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Chronic Renal Failure
Chronic Kidney Disease
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Defined as either renal injury (proteinuria) and/or a glomerular filtration rate <60 ml/min/1.73m² for >3mo

Prevalence: 18 per 1 million
Etiology:

Under 5 yr (most commonly Congenital abnormalities)

* Renal Hypoplasia
* Renal Dysplasia
* Obstructive Uropathy
* Congenital Nephrotic Syndrome
* Prune Belly Syndrome
* Cortical Necrosis
* FSGS
* Polycystic Kidney
* Renal Vein Thrombosis
* Hemolytic Uremic Syndrome
Etiology

After 5 yrs (Acquired and inherited disorders)

* Glomerulonephritis
* Nephronophthisis
* Alport Syndrome

Throughout Childhood years

* Cystinosis
* Hyperoxaluria
* Polycystic Kidney Disease
Pathogenesis

Hyperfiltration Injury

* Final common pathway of glomerular destruction
* Hypertrophy of remaining nephrons
* Increase glomerular blood flow
* ↑ glomerular filtration in surviving nephrons
* Progressive damage to surviving nephrons (due to elevated hydrostatic pressure / toxic effect)
* ↑ excretory burden on surviving nephrons
* Sclerosis of nephrons
Pathogenesis (Continued)

Proteinuria:
* Exerts a direct toxic effect
* Infiltration of monocytes / macrophages
* Enhancing glomerular sclerosis

Hypertension:
* Exacerbate disease progression
* Arteriolar nephrosclerosis
* Hyperfiltration injury

Hyperphosphatemia:
* Calcium phosphate deposition

Hyperlipidemia:
* Oxidant medicated injury
## Stages of CKD

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR</th>
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<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>&gt; 90</td>
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<tr>
<td>2</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60-89</td>
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<tr>
<td>3</td>
<td>Moderate ↓ in GFR</td>
<td>30-59</td>
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<tr>
<td>4</td>
<td>Severe decrease in GFR</td>
<td>5-29</td>
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<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
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Pathophysiology of Chronic Kidney disease

Accumulation of nitrogenous waste products
  Decrease in glomerular filtration rate

Acidosis
  Decrease ammonia synthesis.
  Impaired bicarbonate reabsorption
  Decrease net acid excretion

Sodium Retention
  Excessive renin production, oliguria

Sodium Wasting
  Solute diuresis, tubular damage
Hyperkalemia
Decrease in GFR
Metabolic acidosis
Excessive potassium intake
Hyporeninemic hypoaldosteronism

Renal Osteodystrophy
Impaired renal production 1,25-Dihydroxycholecalciferol
Hyperphosphatemia
Hypocalcemia
Secondary hyperparathyroidism

Growth Retardation
Inadequate caloric intake
Renal osteodystrophy, Metabolic acidosis
Anemia, Growth hormone resistance
Anemia

- Decreased erythropoietin production
- Iron deficiency, Vitamin $B_{12}$ deficiency
- Decreased erythrocyte survival

Bleeding tendency
- Defective platelet function

Infection
- Defective granulocyte functions
- Indwelling dialysis catheters

Neurologic symptoms (fatigue, poor concentration, headache, drowsiness, memory loss, seizures, peripheral neuropathy)
- Uremic factors, Aluminum toxicity
- Hypertension
Gastrointestinal symptoms (feeding intolerance abdominal pain)
  Gastroesophageal reflux
  Decreased gastrointestinal motility

Hypertension
  Volume overload, Excessive renin production

Hyperlipidemia
  Decreased plasma lipoprotein lipase activity

Pericarditis / cardiomyopathy
  Uremic factors, Hypertension
  Fluid overload

Glucose intolerance
  Tissue insulin resistance
Clinical Manifestation

Depends upon underlying renal disease

* Lethargy, Anorexia, Vomiting
* Growth failure / short stature
* Failure of thrive
* Pallor
* Edema
* Hypertension
* Hematuria
* Proteinuria
* Polyuria
* UTI
Physical Examination

* Pallor & sallow appearance
* Short stature
* Bony abnormality of renal osteodystrophy
* Edema
* Hypertension
Laboratory Findings

* Elevated BUN and creatinin
* ↓ GFR
* Hyperkalemia
* Hyponatremia
* Acidosis
* Hypocalcemia
* Hyperphosphatemia
* Elevated uric acid
* Hypoproteinemia (if proteinuria)
* Normocytic, normochromic anemia
* Elevated serum cholesterol and triglyceride
* Hematuria & Proteinuria (glomerulonephritis)
GFR (ml/min /1.73m²) = \frac{k \times \text{height (cm)}}{\text{S. Creatininin (mg/dl)}}

k = 0.33 \text{ LBW < 1 yr}
0.45 \text{ term AGA < 1yr}
0.55 \text{ children & adolescent female}
0.70 \text{ adolescent male}
Treatment

Aims

* Replacing absent / diminished renal function
* Slowing progression of renal dysfunction
Fluid & Electrolyte Management

* Most patients maintain normal sodium & water balance
* Polyuric with urinary sodium loss: give high volume, low caloric density feeding with sodium supplements
* High BP, edema or heart failure: require sodium restriction & diuretic therapy
* Fluid restriction is rarely necessary until ESRD
* Hyperkalemia: restriction of dietary K+ intake
  oral alkalinizing agent kayexalate
Acidosis

Sodium bicarbonate tab. (650mg = 8 mEq base)

Bacitra (1mEq sodium citrate / ml)
Maintain serum bicarbonate > 22 mEq/L
Nutrition

* Progressive restriction of various dietary components
* Dietary restriction of phosphorus, potassium and sodium
* RDA of caloric intake for age
* Protein intake 2.5g/kg/day
* High biologic value protein (egg, milk, meat, fish, fowl)
* Supplement carbohydrate (polycose), fat (MCT) and protein (pro-Mod)
* Nasogastric, gastrostomy, or gastrojunal tube feeding
* Continuous overnight infusions
* Water soluble vitamins, routinely supplied
* Zinc and iron only if deficiency
* Supplement with fat soluble vitamins – usually not required
Growth

* Short stature is long term sequela
* Growth hormone resistant state (GH ↑, IGF ↓)
* Abnormality of IGF binding protein
* Recombinant human GH (0.05mg/kg/24hrs)
* Continue until 50th percentile for MPH or achieves a final adult height or undergoes renal transplantation
Renal Osteodystrophy

* Spectrum of bone disorders in CKD
* High turnover bone disease
* Secondary hyperparathyroidism
* Osteitis fibrosa cystica
Pathophysiology

* When GFR decline to 50% of normal
* Decline in $1\alpha$ hydroxylase
* Decreased production of activated Vit. D
* ↓ intestinal absorption of calcium
* Hypocalcaemia
* Secondary hyperparathyroidism (to correct hypocalcemia)
* Increased bone resorption
* When GFR declines to 25% of normal
* Hyperphosphatemia – further promotes hypocalcemia and increased PTH
Clinical Manifestations of Renal Osteodystrophy

* Muscle weakness, Bone pain
  Fractures with minor trauma
  Rachitic changes, varus or valgus deformity
* Ca ↓ Ph ↑, alkaline phosphate ↑, PTH normal
* Subperiosteal reorption of bone with widening of metaphysis
Treatment of Renal Osteodystrophy

* Low phosphorus diet
* Phosphate binders
* Calcium carbonate & calcium acetate
* Sevelamer (Renagel) non calcium binder
* Avoid aluminum based binder
* Vitamin D therapy
* Maintain calcium / phosphorus product $(Ca \times PO_4)$ at $< 55$
Adynamic Bone disease

- Low turnover bone disease
- Osteomalacia
- Oversuppression of PTH
Anemia

* Inadequate erythropoietin production
* Iron deficiency
* Folic acid, Vitamin B₁₂ deficiency
* Decreased erythrocyte survival
* Erythropoietin of Hb < 10g/dl
* Dose 50-150 mg/kg/dose S/C 1-3 times/wk
* Keep Hb between 12-13 g/dl
* Darbopoeitin alfa (longer acting)
* Dose 0.45μg/kg/wk
Hypertension

* Salt-restriction
* Diuretic therapy
* Hydrochlorothiazide 2 mg/kg/24hrs
* Furosemide 1-2 mg/kg/dose
* ACE inhibitors - angiotensin II blockers for proteinuric renal disease (Enalapril, lisopril, losartan)
* Calcium channel blockers (Amlodipin)
* B-Blockers (propranolol, atenolol)
Immunizations

* Immunization according to the schedule
* Avoid live vaccine if on immunosuppressive drugs
* Give live vaccine before renal transplantation
* Yearly influenza vaccine
* Suboptimal response
Adjustment in drug dose
adjust doses as per GFR
Strategy to slow the progression

* Optimal control of hypertension
* Maintain serum phosphorus (Ca x Ph=<55)
* Prompt treatment of infectious and episodes of dehydration
* Correction of anemia
* Control of hyperlipidemia
* Avoidance of smoking
* Prevention of obesity
* Avoid use of NSAID
* Dietary protein restriction helpful but not recommended in children
Thank You