Renal function tests

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Role of kidney

Maintainance of body homeostasis:

- Removal of metabolic waste products
- Regulating body's water and electrolyte balance
- Role in hormone synthesis in bone metabolism and BP control

An early identification of reduction in kidney function is important to decrease morbidity and mortality related to renal failure

Indications of kidney function test

To assess how well the kidneys are functioning

- Kidney problems are common
- Abnormal urinalysis (persistent proteinuria)
- Newly discovered high blood pressure or diabetes
- All seriously sick patients will need their kidney function evaluated

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Lab tests for kidney disease

Urinalysis:

- Protein ,blood glucose,ketone,bili,Hb
- PH,SG,nitrite

Routine laboratory tests:

- Blood Urea and creatinine
- Electrolyte(Na,K,Cl)

Others:

- Creatinine clearance
- Estimated GFR (eGFR)
- Beta 2 microglobulin
- Cystatin C

Urinalysis

Evaluation of proteinuria:

- Most +ve dipsticks ur protein are of benign proteinuria(no morbidity or mortality)

RR of ur protein < 150 mg/day, **composed:**

- **20% LMW proteins such Igs(20,000Da)**
- **40% HMW albumin(65,000Da)**
- **40% of tubular mucoproteins (tamm horsfall)**

Proteinuria

Persistent proteinuria (1+ or greater):

- **Early sign of CKD(e.g diabetes nephropathy, HT, GN)**

Proteinuria >300 mg/day:

- **Random fresh urine can be used for protein levels but to be correlated with creatinine levels**

Microalbuminuria:

- **Sensitive test ,can detect small amount of protein in urine (-ve on urine dipsticks)**
- **30-300mg/day or 20 –200 ug/min**
- **Indication of early nephropathy**

Types of proteinuria

Glomerular proteinuria:2-3 gr /day

- Heavy proteinuria (mainly albuminuria)
- Indication of chr kidney damage(DM,glomerular disease or HT)

Tubular proteinuria (LMW:<2 gr/day)

- Beta 2 microglobulin
- RBP

Overflow proteinuria:

- Increased in LMW proteins
- Igs light chains in MM

Renal function tests

- Sodium:130-147 mmol/L
- Potassium: 3.3-5.3 mmol/L
- Chloride: 99-113 mmol/L
- Carbon dioxide:18-29 mmol/L
- Urea: 2.6-7.0 mmol/L
- Creatinine (Creat):60-120 umol/L

Pl.Creatinine

RR:

- 45-90 umol/l for women
- 60-110 umol/l for men

- By-product of muscle energy metabolism
- Production depends of muscle mass
- Mainly filtered by the kidney
- Small amount is actively secreted
- No tubular reabsorption of creatinine
- More sensitive and specific test of RFT than BUN

Pl.Creatinine (cntd)

High pl.creat levels:

- With marked damage to functioning nephrons
- Massive rhabdomyolysis/crush injury
- Lot of meat in the diet(high creatine content)
- Very large muscle mass(body builder ,adult men)
- Drugs probenecid,cimetidine,trimetoprime,amiloride: block the tubular secretion
- Cephalosporine and ketone bodies(lab interference)

A baseline s-Cr of 150 umol/l may be normal in a male body builder

Pl.creat of 60 umol/l can indicate significant renal disease in a frail old woman

Pl.creatinine(cntd)

Low pl Creat levels:

- Elderly and infants
- Chronically ill patients with LOW
- High bilirubin levels (falsely low pl.creat level): lab interference
- Vegetarians:no creatine in diet

Creatinine clearance(CrCl)

- GFR is the best measure of renal function
- GFR is estimated by CrCL
- Cr Cl always needed in persistent proteinuria
- CrCl= Ur Cr/S-Cr x Ur.Vol(ml/min)

RR varies on age,gender and body size:

- Adult males:90-140ml/min
- Adult female:80-125 ml/min

CrCl (cntd)

- Mild decrease GFR:60-89 ml/min
- Moderate decrease:30-59 ml/min
- Severe decrease :15 ml/min (for dialysis)

In severe renal dysfunction,overestimation of CrCl rate due to active secretion of creatinine

Estimated GFR (eGFR)

For most patients eGFR is more accurate than CrClr based on serum and urine values

E.GFR by MDRD study equation

- Modification of Diet in Renal Disease equation based on 4 variables
  - Serum creatinine (S_{cr})
  - Age (18y or older)
  - Sex
  - Race (African American or not) – not used for SA Blacks

- Best available S_{cr}-based equation to assess kidney function in adults aged 18-70y
- Extensively validated in impaired kidney function, but significantly underestimates GFR when kidney function is normal

MDRD study equation (cntd)

- Unreliable in the following circumstances:
  - Patients with normal kidney function
  - Patients < 18y or older than 70y
  - Pregnancy
  - Acute renal failure
  - Serious comorbid conditions
  - Extremes of body habitus (obesity or malnutrition)*
  - Muscle wasting diseases, amputees, paraplegics*
  - Atypical dietary intake (vegetarian or creatine supplements)*
- In these* patients, GFR should be estimated from U_{cr} and S_{cr} values

MDRD study equation (cntd)

- NKDEP eGFR reporting recommendations:
  - S_{cr} for eGFR calculation should be rounded to nearest whole number
  - eGFR >60 mL/min/1.73 m^2 should be reported as >60
  - eGFR $\leq$60 should be reported as an absolute figure rounded to a whole number
- Three reasons for this recommendation:
  - Equation less accurate when kidney function is normal or mildly impaired
  - Calibration differences and S_{cr} assay imprecision have greatest impact in near-normal range
  - eGFR quantification for values $\leq$60 are used

    to classify CKD severity

Blood urea

- **Secreted and reabsorbed in nephron**
- **Less specific than pl.Creat in RFT due :**

  -effect in ECF volume (dehydration,CCF etc..)

  -Protein intake and catabolism

  -renal blood flow
- **BUN and pl.creat (more complete estimation of RFT)**
- **Urea /Creat ratio can indicate other problems besides those intrinsic to the kidney**

- **High Urea levels out of proportion to Creat:pre-RF (e.g dehydration)**
- **In renal failure or CKD,BUN will only be raised outside"normal" when more than 60 % of kidney cells are no longer functioning**

Beta 2 microglobulin

- **S-B2M is freely filtered by the glomerulus and freely reabsorbed by the PCT**
- **Good as a measure of GFR (similar to pl-creat)**

- **Ur.B2M: very sensitive indicator in renal tubular disease**

- **No specific but relatively sensitive marker of various neoplastic,inflammatory and infection condition**
- **Has a prognostic value in MM**

Cystatin C

- **Freely filtered by the glomerulus and completely reabsorbed and catabolysed by the PCT cells**
- **Single RR for adult men and female under 50 Yr of age**
- **More practical for monitoring GFR changes in the pediatric population**
- **Sensitive screening test than pl-Creat for early assessment of changes in the GFR**

Biochemical tests in differentiating types of ARF

- **Fractional excretion of Na(FENa):**

  FE Na = 100 X (UNa X PCr) / (PNa X UCr)

- **Renal function index (RFI):**

  RFI = (UNa X PCr) / Ucr

- **Urea/Creatinine ratio**

- **Urinary Na (mmol/L)**

- **Urinary osmolality (mosmol/kg)**

ARF indices

Indices interpretation

	Pre-renal	ATN	Post-renal
UNa(mmol/l)	<20	>40	>40
FE Na	<1%	>1%	>4%
RFI	<1%	>1%	>1%
Urea/Creat	>70	<70	
Ur.Osmolality	>500	<350	

Indices pitfalls

Urea/Creat ratio >70:

- Common finding in elderly
- Marker of ill health

FE Na<1%:

- Diuretics will increase the excretion of **filtered Na**
- In secondary hyperaldosteronism (as in cirrhosis), there will be a decrease Na excretion

Effect of CRF on biochemistry tests

- BUN and pl.Creat may only rise until the GFR < **50 %**

- **Water :Inability to concentrate or dilute urine:**
  Polyuria,nocturia

- **Potassium imbalance**

- **Anemia: due to decrease erythropoietin production (normocytic)**

- **Hyperphoshatemia,hypocalcemia,decrease Vit D production and secondary hyperparathyroidism**

- **Renal osteodystrophy: (osteitis fibrosa cystica)**

- **NAGMA progressing when GFR IS 20 % of normal**