dL indicates impairment of renal function.*
- Creatinine is quantitated by
- **Jaffe's test** (alkaline picrate), or Test kit based on specific enzymatic reaction.

Estimated GFR (eGFR)

- A simpler technique of estimating creatinine clearance
- and there by GFR is by using serum creatinine
- level. This would eliminate the need for timed urine
- collections. A commonly used formula is **Cockcroft-**
- **Gault equation.**
- Ccr = (140 – age in years) × weight in Kg (0.85 in
- females)/72 × Pcr in mg/dL
- The factor 0.85 is used in females assuming
- that they have 15% less muscle mass.
- eGFR can be used for staging of patients with
- chronic kidney disease. and neither in healthy individuals, nor in children and obese people.

- *Creatinine Co-efficient*
- It is the urinary creatinine expressed in mg/kg body
- weight. The value is elevated in muscular dystrophy.
- Normal range is 20–28 mg/kg for males and 15–21
- mg/kg for females.
- **Cystatin C as a Filtration Marker**
- It is a marker which has advantages over serum
- creatinine. Normal blood level of cystatin is
- (0.8 -1.2) mg/L. It is expressed in virtually all organs of the body, and most abundant extracellular Cysteine protease inhibitors.

Cystatin C as a Filtration Marker

- Creatinine sometimes, it is inaccurate in detecting mild renal impairment.

- tubular secretion contributes approximately 20% of the total creatinine excretion by the kidney, and this contribution can increase as GFR decreases. Serum creatinine does not increase until the GFR has moderately decreased.
- This insensitivity to moderate decreases in GFR is called
- creatinine blind GFR area (40–70 mL/min/1.73 m2).
- So, serum creatinine may not be a good parameter for determination of GFR.
- Cystatin C is an excellent GFR marker. The blood levels are not depended on
- age, sex, muscle mass or inflammatory processes.
- It is sensitive to changes in the so-called creatinine
- blind area of GFR rather than sCreatinine levels.
- Since, there is no tubular secretion of Cystatin C, it is extremely sensitive to minor changes in GFR in the earliest
- stages of chronic kidney diseases.

Chronic Kidney Disease (CKD)

- CKD is a silent killer. CKD is a growing problem
- ~ 12 % of the adult population.
- Major risk factors of CKD: diabetes mellitus, hypertension, glomerular nephritis, urinary
- tract infection, autoimmune diseases, kidney stones
- and toxic effects of some drugs.

- Markers for CKD:
- serum creatinine, eGFR, microalbumin and
- Cystatin C

Acute Kidney Injury (AKI)

- AKI is characterised by a rapid rise of serum creatinine with low urine output.
- Onset of AKI can be swift and often deadly. In acute kidney injury, serum creatinine (sCr), can take days to show an increased level.
- Novel biomarkers of tubular injury such as urinary
- neutrophil gelatinase-associated lipocalin (uNGAL)
- may enable the early detection of acute kidney injury before a change in GFR is observed.
- The uNGAL is very useful when sCr level is not increased.

Factors impact on sCr.

- **Causes of an abnormal plasma**
- **[creatinine].**
- *Reduced plasma [creatinine]*
- Physiological: Pregnancy
- Pathological: Reduced muscle bulk (e.g. starvation wasting diseases,
- steroid therapy)
- *Increased plasma [creatinine]*
- No pathological:
- Significance High meat intake, strenuous exercise
- Drug effects (e.g. salicylates)
- Analytical interference (e.g. due to cephalosporin antibiotics)
- Pathological:

Renal causes, i.e. any cause (acute or chronic) of a reduced GFR

Blood Urea Level

- Normal serum urea value is 20 – 40 mg/dL.
- Urea is the end-product of protein metabolism
- The serum concentration of urea generally increases as the age advances.
- The lower range is usually seen in young adults and the upper limit is normal for elderly people.
- Therefore, a value of
- 40 mg/dL in a patient of 25 years may be considered
- as suspicious, while the same value in a person of 60 years can be considered as perfectly normal.

- *Decreased Blood Urea*
- Urea concentration in serum may be low in late
- pregnancy, in starvation, in diet grossly deficient in
- proteins and in hepatic failure.

- **Azotemia**
- Increase in the blood levels of NPN is referred to as
- azotemia and is the hallmark of kidney failure.

Causes for increased blood urea

- 1. Prerenal conditions:
- Dehydration: Severe vomiting, intestinal obstruction, diarrhea
- Diabetic coma and severe burns
- Fever and severe infections
- 2. Renal diseases:
- Acute glomerulonephritis
- Nephrosis
- Malignant hypertension
- Chronic pyelonephritis
- 3. Postrenal causes:
- Stones in the urinary tract
- Enlarged prostate
- Tumors of bladder
- 4. Medications:
- ACE inhibitors
- Acetaminophen
- Aminoglycosides
- Amphotericin B
- Diuretics
- NSAIDs

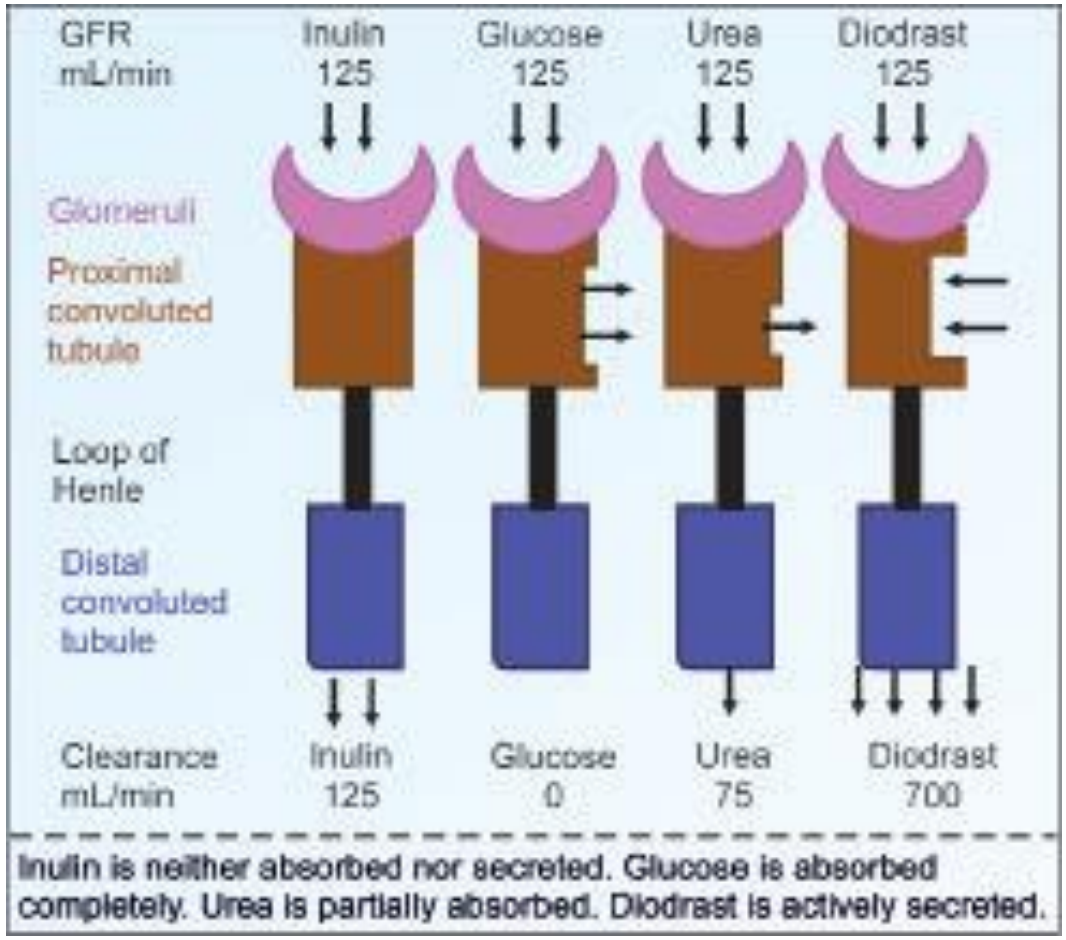
Urea Clearance Test

- *Importance of Urea Clearance*
- The urea clearance is less than GFR, because urea
- is partially reabsorbed.
- Urea clearance is the number of mL of blood, which contains the urea excreted in a minute by kidneys.
- *Maximum Urea Clearance*
- The urea clearance is calculated by the formula
- U × V/P
- where U = mg of urea per mL of urine; P = mg of urea
- per mL of plasma and V = mL of urine excreted per
- minute. This is called maximum urea clearance and
- the normal value is found to be 75 mL/min.

- **Inulin Clearance**
- Inulin is a polysaccharide of fructose. It is not
- appreciably metabolized by the body. It is neither
- absorbed nor secreted by the tubules. Therefore,
- inulin clearance is a measure of GFR. The test needs
- continuous infusion of inulin so as to keep the plasma
- level adequate. Since it involves administration of an
- extraneous compound, this procedure is not used
- routinely.
- Inulin clearance (GFR) = 125 mL/min and urea clearance
- = 75 mL/min.

Diodrast Clearance

- Diodrast is a contrast medium usually used in taking
- X-ray of urinary tract. Diodrast and PAH (para-amino
- hippurate) are filtered and excreted, so that these
- substances are removed by one passage of the blood
- through kidney. PAH clearance is a measure of **renal**
- **plasma flow***.*
- Since, renal plasma flow is 700 mL/min and the
- GFR is 125 mL/min, it is obvious that about 1/5th
- of the plasma brought to the glomeruli becomes
- the glomerular filtrate. This is called the **filtration**
- **fraction.**


GFR
mL/min
Inulin
125
Glucose
125
Urea
125
Diodrast
125
Glomeruli
Proximal convoluted tubule
Loop of Henle
Distal convoluted tubule
Clearance
mL/min
Inulin
125
Glucose
0
Urea
75
Diodrast
700
Inulin is neither absorbed nor secreted. Glucose is absorbed completely. Urea is partially absorbed. Diodrast is actively secreted.

Proteinuria

- *Glomerular Proteinuria*
- Albuminuria is always pathological.
- Overnight first voided sample (early morning urine-
- EMU) may be used for the measurement of protein.
- Detection limit with Dipstick is 200–300 mg/L.
- 300 mg/day = Benign proteinuria
- 300 mg – 1000 mg = Pathological proteinuria
- > 1000 mg/day = Glomerular proteinuria

Kidney failure, early symptoms

- Polyuria (passing more urine)
- Nocturia (passing more urine during night)
- Pedal edema, puffiness of face
- High blood pressure
- Unexplained anemia
- Fatigue, lassitude and tiredness
- Microalbuminuria
- Mild elevation of serum creatinine

- Reference :
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- Lecture Notes
- Simon Walker
- Geoffrey Beckett
- Peter Rae
- Peter Ashby
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- 2- https://www.researchgate.net/publication/327245449_Chapter-25_Kidney_Function_Tests