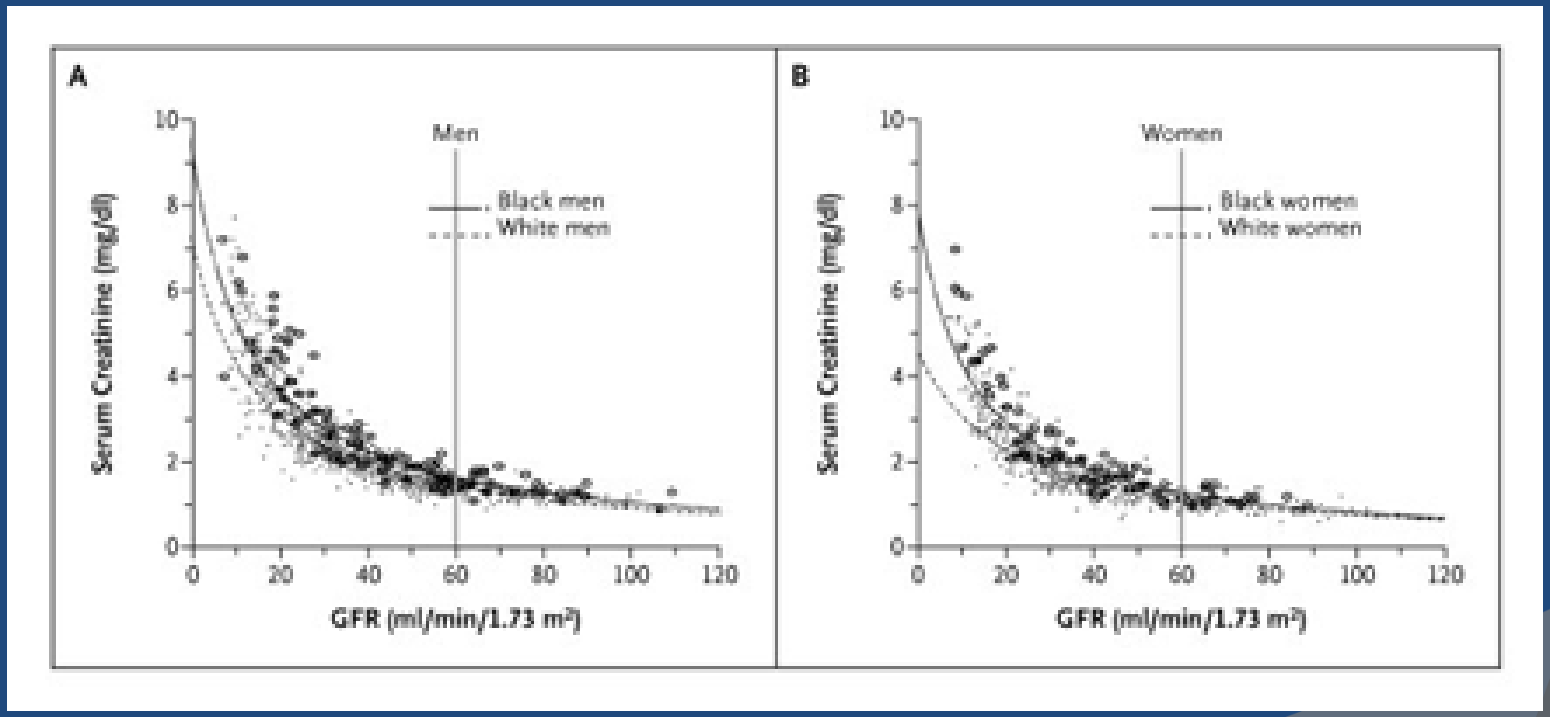
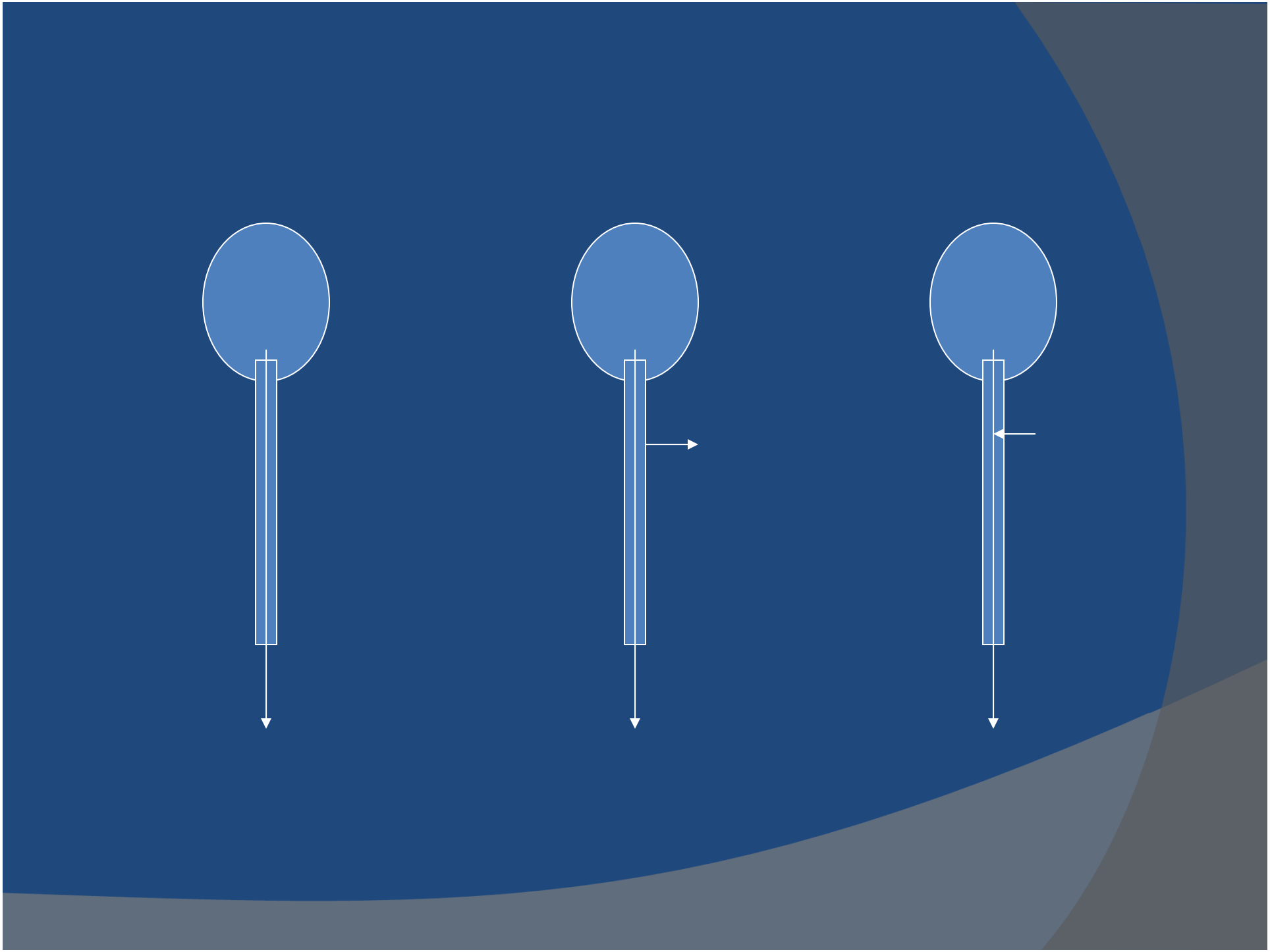
MANAGEMENT OF CKD WITH REFERENCE TO DIABETIC NEPHROPATHY

Madhivanan Sundaram MD DM DNB
Assistant Professor
Dept of Nephrology

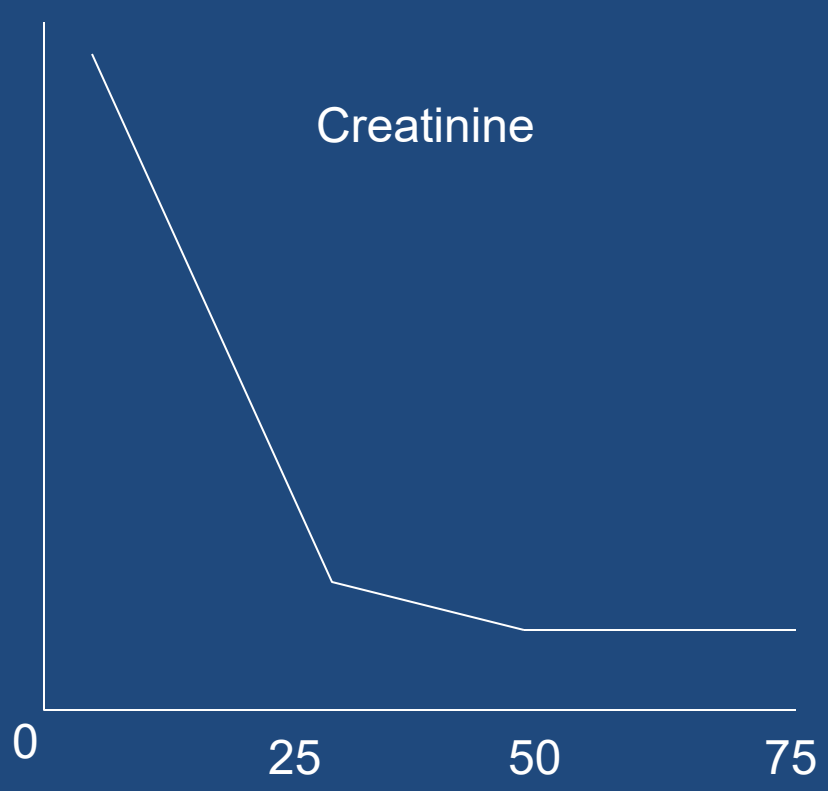
Assessment of renal function

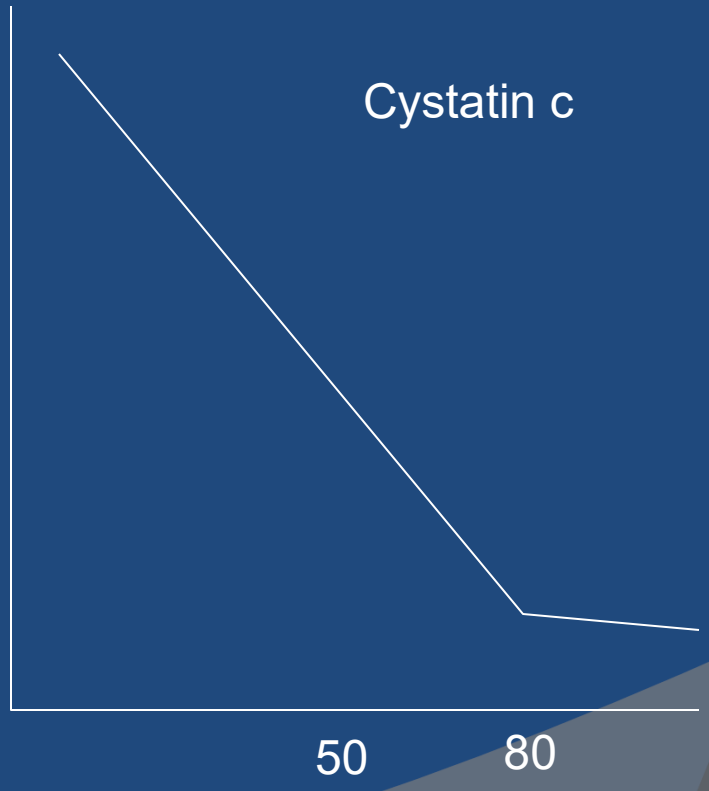
Creatinine- it's the best we have!





The alternative





Options aplenty !

Equation Author, Year (No. of Subjects)	Equation
Cockcroft-Gault Equation Cockcroft,[121] 1976 (N = 236)	$C_{Cr}\,(\text{ml/min}) = \dfrac{(140 - Age) \times Weight}{72 \times S_{Cr}} \times (0.85 \text{ if female})$
MDRD, Serum Variables Levey,[17] 1999 (N = 1,070, 558 in validation set)	$GFR\,(\text{ml/min/1.73 m}^2) = 170 \times (S_{Cr})^{-0.999} \times (Age)^{-0.176} \times (SUN)^{-0.170} \times (Alb)^{+0.318}$ $\times (0.762 \text{ if female}) \times (1.180 \text{ if black})$
Jelliffe Equation, 1973 Jelliffe,[130] 1973 (No data)	$C_{Cr}\,(\text{ml/min}) = \dfrac{98 - 0.8 \times (Age - 20)}{S_{Cr}} \times (0.90 \text{ if female})$
Mawer Equation Mawer,[131] 1972 (N = 16)	Men: $C_{Cr}\,(\text{ml/min}) = \dfrac{Weight \times \left[29.3 - (0.203 \times Age)\right] \times \left[1 - (0.03 \times S_{Cr})\right]}{(14.4 \times S_{Cr})} \times \dfrac{Weight}{70}$ Women: $C_{Cr}\,(\text{ml/min}) = \dfrac{Weight \times \left[25.3 - (0.175 \times Age)\right] \times \left[1 - (0.03 \times S_{Cr})\right]}{(14.4 \times S_{Cr})} \times \dfrac{Weight}{70}$
Hull Equation Hull,[132] 1981 (N = 103, 144 measurements)	$C_{Cr}\,(\text{ml/min}) = \left(\dfrac{145 - Age}{S_{Cr}} - 3\right) \times \dfrac{Weight}{70} \times (0.85 \text{ if female})$
Jelliffe Equation, 1971 Jelliffe,[122] 1971 (No data)	Men: $C_{Cr}\,(\text{ml/min}) = \dfrac{100}{S_{Cr}} - 12$ Women: $C_{Cr}\,(\text{ml/min}) = \dfrac{80}{S_{Cr}} - 7$
Reciprocal Serum Creatinine Equation	$C_{Cr}\,(\text{ml/min}) = \dfrac{100}{S_{Cr}}$
Gates Equation Gates,[133] 1985 (N = 90, 100 measurements)	Men: $C_{Cr}\,(\text{ml/min}) = (89.4 \times S_{Cr}^{-1.2}) + \left((55 - Age) \times (0.447 \times S_{Cr}^{-1.1})\right)$ Women: $C_{Cr}\,(\text{ml/min}) = (60 \times S_{Cr}^{-1.1}) + \left((56 - Age) \times (0.3 \times S_{Cr}^{-1.1})\right)$
Bjornsson Equation Bjornsson,[134] 1983 (N = 50, validation set)	Men: $C_{Cr}\,(\text{ml/min}) = \dfrac{27 - (0.173 \times Age) \times Weight \times 0.07}{S_{Cr}}$ Women: $C_{Cr}\,(\text{ml/min}) = \dfrac{25 - (0.175 \times Age) \times Weight \times 0.07}{S_{Cr}}$

Prediction equations

- CGCrCl:
  - a) Men: CrCl = [(140-age)∗ Weight (Kg)]/[SCr ∗ 72] ∗ 1.73/BSA
  - b) Women: CrCl = [(140-age)∗ Weight (Kg)]/[SCr ∗ 72] ∗ 0.85 ∗ 1.73/BSA
- CGGFR estimate:
  - GFR = 0.84 ∗ CGCrCl
- MDRD1:
  - GFR = 170 ∗ [SCr] $^{-0.999}$ ∗[age] $^{-0.176}$ ∗[0.762, for female] ∗[1.18, for blacks] ∗[BUN] $^{-0.170}$ ∗[ALB]$^{0.318}$
- MDRD2:
  - GFR:186 ∗[SCr] $^{-1.1154}$ ∗[age] $^{-0.203}$ ∗[0.742, for female] ∗[0.212, for blacks]

Computerised calculators

Rough GFR

- Equations should be used only in the steady state
- Not useful in ARF
- Reasonable criteria
  - CrCl> 50ml/min
  - CrCl 10 – 50 ml/min
  - Crcl< 10 ml/min
  - Oliguric and non oliguric

Creatinine	GFR
1	100
2	50
3	25
4	12.5
5	6.125
6	3.06125

What we know and we don't

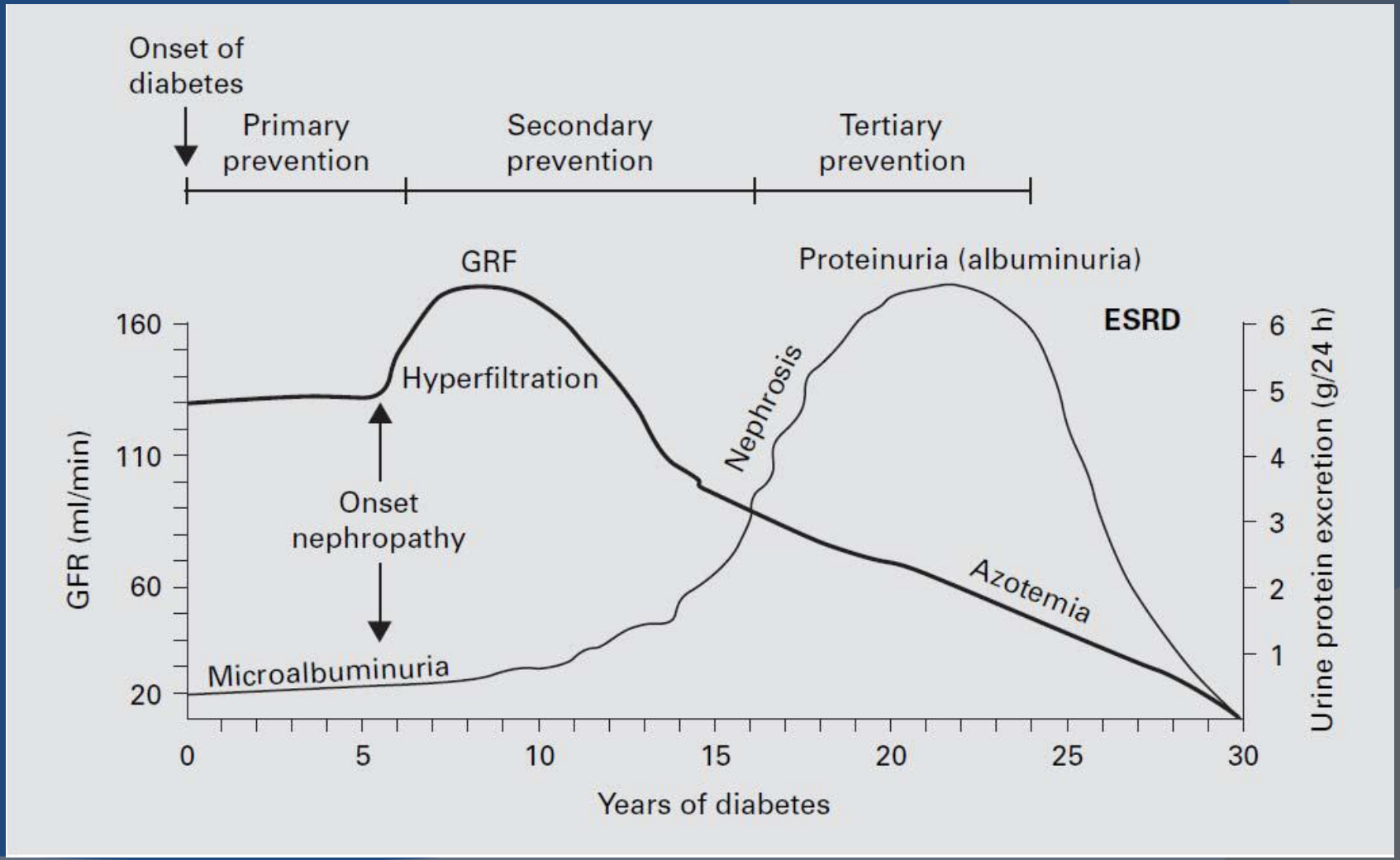
- What is the normal GFR?
  - 125 ml/min/1.73 m^2
- Is the indian normal the same?
  - Do not know
  - Probably less !!
- How low?
  - 82.3 +/- 21.3-ml/min/1.73 m2 BSA
  - 80.8 +/- 18.1-ml/min/1.73 m2

    Barai S, Bandopadhyaya GP, Patel CD et al. Do healthy potential kidney donors in india have an average glomerular filtration rate of 81.4 ml/min?

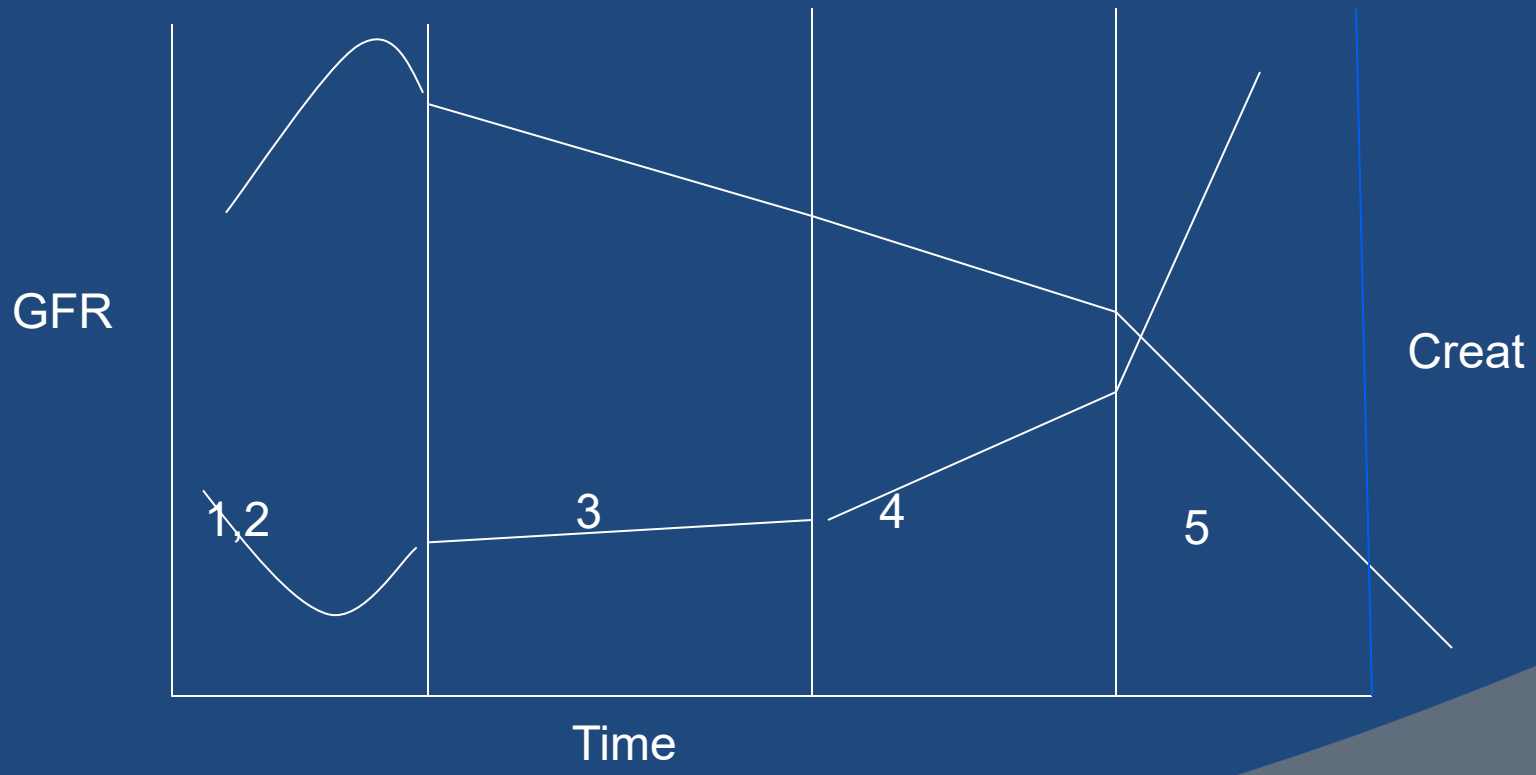
    Nephron Physiol. 2005; 101(1):21-6.

GFR- proteinuria- Creatinine connection

Natural history of DN



Diabetes



Staging CKD

Table 11. Definition of Chronic Kidney Disease

Criteria
1. Kidney damage for ≥3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either*: • Pathological abnormalities; or • Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR <60 mL/min/1.73 m^2 for ≥3 months, with or without kidney damage

Methods to estimate GFR are discussed in Guideline 4. Markers of kidney damage are discussed in Guidelines 5–6.

Table 10. Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m^2 for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

CKD management

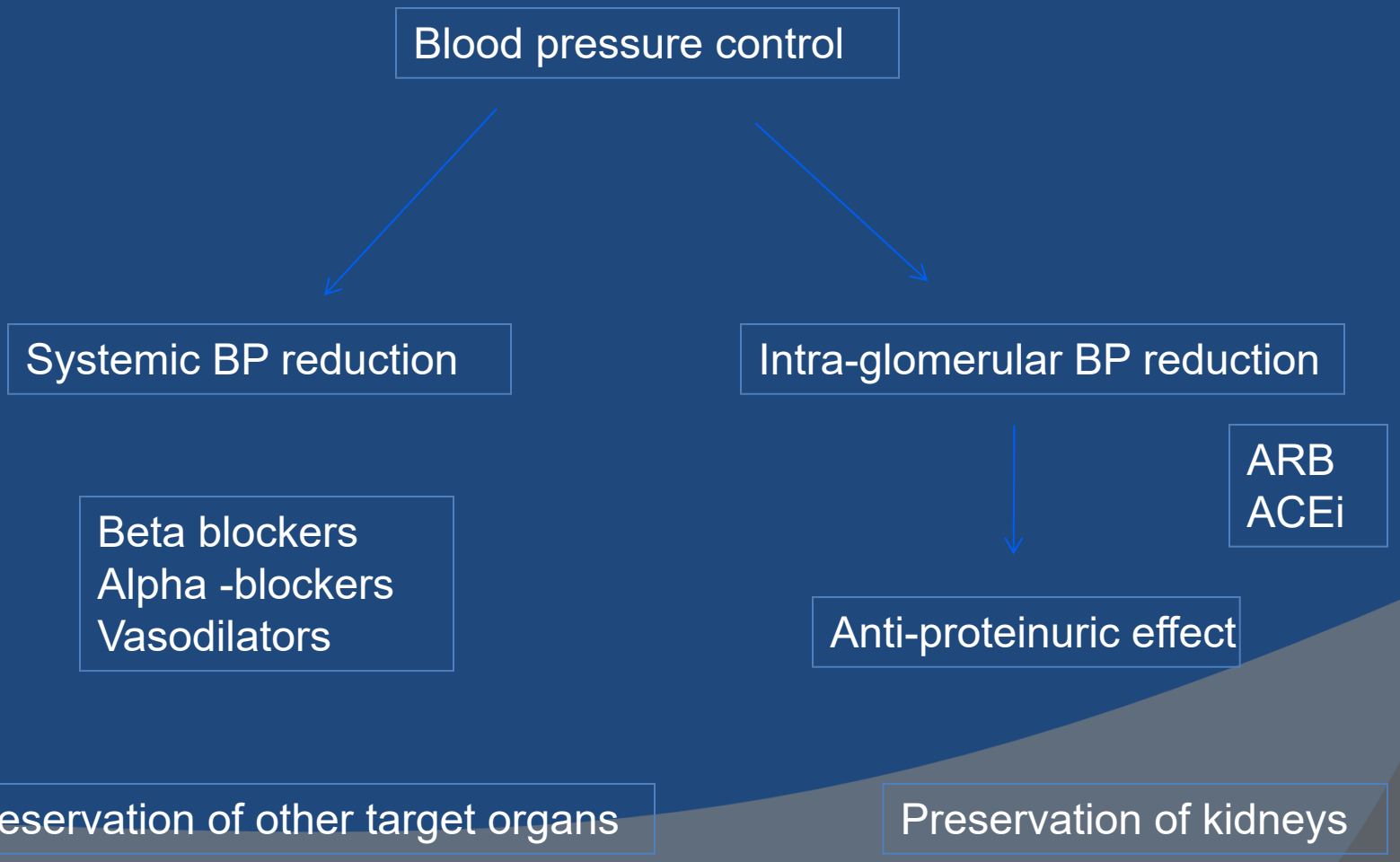
Problems

- Precautions
- Blood pressure control
- Dietary protein restriction
- Management of MBD
- Management of anemia
- Vaccination
- Volume control
- Cardiovascular disease screening
- Options of renal replacement

Precautions

- No nephrotoxics
  - Impair glomerular function: NSAIDS
  - Impair tubular function: Aminoglycosides
  - NO contrast agent exposure
- Drug dose adjustment
- Treat intercurrent infections properly
- Educate about native drugs
- Early referral to nephrologist

Blood pressure management



Protein restriction

- Preservation of organ repair
- Daily dietary requirement (FAO)
  - 0.6 g/Kg/d plus 2 SD= 0.8 g/Kg/d
- MDRD study
  - Dietary protein restriction may offer a benefit
- Remember to preserve adequate calories

Secondary hyperparathyroidism

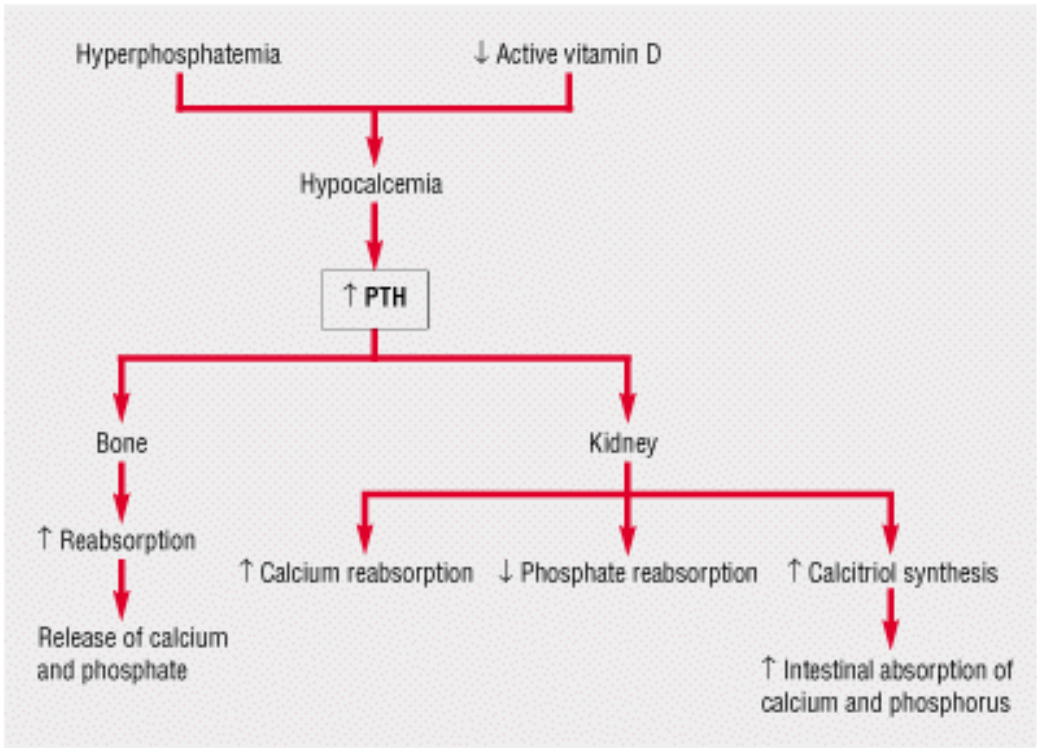
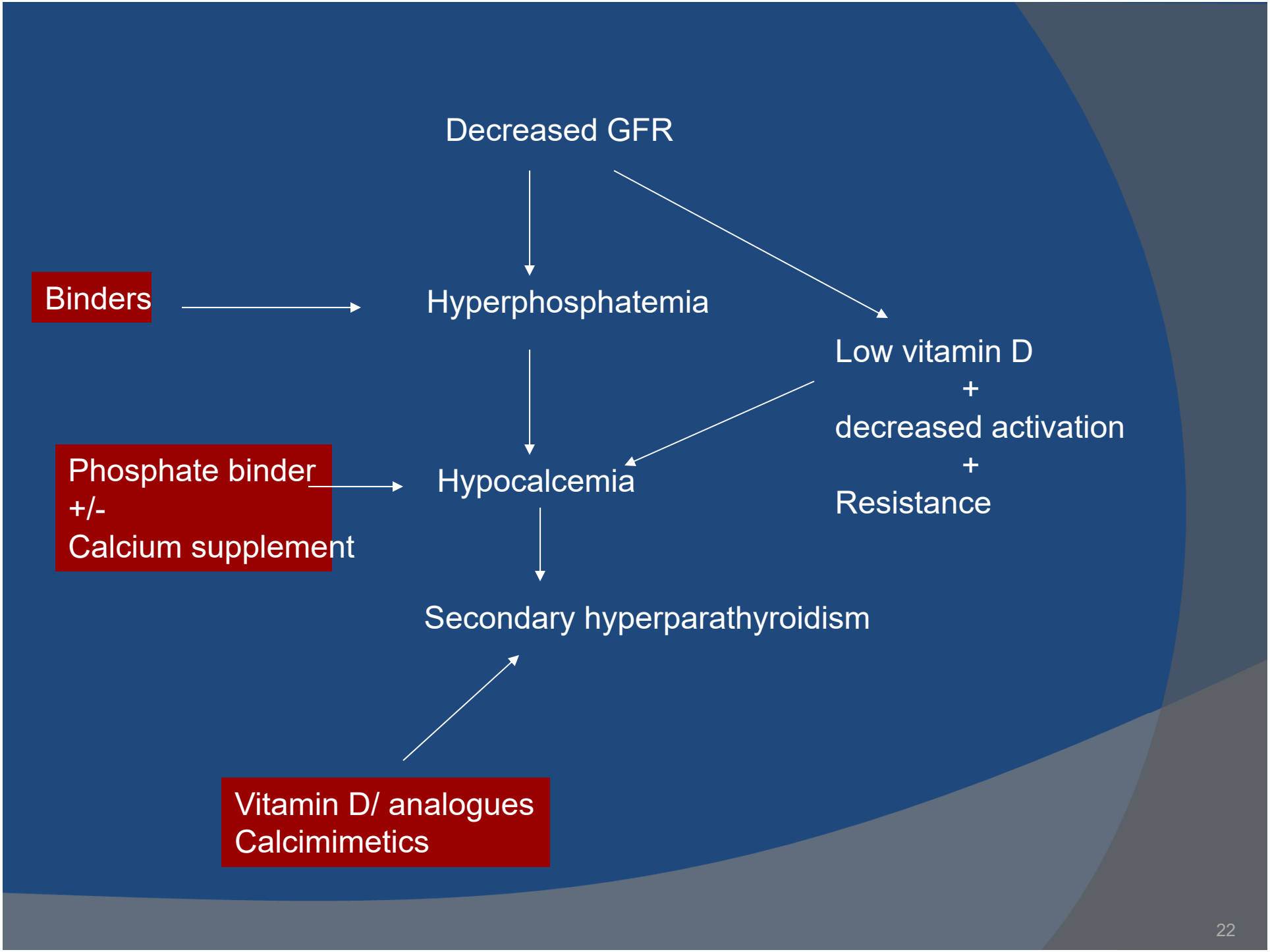


Figure 1. Abnormalities in metabolism of calcium and phosphorus in patients with chronic kidney disease. PTH, parathyroid hormone.


Decreased GFR
Binders
Hyperphosphatemia
Low vitamin D
+
decreased activation
+
Resistance
Phosphate binder
+/-
Calcium supplement
Hypocalcemia
Secondary hyperparathyroidism
Vitamin D/ analogues
Calcimimetics

Targets

Stage	Calcium*	Phosphorous	PTH
Stage 3	8.4 to 9.5	2.7 to 4.6	35-70
Stage 4	8.4 to 9.5	2.7 to 4.6	70-110
Stage 5	8.4 to 9.5	3.5 to 5.5	150 to 300

*Corrected calcium

BMD

- Dietary phosphate restriction
- Phosphate binders
  - Aluminium
  - Calcium
  - Magnesium
  - Non aluminium, calcium, magensium binders
- Replenishment of vitamin D stores
- Activated vitamin D 1, 25 (OH)2D3
- Vitamin D analogues
  - Paricalcitrol
  - Doxercalcitriol

Anemia management

EPO deficiency

Blood loss

Defect in iron absorption

Aluminum toxicity

B12 and folate deficiency

Hemolysis

Hyperparathyroidism

Drugs like ARB

Diseases like myeloma

Pure Red Cell Aplasia

Correction of anemia

- Identify iron deficiency
- Oral iron vs parenteral iron
- Iron sucrose
- Don’t overload iron
- Avoid transfusions
- EPO therapy if iron replete
- Target 11 to 12 g/dl
- Start at small dose and titrate upwards
- Twice weekly to thrice weekly
- Newer analogues may be used less frequently

Vaccinations

- Hepatitis B
  - 20 mcg each deltoid IM 0, 1, 2, 6 months
  - Check Anti HBS titre post vaccination after 3rd dose
  - Only 60 % seroconvert in ESRD
- Pneumococcal vaccine
- Influenza vaccine

Volume control

- Problems with salt and water excretion in CKD is relatively later
- Proteinuric conditions may develop this problem early
- Diabetic remain proteinuric even while fibrosis continues to proceed
- Fluid restriction and salt restriction is important

Restriction water intake

- Water 1500
- Other food 1000

- Urine 1500
- Sweat 500
- Stool 500

Salt absorption enhances fluid absorption

Cardiovascular disease screen

- Renal disease is a cardiovascular risk factor
- CKD promotes vascular calcification
- Non invasive evaluation important
- Contrast agents carries risk of RCIN- benefits to risk

Options of renal replacement

- Hemodialysis
- Peritoneal dialysis
- Renal transplantation

Hemodialysis

- Vascular access
  - Arterivenous fistula
  - Arteriovenous graft
  - Permacath
- Co-morbidities
  - Cardiovascular compromise
  - Autonomic neuropathy
  - Other diabetic complications- PVD, Neuropathy, Foot problems, vision
  - Infections
- Patient compliance with fluid ingestion

Adequacy of dialysis

Dialysis units problems
Dedicated technicians
Machine maintenance
Time constraints
CQI

Disease
Co- morbidities
AVF
Residual renal function

Solute removal | Fluid removal

Patient factors
Punctuality
Motivation
Adherence to prescription
Compliance to food and fluids

Peritoneal dialysis

Advantages

- Slow, gentle
- Round the clock clearance
- Greater salt, fluid and dietary freedom
- Mobility
- No need for vascular access

Disadvantages

- Visual acuity important
- Metabolic problems and some mechanical problems
- Peritonitis

Transplantation

- Cardiovascular status
  - Angiogram and repair important before transplanting
- Gastropaeresis
  - Pose problems in immunosuppression absorption
- Cystopathy
  - May lead to UTI- graft pyelonephritis
- Vascular disease
  - Anastamosis
- Donor availability
  - Smaller family norms, familial diabetic tendency
  - Spouse/ deceased donors

Diabetes

- Asymptomatic bacteriuria is more common (20%)
- UTIs are likely to be more severe in diabetic than nondiabetic women
- Asymptomatic bacteriuria often precedes symptomatic UTI in type 2 diabetes [RR] 1.65
- Risk factors for UTI in diabetics includes those
  - who take insulin (relative risk 3.7)
  - longer diabetes duration (>10 years, relative risk 2.6)
    - but not glucose control
- Emphysematous pyelonephritis, xanthogranulomatous UTI and fungal UTI are common

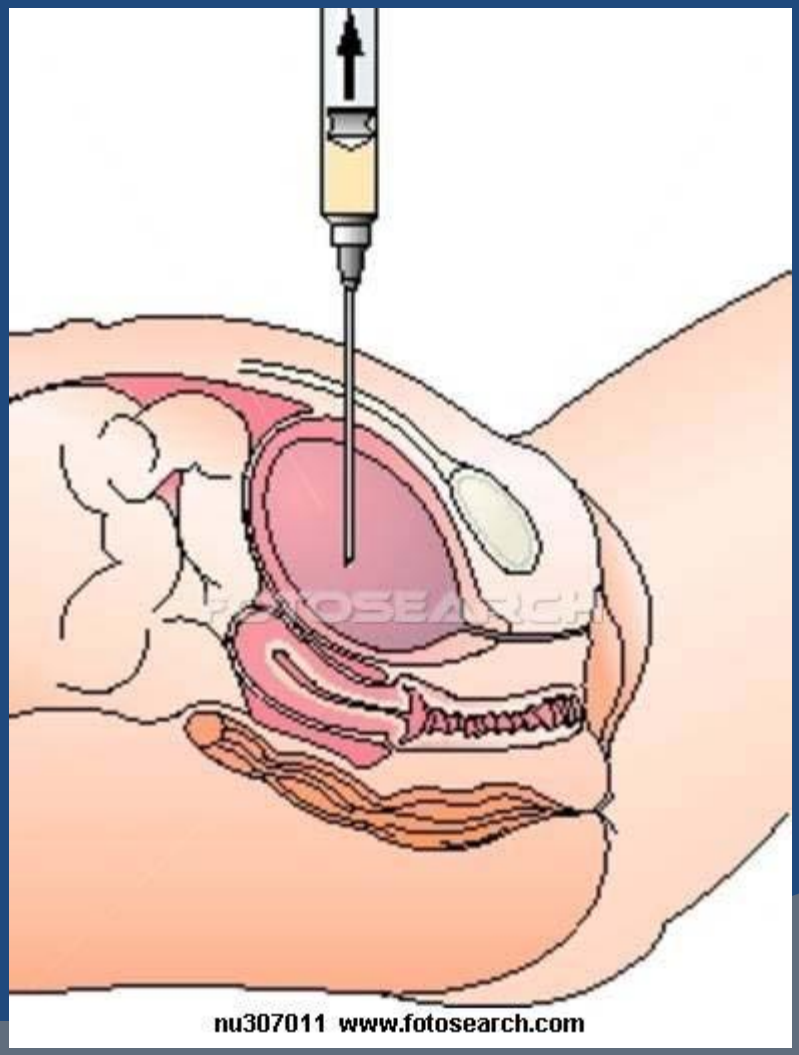
To treat or not to treat:that is the question

- Pregnancy
- Urological intervention

- Diabetes
- Non pregnant women
- Spinal cord injury
- Indwelling catheter
- Elderly

Yes **No**

Other option



Evaluate for cystopathy

- Uroflowmetry
- Residual volume
- Urodynamic study

- If significant may have to use promotility drugs
- Clean intermittent catheterisation

Thank you