ACUTE KIDNEY INJURY

&

CHRONIC KIDNEY DISEASE

Renal Failure

Partial or complete impairment of Kidney function resulting in an inability to excrete metabolic waste products and water

Results in functional disturbances of all body systems

Acute Renal Failure (ARF) has :

- Rapid onset
- Reversible
- Mortality Rate~50%.

Chronic Kidney Disease (CKD) develops :

- Slowly & Progressive .
- Irreversible .
- Requires dialysis or transplant.

Terms

- Azotemia
  - Insufficient filtering of blood by kidneys
- Uremia
  - Azotemia + “uremic” symptoms

Acute Renal Failure

Definition:

Rapid (hours to weeks) decline in GFR and retention of waste products

It is a clinical syndrome cause by many renal or extrarenal diseases

Early sign of ARF is oliguria.

Only seen in 2/3 of ARF patients.

Symptoms and signs depend on cause.

ARF is a common complication in hospitalized patients

Acute Renal Failure

Serum creatinine concentration will typically increase by ↑ >0.5mg/dl daily

Increase in serum Creatinine of >50% from baseline.

Reduction in the calculated Creatinine Clearance of 50%

Significant (>50%) decrease in GFR with an associated accumulation of nitrogenous wastes (BUN & Creatinine) in the body (Azotemia)

Urine output <0.5ml/kg/hr

Cr increase ≥ 1.0 mg/dl/2d

Any decrease in renal function that requires dialysis.

ARF Epidemiology

Incidence:

In healthy population Annual incidence ~0.02%

13% in patients with preexisting CKD

2-5% of hospitalized patients(55% Iatrogenic)

7-23% of ICU patients

20-60% Require dialysis;

Of those who survive initial dialysis

<25% require long-term dialysis

Still, Mortality very high (~60%)

Most common cause of death : Sepsis, Cardiac failure and Respiratory failure.

Mortality rates are lower for nonoliguric (>400ml/day) then oliguric ARF (<400 ml/day).

Acute Renal Failure

Serum creatinine provides the most accurate and consistent estimation of GFR.

ARF categorized based on anatomic area of injury or malfunction

- **Prerenal**
- **Renal (Intrinsic)**
- **Postrenal**

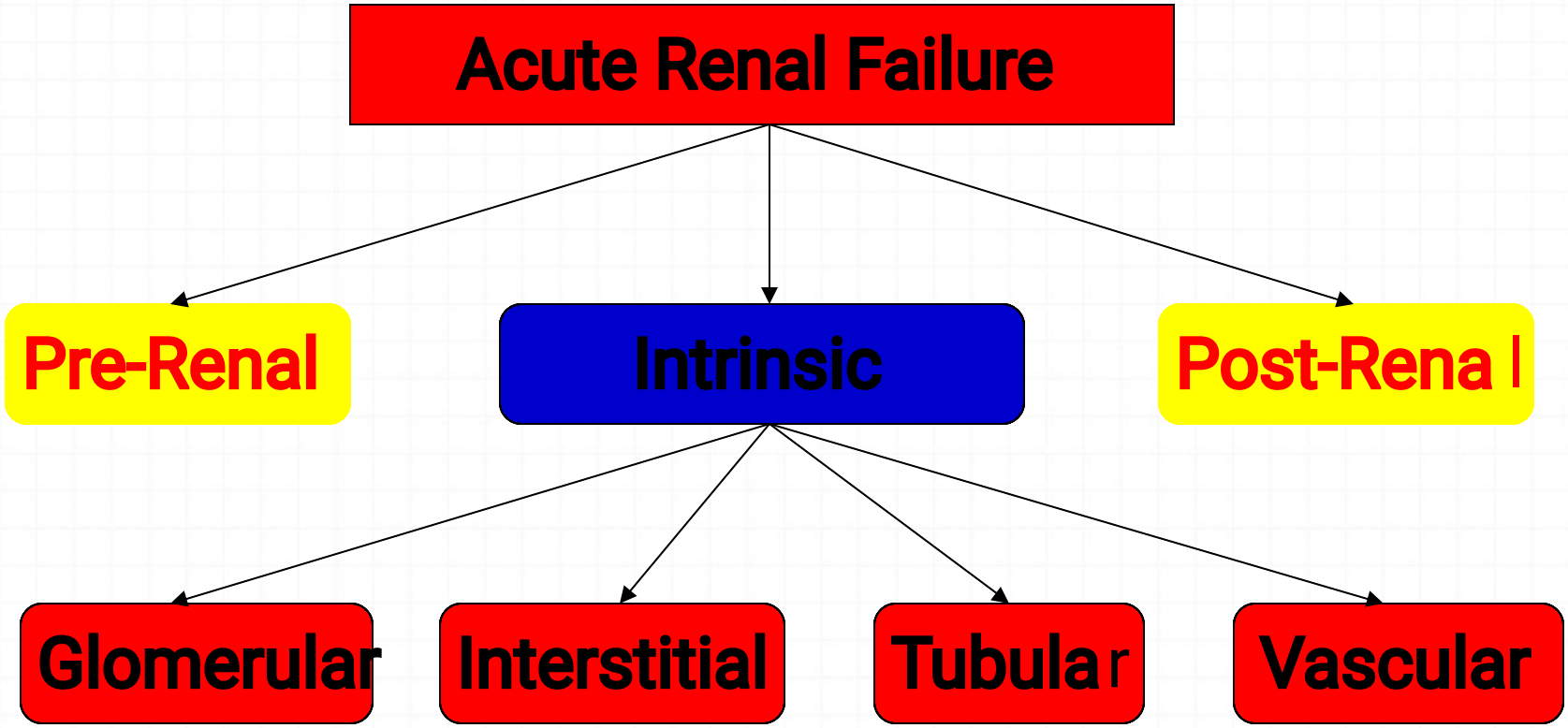
Clinical Description of Acute Renal Failure

NON-OLIGURIC > 400 mL urine output in 24 h

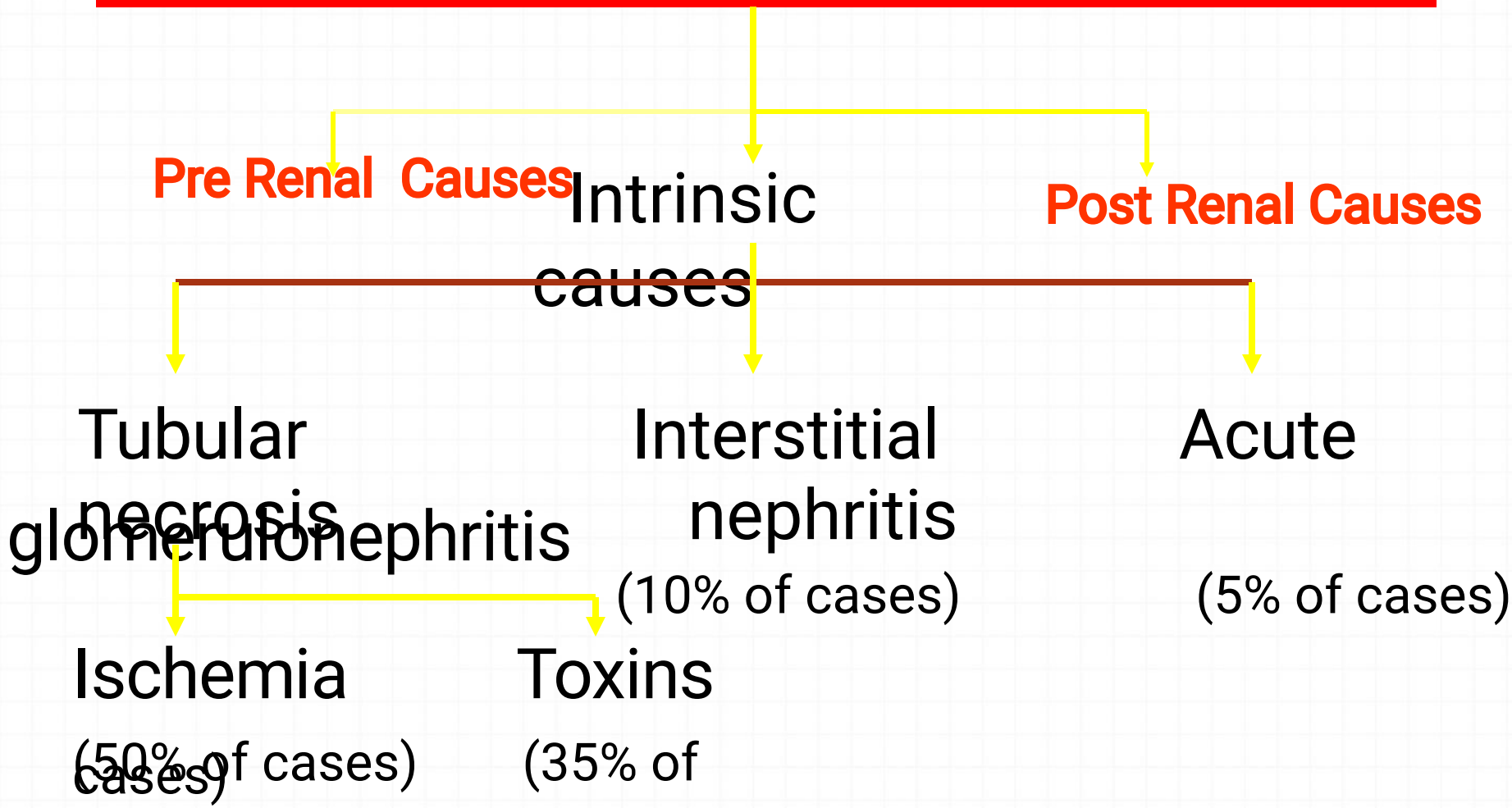
OLIGURIC < 400-500 mL urine output in 24 h

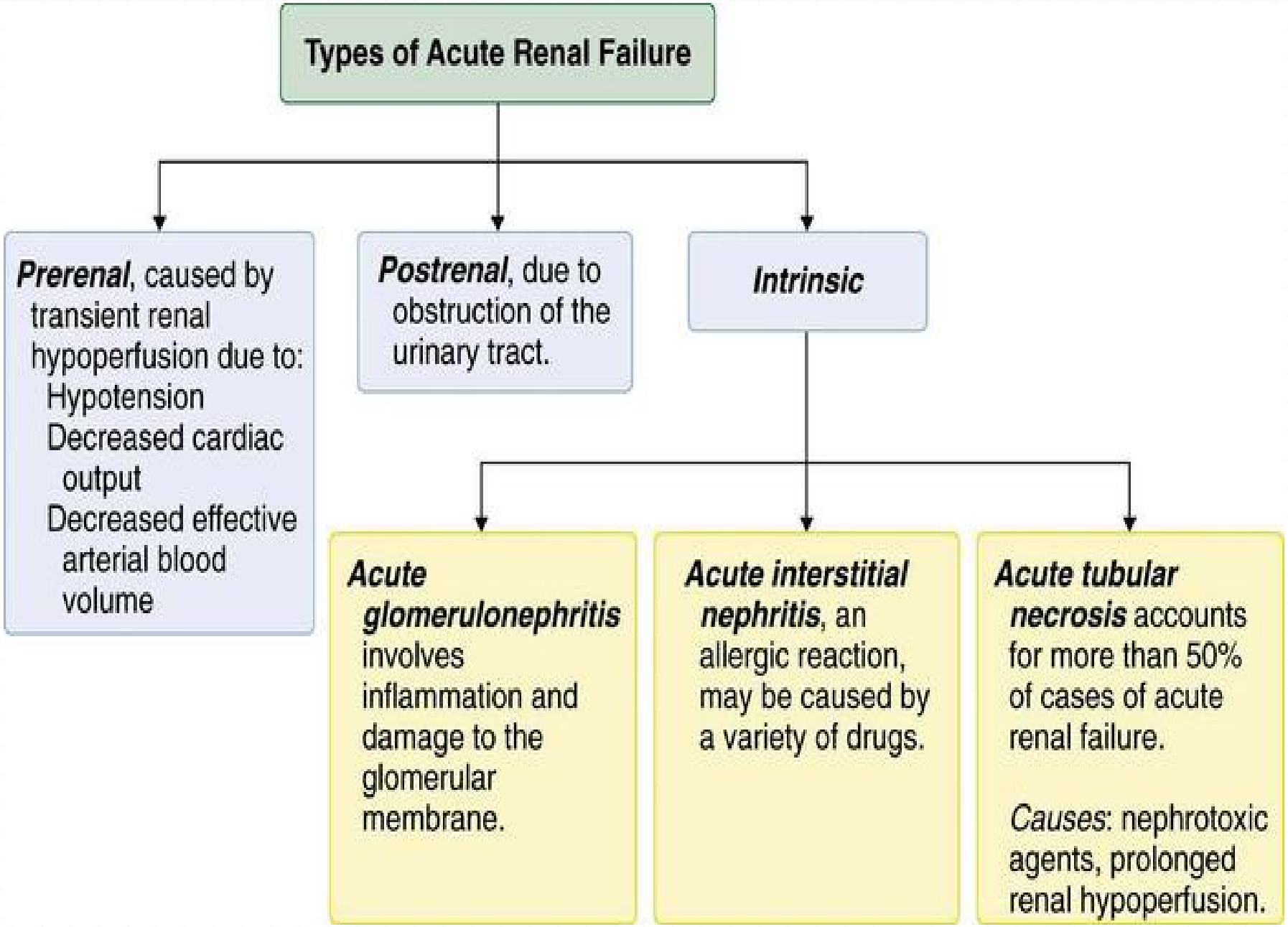
ANURIC < 100 mL urine output in 24 h

Classification of ARF



Acute Renal Failure



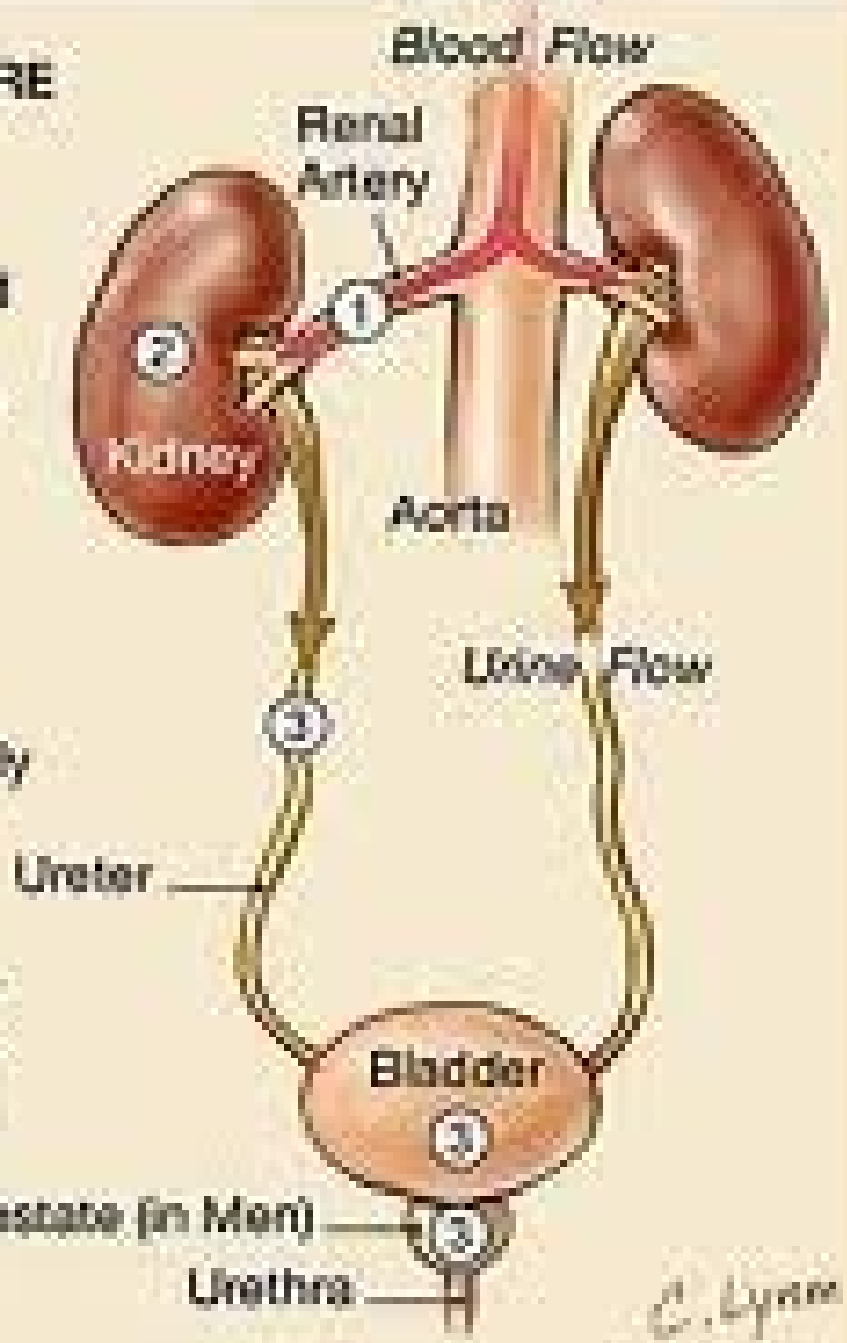

Types of Acute Renal Failure
Prerenal, caused by transient renal hypoperfusion due to:
Hypotension
Decreased cardiac output
Decreased effective arterial blood volume
Postrenal, due to obstruction of the urinary tract.
Intrinsic
Acute glomerulonephritis involves inflammation and damage to the glomerular membrane.
Acute interstitial nephritis, an allergic reaction, may be caused by a variety of drugs.
Acute tubular necrosis accounts for more than 50% of cases of acute renal failure.
Causes: nephrotoxic agents, prolonged renal hypoperfusion.

CAUSES OF ACUTE RENAL FAILURE

(1) Prerenal
Sudden and severe drop in blood pressure (shock) or interruption of blood flow to the kidneys from severe injury or illness

(2) Intrarenal
Direct damage to the kidneys by inflammation, toxins, drugs, infection, or reduced blood supply

(3) Postrenal
Sudden obstruction of urine flow due to enlarged prostate, kidney stones, bladder tumor, or injury



Etiology

Prerenal- 70%

- Kidney hypoperfusion due to:
  - Absolute decrease in blood volume (Dehydration, hemorrhage, GI losses,)
  - Relative decrease in blood volume (sepsis, vasodilatory drugs, renal artery stenosis)

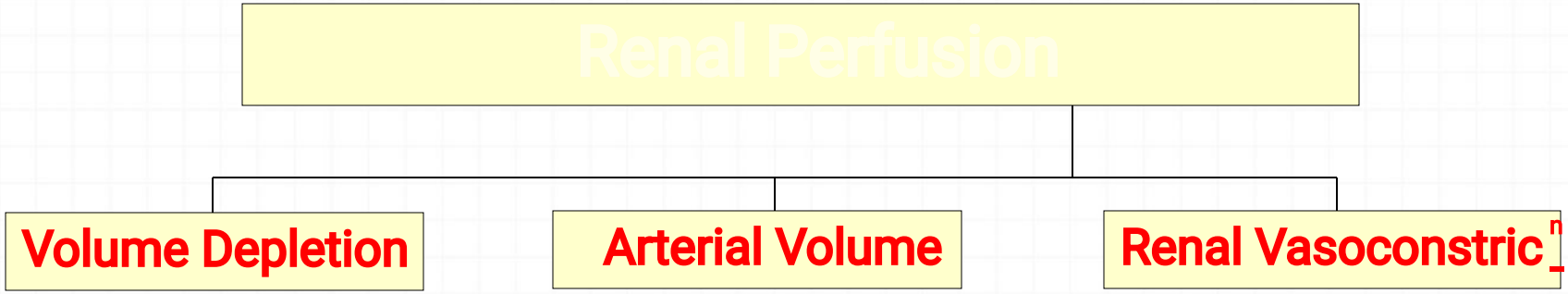
Intrinsic – 25- 40 %

- Parenchymal injury due to:
  - Acute Glomerulonephritis
  - Interstitial Nephritis
  - Acute Tubular Necrosis (ischemia, drugs, or toxins)

Postrenal

- Obstruction due to
  - Calculi, Tumor, etc.

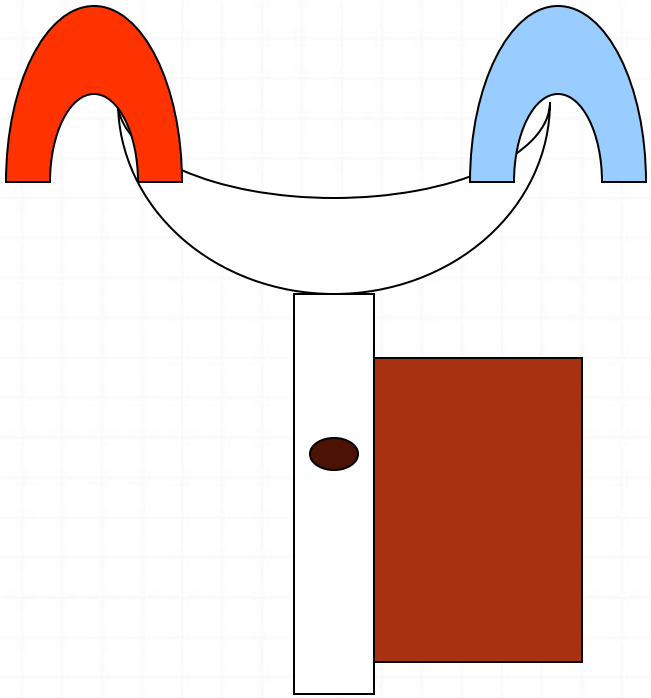
Pre-renal ARF



Effects of NSAIDS and ACE inhibitors on Glomerular Hydrostatic Pressure

Prostaglandins cause afferent vaso dilation

Locally produced AII causes efferent vaso constriction



Blocked by NSAIDS

Blocked by ACE inhibitors

Pre-Renal Failure

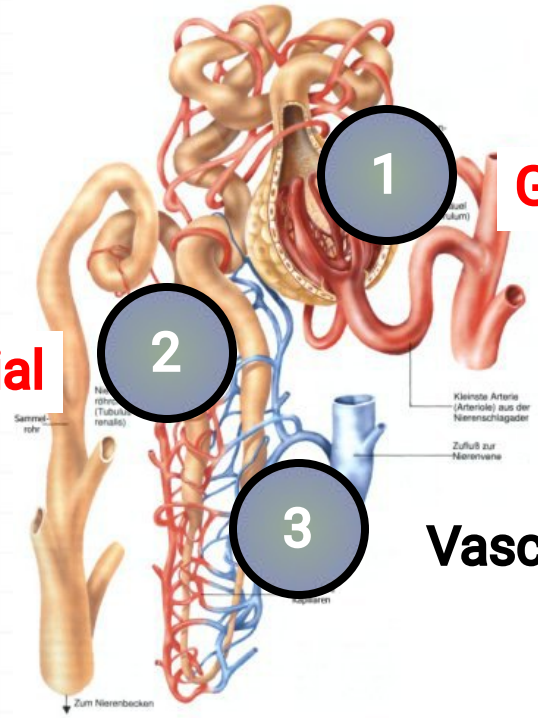
Urinary Findings

- Lots of H2O resorbed
- Concentrated urine
- ↑Uosm
- Lots of Na resorbed
- ↓U_{na}
- ↓Fe_{na}

Pre Renal Failure

	Normal	Pre-Renal Failure
BUN (mg/dl)	20	60
Cr (mg/dl)	1.0	2.0
BUN:Cr	20:1	> 20:1
UNa (mEq/L)	variable	<20
FeNa (%)	variable	<1
Uosm (mOsm/kg)	variable	>550

Intrinsic Renal ARF



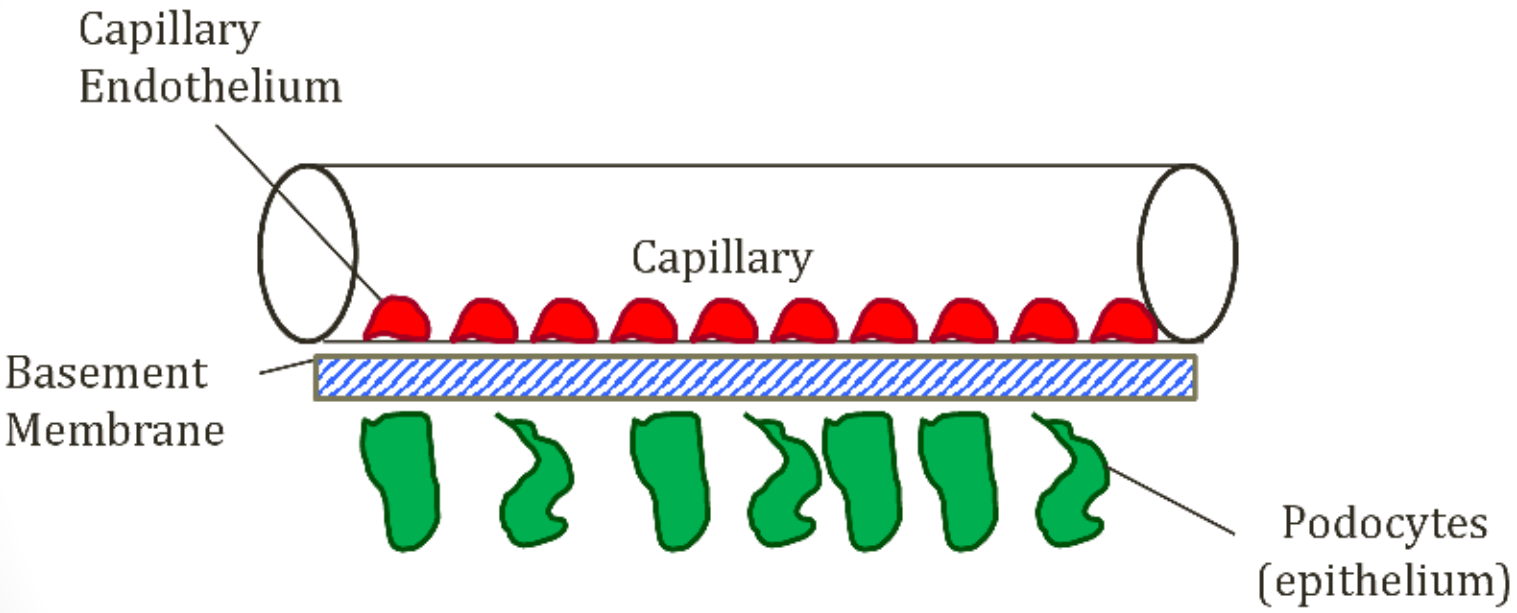
Though in all cases of intrinsic renal failure the kidney is the site of pathology, determining the nature of the problem is critical since **TREATMENT** & **PROGNOSIS** vary considerably.

Glomerular Disease Principles

Glomerulus Functions

- Allow "ultrafiltrate" into Bowman's space
  - Water, electrolytes, glucose, amino acids
- Prevent filtration of most proteins
- Prevent filtration of red blood cells
- Glomerular pathology
  - **Proteinuria**
  - **Hematuria**

Glomerular Filtration Barrier



Capillary Endothelium

- Fenestrated (i.e. has openings)
- Only small (~40nm) molecules pass through
- Repels red cells, white cells, platelets
- First barrier to filtration
- Capillary damage → RBC in urine → **hematuria**
- Capillary damage → inflammation → **nephritis**

Basement Membrane

- Negatively charged molecules
  - Type IV collagen
  - Heparan sulfate
- Repels (-) molecules like albumin
- Also size barrier

Podocytes

- Also called **epithelial cells**
- Long "processes" called "foot processes"
- Wrap capillaries
- Slits between foot processes filter blood
- Further size barrier small molecules
- Damage → loss of protein barrier

Albumin

- Small (~3.6nm)
- Can fit through all size barriers
- Negatively charged
- Repelled by GBM charge barrier
- Podocyte/GBM disease → albumin in urine

Glomerular Diseases

- Breakdown of components of filtration barrier
- Things in urine that shouldn't be there:
  - Red blood cells
  - Protein (especially albumin)

Glomerular Bleeding

- Red cell casts
- Dysmorphic red blood cells
- Acanthocytes
- Proteinuria
- Red, smoky brown or ""coca cola""
- Clots generally not seen

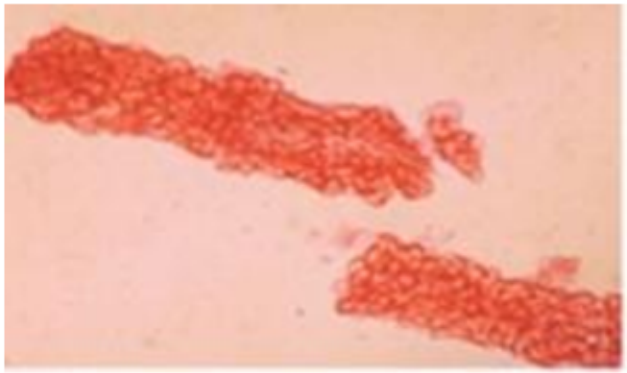


Image courtesy of Anwar Siddiqui

Proteinuria

- Urine dipstick
  - Color change indicates amount of protein
  - Primarily detects albumin (good for glomerular disease!)
  - 1+, 2+, 3+, 4+
  - Affected by urine concentration

Proteinuria

- Urine protein-to-creatinine ratio
  - "Spot urine"
  - 1st or 2nd morning urine sample after avoiding exercise
  - Normal ratio less than 0.2 mg/mg

Proteinuria

- 24-hour urine collection
  - Gold standard for protein evaluation
  - Gives you grams/day of protein excretion
  - Normal is less than 150 mg/day
  - Cumbersome for patients
  - Errors in collection common

Glomerular Diseases

Spectrum

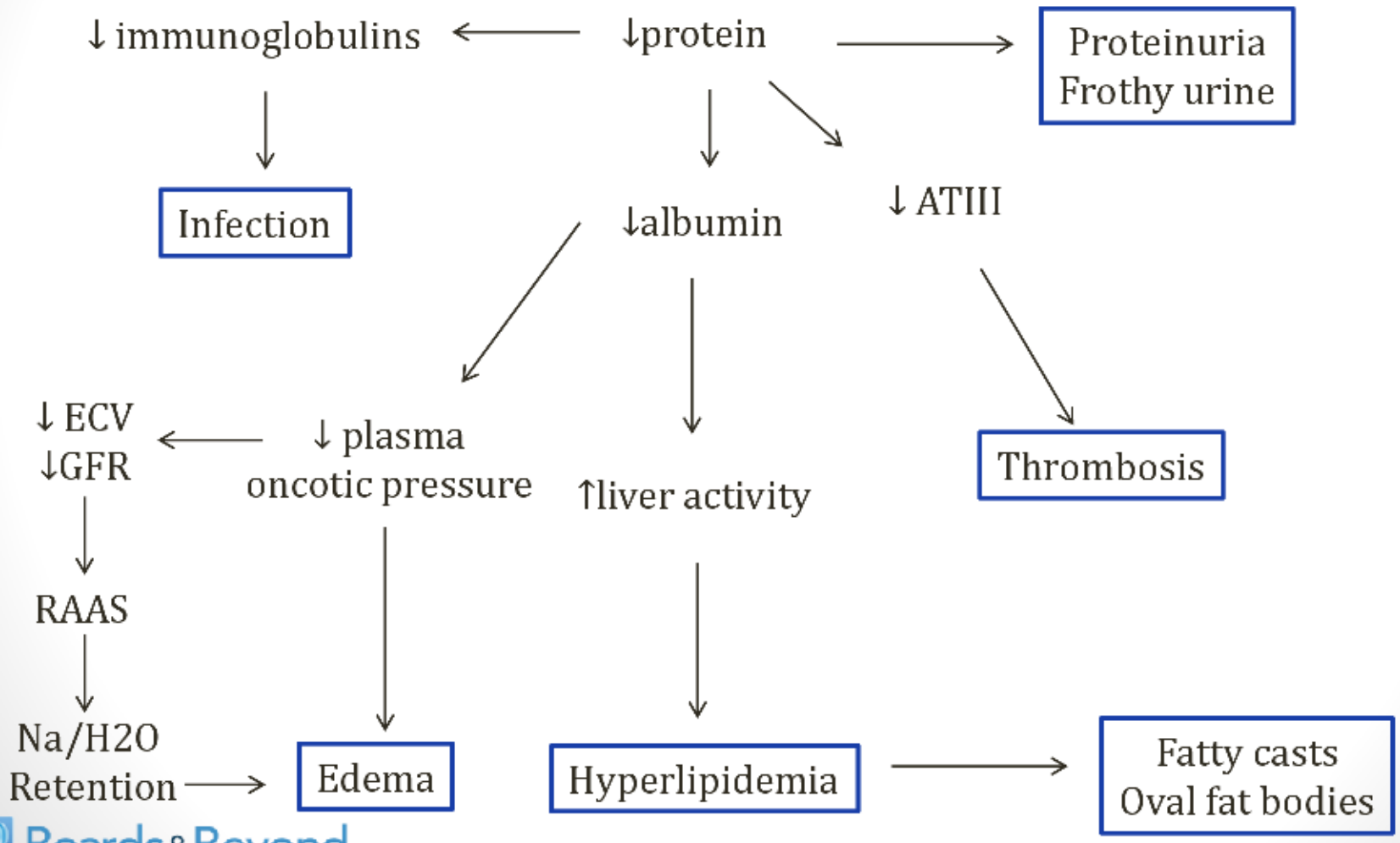
Nephritic Syndrome
RBC casts
Mild proteinuria
Renal Failure

Nephrotic Syndrome
Massive proteinuria
Hyperlipidemia

Nephrotic Syndrome

- Filtration barrier to protein is lost
- RBC filtration barrier remains intact
- Massive proteinuria
  - 4+ on dipstick
  - >3.5g/day
- Triggers cascade of pathology

Nephrotic Syndrome



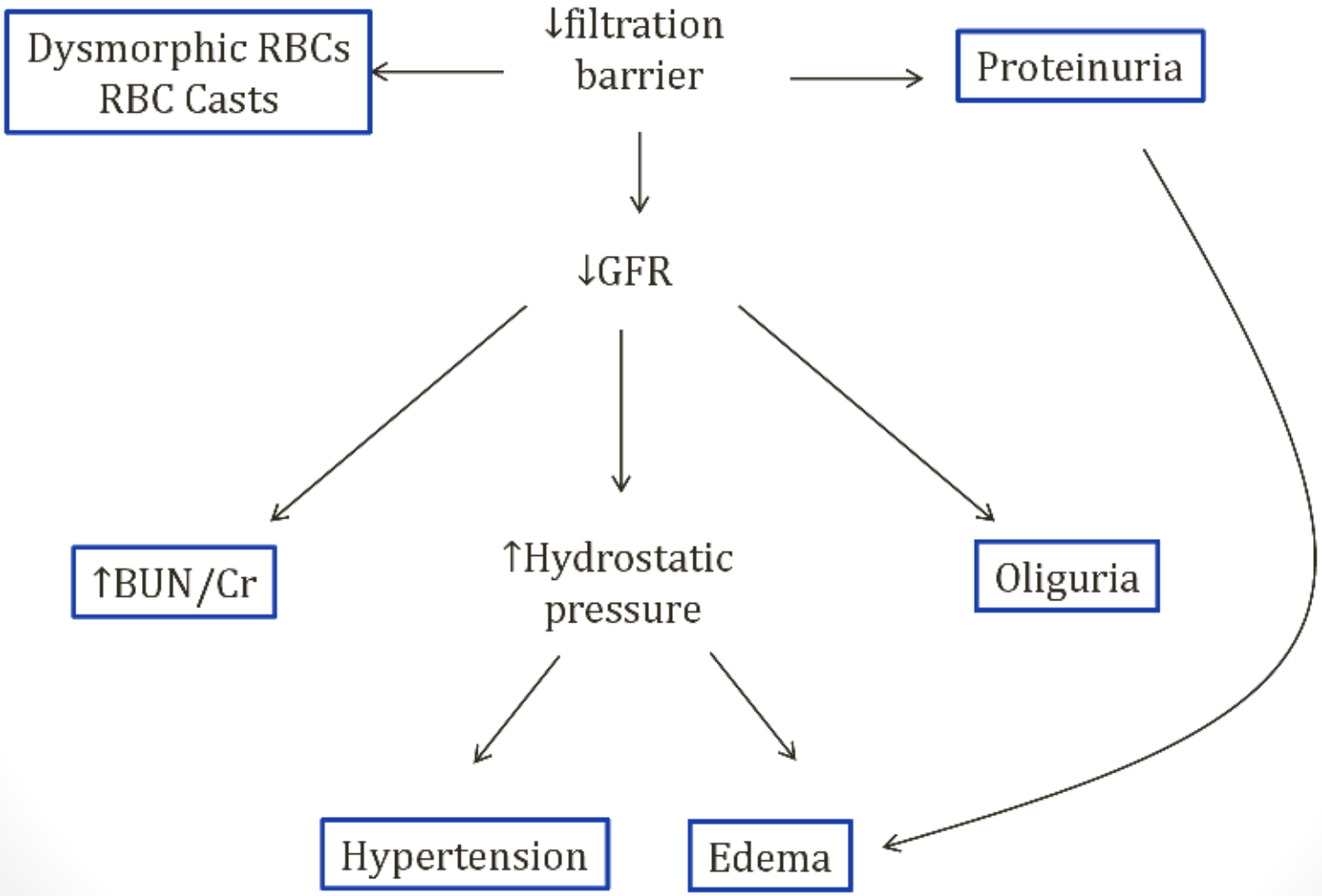
Nephrotic Syndrome

- Classic presentation
  - Frothy urine
  - Swelling of ankles
  - Swelling around eyes (periorbital)
  - Often mistaken for allergic reaction
  - Serum total cholesterol >300mg/dl
  - Proteinuria (>3.5g/day)

Nephritic Syndrome

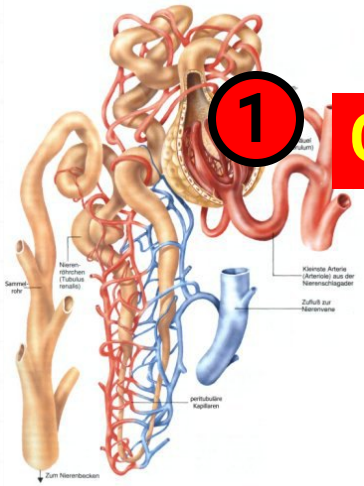
- Inflammatory process damages entire glomeruli
- Filtration barrier to RBCs and protein lost
- Glomerular damage: ↓GFR
- RBC in urine
  - Dysmorphic
  - RBC Casts
- Protein in urine
  - Less than nephrotic syndrome due to lower GFR
  - <3.5g/day

Nephritic Syndrome



Nephritic Syndrome

- Classic presentation
  - Dark urine (RBCs)
  - Swelling
  - Fatigue (uremia)
  - Proteinuria (<3.5g/day)



Glomerular: 5%

NEPHROTIC ⟷ NEPHRITIC

- Diabetes
- Amyloidosis
- Minimal Change
- Membranous
- IgA Nephropathy
- RPGN
- FSGS
- MPGN I & II

Rapidly Progressive Glomerulonephritis

Anti-GMB Diseases

Goodpasture's Syndrome

Anti-GBM nephritis

Immune Complex

SLE

IgA

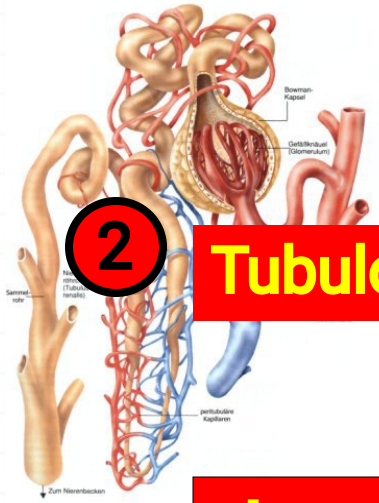
Cryoglobulinemia

Infectious (hepatitis B/C, post-streptococcal, endocarditis)

Pauci-immune/ANCA

Wegener's Granulomatosis

Microscopic Polyangiitis



2 Tubulointerstitial

Interstitial

Acute Interstitial Nephritis (AIN)

~ 30 % AIN associated with systemic Sx of fevers, arthralgias, maculopapular erythematous rash & eosinophilia

- Drugs: penicillins, cephalosporins, NSAIDs, sufonamide analogues
- Infections: renal parenchymal or systemic
- Immunologic disorders: SLE, Sjorgren's, mixed cryoglobulinemia
- Idiopathic: 10 – 20 % of Bx-proven AIN

Tubular (85%)

Acute Tubular Necrosis (ATN)

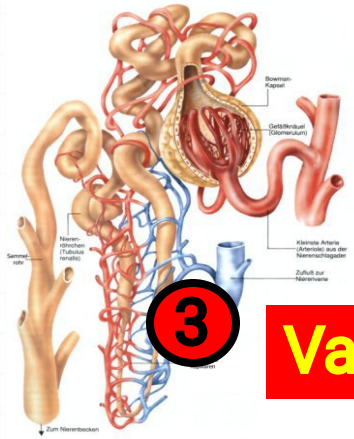
~ 45 % ARF in hospitalized patients is from ATN

Ischemic ATN

- Most common
- Often following prolonged hypoperfusion

Nephrotoxic ATN

- Drugs: aminoglycosides, amphotericin B, chemotherapeutic agents
- Endogenous toxins: hemoglobin, myoglobin, light chains



Vascular

Macrovascular

Renal artery stenosis
Renal vein thrombosis
Renal infarction

Microvascular

Malignant hypertension
Scleroderma crisis
Cholesterol emboli syndrome
Vasculitis
Microangiopathy (HUS/TTP)
Pre-eclampsia/eclampsia
Hyperviscosity syndrome

Intrinsic Renal Failure

BUN/Cr

- Kidney cannot filter blood
- Less BUN/Cr filtered
- Rising BUN/Cr in blood
- No extra rise in BUN from ↑resorption
- Normal ratio (20:1)

Intrinsic Renal Failure

	Normal	Intrinsic Failure
BUN (mg/dl)	20	40
Cr (mg/dl)	1.0	2.0
BUN:Cr	20:1	20:1
UNa (mEq/L)	variable	>20
FeNa (%)	variable	>2
Uosm (mOsm/kg)	variable	<350

Post-renal ARF

Obstruction

Ureteral

- Crystals
- Stones
- Clots
- Tumor
- Papillary necrosis

Urethral

- Clots
- Tumor
- Prostate
- Endometrial
- Neurogenic bladder

Retroperitoneal

- Fibosis

Diagnosis

ARF signs and symptom highly variable, depending on etiology

Patients may have acute change in voiding habits

Onset of flank pain Urinary stone

Severe headaches Severe hypertension as result of ARF

Determine if renal complication is Acute, Chronic, or result of acute changes in a CKD patient

Patient Assessment

- Past medical history to differentiate between acute and chronic renal failure
- Medication and recent procedure history may suggest causes for acute interstitial nephritis or other nephrotoxic effects
- Medications
  - Diuretics
  - NSAIDs
  - Antihypertensives
  - Contrast dye
  - Other recent additions or changes

Patient Assessment

Patients who develop renal insufficiency while hospitalized usually have acute initiating event

- Identified from laboratory data, urine output record, medication administration records, procedure records

Acute anuria: Caused by complete urinary obstruction or catastrophic event (shock, acute cortical necrosis)

Oliguria (urine output < 500 mL/day) develops over several days, suggests prerenal azotemia

Nonoliguria (urine output > 500 mL/day) acute intrinsic renal failure, incomplete urinary obstruction

Symptoms and Signs of Renal Failure

Retention of nitrogenous waste products

Nausea, vomiting, diarrhea, hiccup, foul taste, dry crusted mouth, itching,

Drowsiness, clouding of consciousness, pericarditis, GI bleeding,

Coma

Retention of salt and water

Pulmonary edema, peripheral edema, ascites, pleural effusion

Retention of potassium

Weakness,, paralysis, ECG changes with tenting T waves, widening of QRS complex, increased PR interval, sine wave pattern, cardiac arrest, VT

Retention of acid

Kussmaul respiration, hyperreflexia, hypotension

Uremia

An excess in the blood of urea, creatinine and other nitrogenous end products with signs and symptoms listed .

General

- Fatigue, weakness
- Pruritis

Mental status change

- Uremic encephalopathy
- Seizures
- Asterixis

GI disturbance

- Anorexia, early satiety, N/V,

Uremic Pericarditis

Platelets dysfunction/bleeding

Clinical Manifestations

Clinical Course of ARF

Initiating phase

Hours to days

Begins at time of insult and continues until symptoms become apparent.

Generally divided into 3 stages:

Oliguria

Diuresis

Recovery

Oliguric Stage

- Most common
- Oliguria within 24-48 hours of initial injury
  - May take several days to develop with nephrotoxic chemicals
  - Azotemia accompanies oliguria
- Critical to recognize, determine cause and begin treatment
  - Oliguria caused by acute-on-chronic RF usually easy to detect from history
  - Post renal obstruction must be ruled out

Oliguric Stage

Reduction of GFR

Other changes:

- Fluid volume excess
- Metabolic acidosis
- Hyponatremia
- Hyperkalemia
- Waste accumulation (Increase BUN, Creatinine)
- Neuro disorders.

Diuretic Stage

- Begins when urine output increases to >400 ml/ day
- Usually lasts 2-3 weeks
- Urine output rarely exceeds 4 L/day
- Caused partly by osmotic diuresis due to high blood urea and partly by impaired ability of recovering tubules to conserve salts and water
- May develop K^+, Na^+ and water deficits
  - **Must replace loses or death**
- BUN may continue to rise as clearance does not keep up with production
- With continued diuresis azotemia gradually disappears and get clinical improvement

Recovery Stage

Lasts up to one year

Anemia and concentrating ability gradually improve

- Some have permanent reduction in GFR

Clinical course of ARF

Diuretic phase

- Increase in u/o of 1-3 L/day
- May result hypovolemia, hypotension, hyponatremia, hypokalemia, dehydration.
- Lasts 1-3 wks.

Recovery phase

- Begins when GFR increases, allowing BUN and serum creatinine levels to decrease
- Up to 12 months to stabilize.

Outcome influenced by overall health.

Urine Indices in ARF

	Pre Renal	Intrinsic ATN	Post Renal
Uosm	> 500	< 350	< 350
Na (meq/L)	< 20	> 20	> 20
Bun/Cr (mg/dL)	> 20:1	< 10:1	< 10:1
FENa	< 1%	>3%	>3%
FEUrea	<35%	>55%	>55%
Sediment	Hyaline casts	Brown, Granular casts,	Bland

Systemic Complications of ARF

Infections of urinary tract & lungs due to uremia

Up to 70% of pts. with ARF.

Anemia

Kidney makes EPO, ↓ EPO Anemia

"3rd space disease"

Salt and Water retention (esp. in prerenal failure)

Pulmonary edema, Pleural effusion, & ascites

Hypocalcemia

↓ Excretion of phosphate impaired GI absorption of Calcium.

Systemic Complications of ARF

Hyperkalemia

- ↓Glomerular filtration
- ↓Tubular secretion
- Malaise, nausea, and muscle weakness.
- A cardiac emergency

Metabolic Acidosis w/ ↑Anion Gap

- ↓ Excretion of acids & ↓ tubular reabsorption of bicarbonateresults in metabolic acidosis with a high anion gap.
- Hypotension
- Kussmaul's respirations

Treatment of ARF

Short-Term Goals

- Minimize degree of insult to the kidney
- Reduce extrarenal complications
- Expedite renal function recovery

Ultimate goal

- Restore renal function to pre-ARF baseline

Prerenal – Hemodynamic support and volume replacement

Immune related (Interstitial nephritis, GN) – promptly initiate immunosuppressive therapy

Postrenal – Remove cause of obstruction

Treatment of Acute Renal Failure

- Treat underlying cause
  - Blood pressure
  - Infections
  - Stop inciting medications
  - Nephrostomy tubes/ureteral stents if obstruction
- Hydration
- Diuresis
- Dialysis
- Renal Transplant

Primary consideration is maintenance of fluid and electrolyte balance – during all stages

Treatment of Hyperkalemia

ECG
Calcium Gluconate
Glucose and Insulin
Sodium Bicarbonate
Diuretics
Cation-exchange resins (Kayexalate)
Dialysis

Drug Therapy

- IV insulin
  - IV glucose to manage hypoglycemia
- IV 10% calcium gluconate
- Sodium bicarbonate
  - Shift potassium into cells
  - Correct acidosis
- Sodium polystyrene sulfonate (Kayexalate)
  - Cation-exchange resin
  - Resin in bowel exchanges potassium for sodium
    - Evacuates potassium-rich stool from body
    - Educate patient that diarrhea may occur due to laxative in preparation

Dopamine Agonists

Theoretical benefits:

- Low doses of IV dopamine (≤2 mcg/kg/min) should renal blood flow and induce natriuresis and diuresis
- Dopamine 2 mcg/kg/min worsened renal perfusion indices compared to saline in a crossover study in ARF patients

Current evidence does not support use of low-dose dopamine for prevention of AKI

Management of ARF - Dialysis

Indications:

- Early dialysis is better than late
- Refractory fluid overload
- Hyperkalemia (Plasma K >6.5 meq/L) or rapidly rising potassium levels
- Metabolic acidosis (pH less than 7.1)
- Uremia (Pericarditis, Seizures, Encephalopathy)
- Intoxication (Methanol, Ethylene glycol, Isopropanol, Theophylline, Lithium, Salicylates)

Chronic Kidney Disease (CKD)

Progressive, Irreversible loss of kidney function

- Progressive Azotemia over months to years.
- Culminates in End Stage Renal Disease
  - Symptoms and signs of uremia

Defined as either presence of :

- Kidney damage
  - Pathologic abnormalities
  - Markers of damage
    - Blood, Urine, Imaging tests
- GFR : <60 ml/min for 3 months or longer

Chronic Kidney Disease (CKD)

Lab abnormalities precede symptoms

Symptoms (Usually) evolve in orderly sequence

Hypertension in the majority.

- Isosthenuria (Fixed Specific Gravity)
- Broad Casts in urinary sediment are common.
- Bilateral small kidneys on US are diagnostic.

Disease staging based on decrease in GFR

- CKD defined as SCr > 1.2 to 1.5 mg/dL

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.

CKD : Diagnostic Criteria

GFR < 60 mL/min that is present for 3 or more months

With or without, evidence of kidney damage

OR

Evidence of kidney damage (with or without decreased GFR that is present for > 3 months, as evidenced by any of the following

- Microalbuminuria
- Proteinuria
- Glomerular haematuria
- Pathologic abnormalities (Abnormal Renal Biopsy)
- Anatomical abnormalities (Scarring seen on imaging or polycystic kidneys).

CKD Risk Factors

Susceptibility
Advanced age Family history Low income or education Systemic inflammation Dyslipidemia
Initiation
Diabetes mellitus Hypertension Glomerulonephritis
Progression
Glycemia (among diabetic patients) Hypertension Proteinuria Smoking Obesity

CKD - Causes

- Diabetic
- Non Diabetic
  - Glomerular
    - Nephritic: PIGN, IgA, MPGN
    - Nephrotic: FSGS, Membranous, Amyloidosis
  - Tubulointerstitial: Analgesic
  - Vascular: Vasculitis, HTN, RAS
  - Cystic: ADPKD
  - CKD in transplantation

CKD - Causes

Initiation Factors:

- Result in direct kidney damage
- Modifiable by pharmacologic therapy
  - DM
  - HTN
  - Autoimmune diseases
  - Polycystic kidney disease
  - Systemic infections /Urinary tract infections
  - Urinary stones /Lower urinary tract obstructions
  - Drug toxicity

Predictors of Progressive CKD

Persistence of underlying initiation factors

- DM
- HTN
- Previous kidney damage
- Glomerulonephritis
- Polycystic Kidney Disease

Proteinuria,

Smoking

Supportive Therapies may Slow CKD Progression

Dietary protein restriction

Lipid-lowering medications

Smoking cessation

Anemia management

Limit progression with hyperglycemia & HTN treatment

Stages of Chronic Kidney Disease

Stage 1	**Kidney damage with Normal or ↑ GFR**	**GFR ≥ 90 ml/min**
Stage 2	Kidney damage with mild ↓ GFR	GFR 60-89
Stage 3	Moderate ↓ GFR	GFR 30-59
Stage 4	Severe ↓ GFR	GFR 15-29
Stage 5	Kidney failure	GFR <15 (or Dialysis)

The five stages of chronic kidney disease

	STAGE 1	STAGE 2	STAGE 3	STAGE 4	STAGE 5
Amount of kidney function remaining at each stage	More than 90%	60 to 89%	30 to 59%	15 to 29%	Less than 15%
Description of each stage	Early kidney damage with normal or even increased function.	Worse kidney damage with reduced function.	Even worse kidney damage with less function.	Kidney damage is so severe with such poor function that the kidneys are barely able to keep the person alive.	End-stage Renal Disease: kidney function is severely impaired. The kidneys are not working well enough to keep the person alive.
Symptoms	No symptoms observed. Urea and creatinine levels are normal.	No symptoms observed. Urea and creatinine levels are normal, or mildly elevated.	Early symptoms occur and may include tiredness, poor appetite, and itching. Creatinine level rises, excess urea is present, and anemia may begin to occur.	Tiredness, poor appetite, and itching may get worse.	Symptoms may include poor sleeping at night, difficulty breathing, itchiness, and frequent vomiting. High levels of creatinine and urea are present.
eGFR (estimated Glomerular Filtration Rate)	90 ml/min or more	60 – 89 ml/min	30 – 59 ml/min	15 – 29 ml/min	15 ml/min or less
Treatment options*	Identify cause and try to reverse it.	Monitor creatinine level, blood pressure, and general health and well-being. Try to stop or slow the worsening kidney function.	Continue to try to stop or slow the worsening kidney function. Patient learns more about the disease and treatment options.	Plan and create access site for dialysis. Receive assessment for possible transplant.	Start renal replacement therapy: dialysis or transplantation.

Symptoms of Chronic Renal Failure

Many are symptom free until 2/3 of renal mass lost.

Often no physical examination findings or history.

Several common modes of presentation:

- Progressive lethargy, anorexia, (and later vomiting)
- Hypertension, and /or Heart failure
- Unexplained anaemia
- Abnormal findings on biochemistry
- Development & progression may be insidious

CKD - Manifestations

Abnormal Sodium-Water metabolism

- Edema
- Hypertension

Abnormal Acid-base abnormalities

- Metabolic Acidosis due to uremia or RTA

Abnormal hematopoesis

- Anemia of CKD

CKD - Manifestations

Cardiovascular Abnormalities

- LVH
- CAD
- Diastolic Dysfunction

Abnormal Calcium-Phosphorus metabolism

- Hyperphosphatemia
- Pruritus
- Arthralgia
- Hyperparathyroidism
- Renal Osteodystrophy

CKD : Definition

Final stage of numerous renal diseases

Resulting from progressive loss of glomerular, tubular and endocrine function in both kidneys.

This leads to :

- Disturbed excretion of end products of metabolism
- Disturbed elimination of electrolytes and water
- Disturbed secretion of hormones :
  - (Erythropoietin, Renin, Prostaglandins, Active form of vitamin D)

Chronic Renal Failure

Definitions

Azotemia - Elevated BUN >28mg/dL) and creatinine (Cr>1.5mg/dL)

Uremia - Azotemia with symptoms or signs of renal failure

End Stage Renal Disease (ESRD) - Uremia requiring transplantation or dialysis

Chronic Renal Failure (CRF) - Irreversible kidney dysfunction with azotemia >3 months

Psychologic
Denial
Anxiety
Depression
Psychosis

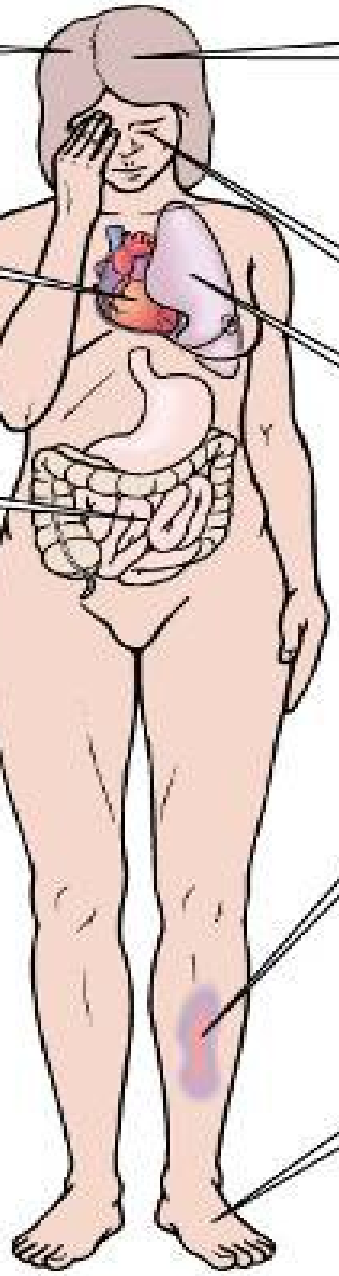
Cardiovascular
Hypertension
Heart failure
Atherosclerotic heart disease
Pericarditis
Myocardiopathy
Pericardial effusion

Gastrointestinal
Anorexia
Nausea
Vomiting
Uremic fetor
Gastrointestinal bleeding
Peptic ulcer
Stomatitis
Gastritis

Endocrine/Reproductive
Hyperparathyroidism
Thyroid abnormalities
Amenorrhea
Infertility
Sexual dysfunction
Azoospermia

Metabolic
Carbohydrate intolerance
Hyperlipidemia
Nutritional deficiencies
Gout

Hematologic
Anemia
Bleeding
Infection



Neurologic
Fatigue
Headache
Sleep disturbances
Lethargy
Muscular irritability
Seizures
Confusion
Coma

Ocular
Hypertensive retinopathy

Pulmonary
Uremic lung
Pulmonary edema
Uremic pleuritis
Dyspnea
Pneumonia
Depressed cough reflex

Integumentary
Pallor
Pigmentation changes
Pruritus
Ecchymosis
Excoriations
$CaPO_4$ deposition
Uremic frost
Dry, scaly skin

Peripheral neuropathy
Paresthesias
Motor weakness
Restless legs syndrome

Consequences of Renal Impairment

Bone disease

- Secondary hyperparathyroidism
- Osteomalacia
- Aluminium toxicity

Haematological

- Anaemia (erythropoietin)
- Bleeding tendency (Platelet function, Anaemia etc try DDAVP)

Endocrine

- GH, Prolactin, LH, reduced testosterone

Consequences of Renal Impairment

Electrolyte & Fluid balance

- Inability to dilute or concentrate urine appropriately
- Acidosis (non anion gap)
- Hyperkalaemia

Cardiovascular

- Hypertension
- Heart failure
- Pericarditis

Gastrointestinal

- Anorexia, Nausea, Vomiting, Diarrhoea

Consequences of Renal Impairment

Dermatological

- Pigmentation, pruritis, ecchymoses

Neurological

- Peripheral neuropathy
- Restless legs
- Stupor, Coma and Fits

Psychological

- Depression
- Anxiety

Complications

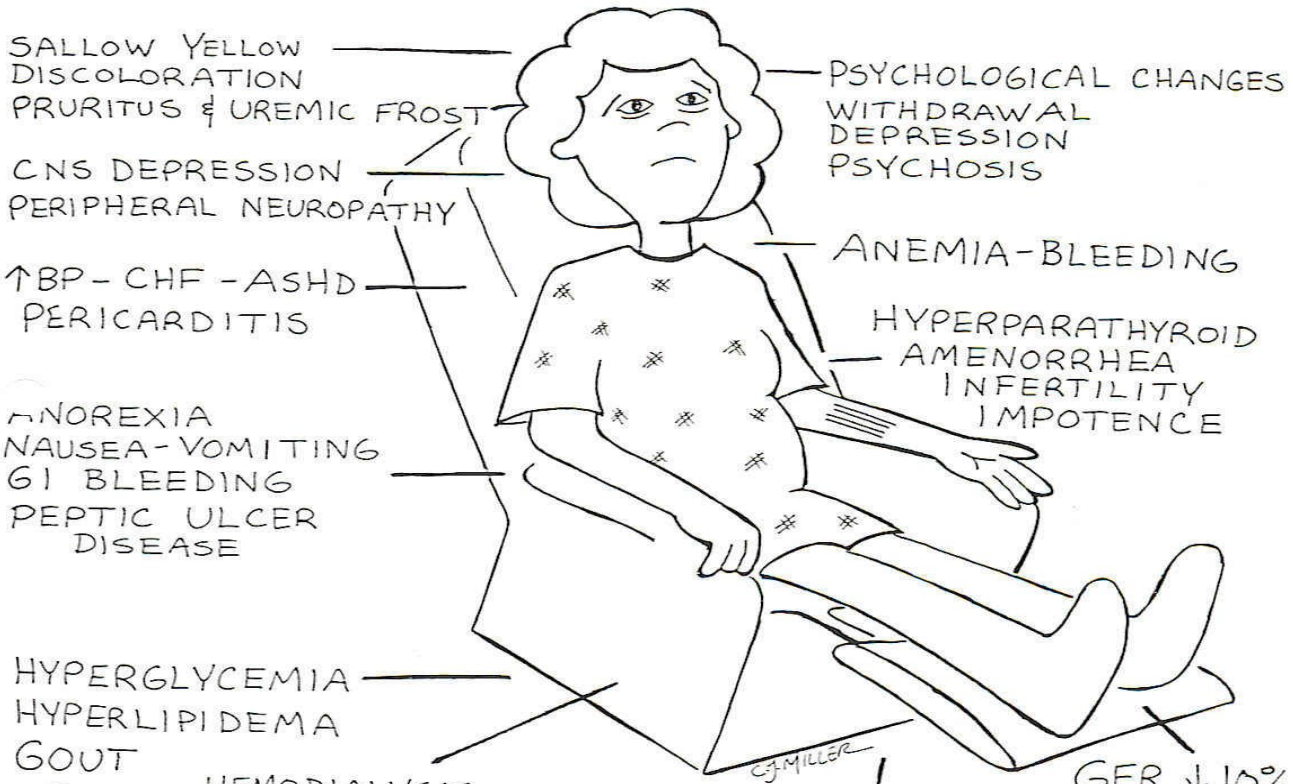
Pericarditis
Cardiac tamponade
CHF
HTN
Edema
Platelet dysfunction
Anemia
Renal encephalopathy
Dementia
Seizures
Peripheral neuropathy

Complications

Hyperparathyroidism
Osteoporosis
Osteomalacia
Decreased immune response
Increased incidence of infection
Hepatitis C, Hepatitis B, liver failure
Electrolyte imbalances:

- Hyperkalemia
- Hyponatremia
- Hypocalcemia

CHRONIC RENAL FAILURE (C.R.F.)
END STAGE (UREMIA)



Fluid - Electrolyte - pH

Water, electrolyte and ABG disturbances

- Potassium
- Sodium
- Calcium
- Phosphate
- Bicarbonate **&** Metabolic Acidosis
- PTH
- Triglycerides
- Magnesium
- Volume expansion and fluid overload

Hyperkalemia

Most serious electrolyte disorder in kidney disease

Fatal dysrhythmias

Results from :

- Decreased excretion by kidneys
- metabolic acidosis
- Food intake
- Medications

Hyperkalemia

Plasma K>5.5mmol/L

Plasma K>7.0mmol/L cardiac arrest

Most common electrolyte disorder in ARF patients

- > 90% of potassium renaly eliminated

Life-threatening cardiac arrhythmias may occur when serum potassium > 6 mmol/L

- Potassium restriction is essential
- Monitor serum potassium at least daily; twice daily for seriously ill patients
- Some medications promote potassium retention by kidneys and should be avoided or closely monitored

Hyperkalemia Symptoms

Weakness
Lethargy
Muscle cramps
Paresthesias
Hypoactive DTRs
Dysrhythmias

Hyperkalemia & ECG

K > 5.5 -6

Tall, Peaked & Tented

Wide QRS

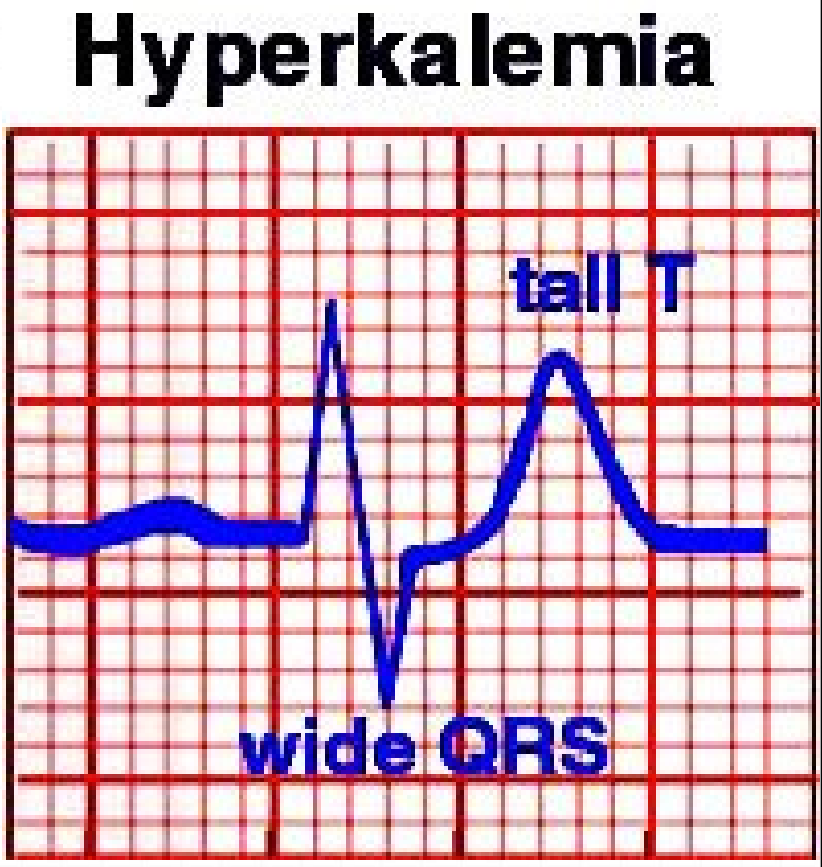
Prolong PR

In Severe cases
Diminished P

Prolonged QT

Loss Of T wave

QRS-T merge – Sine wave



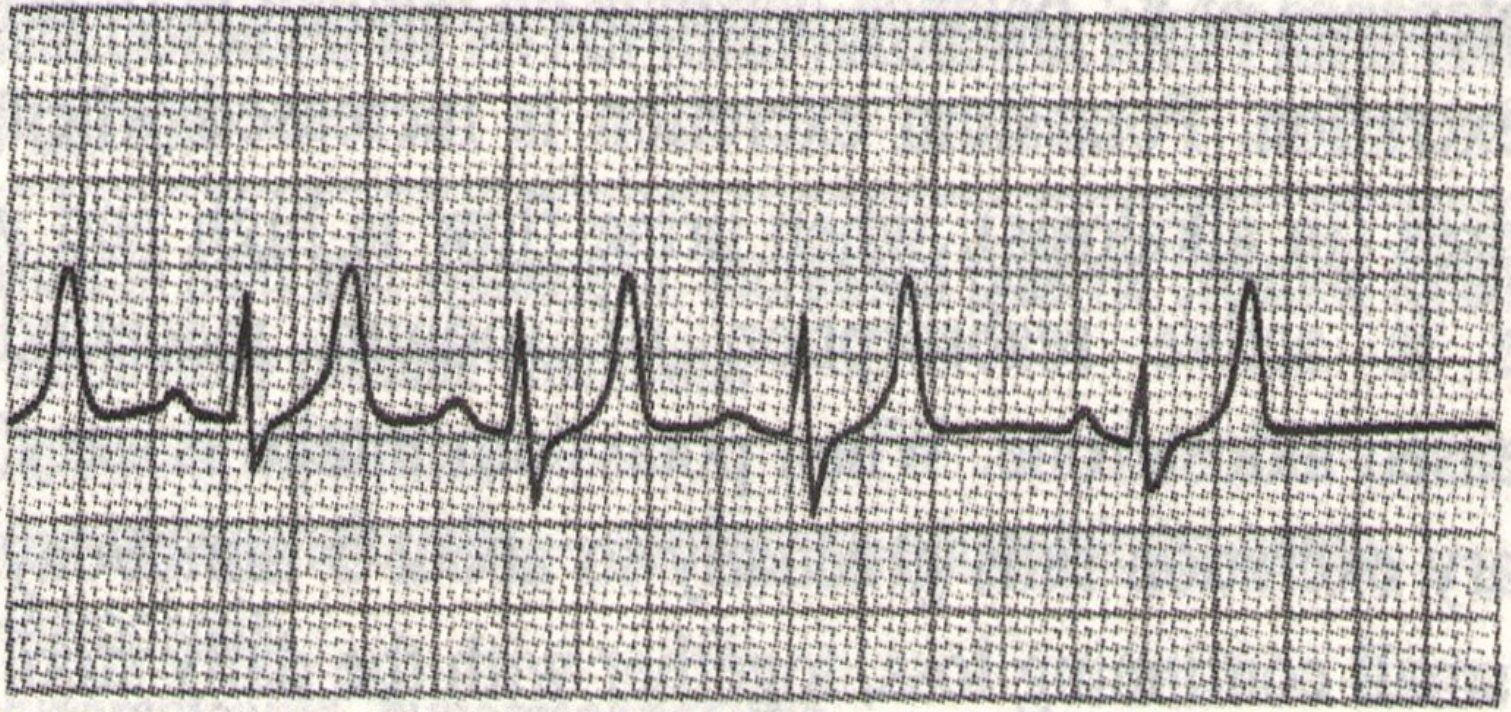


Fig. 5.8 Changes in the ECG associated with hyperkalaemia. The T waves are tall, peaked and tent-like, and the PR interval and QRS complexes are lengthened. In severe cases, the P wave disappears and the QRS complex widens further, with loss of the T wave.

Management of Hyperkalemia

Identify treatable causes

Inject 10-20ml 10% calcium gluconate

50% gluconate 50-100ml I.V.+Insulin 6-12u

Infusion 250ml 5% sodium bicarbonate

Use exchange resin (Kayexalate)

Hemodialysis or peritoneal dialysis

Electrolyte/Acid–Base Imbalances

Sodium

- May be normal or low
- Because of impaired excretion, sodium is retained
  - Water is retained
    - Edema
    - Hypertension
    - CHF

Electrolyte/Acid–Base Imbalances

Metabolic acidosis

- Results from
  - Inability of kidneys to excrete acid load (Primary ammonia)
  - Defective reabsorption/regeneration of bicarbonate

Proteinuria

Single best predictor of disease progression

Normal albumin excretion

- <30 mg/24 hours

Microalbuminuria

- 20-200 g/min or 30-300 mg/24 hours

Macroalbuminuria

- >300 mg/24 hours

Nephrotic range proteinuria

- >3 g/24 hours

Metabolic Disturbances

Waste product accumulation

- As GFR ↓, BUN ↑ and serum creatinine levels ↑
  - BUN ↑
    - Not only by kidney failure but by protein intake, fever, corticosteroids, and catabolism
    - N/V, lethargy, fatigue, impaired thought processes, and headaches occur
  - Serum creatinine and creatinine clearance are more accurate indicators of kidney function than BUN

Metabolic Disturbances

Defective carbohydrate metabolism

- Caused by impaired glucose use
  - From cellular insensitivity to the normal action of insulin
- **Patients with diabetes who become uremic may require less insulin than before onset of CKD**
- Insulin dependent on kidneys for excretion

Elevated Triglycerides

- Hyperinsulinemia stimulates hepatic production of triglycerides
- Altered Lipid Metabolism
  - ↓Levels of enzyme lipoprotein lipase
    - Important in breakdown of lipoproteins

Hematologic System

- Anemia
  - Due to ↓production of erythropoietin
    - From ↓of functioning renal tubular cells
- Bleeding tendencies
  - Defect in platelet function
- Infection
  - Changes in leukocyte function
  - Altered immune response and function
  - Diminished inflammatory response

Cardiovascular System

Hypertension
Heart failure
Left ventricular hypertrophy
Peripheral edema
Dysrhythmias
Uremic pericarditis

Respiratory System

Kussmaul respiration

Dyspnea

Pulmonary edema

Uremic pleuritis

Pleural effusion

Predisposition to respiratory infections

Depressed cough reflex

“Uremic lung”

Gastrointestinal System

Every part of GI is affected

- Due to excessive urea
  - Mucosal ulcerations
  - Stomatitis
  - Uremic fetor (urinous odor of breath)
  - GI bleeding
  - Anorexia
  - N/V

Neurologic System

Expected as renal failure progresses

- Attributed to
  - ↑ Nitrogenous Waste Products
  - Electrolyte imbalances
  - Metabolic acidosis
  - Axonal atrophy
  - Demyelination of nerve fibers
  - Altered mental ability
  - Seizures
  - Coma
  - Dialysis encephalopathy
  - Peripheral neuropathy

Neurologic System

Restless leg syndrome
Muscle twitching
Irritability
Decreased ability to concentrate
Personality and behavioral changes
Emotional ability
Withdrawal
Depression

Skeletal Effects of CRF

Hyperphosphatemia

Hypocalcemia

Hyperparathyroidism

Low bone mass and density

Osteitis fibrosa cystica

SKin

- Most noticeable change
  - Yellow-gray discoloration of the skin
    - Due to absorption/retention of urinary pigments
- Pruritus
- Uremic frost
- Dry, pale skin
- Dry, brittle hair
- Thin nails
- Petechiae
- Ecchymoses

Reproductive System

- Infertility
  - Experienced by both sexes
- Decreased libido
- Low sperm counts
- Sexual dysfunction

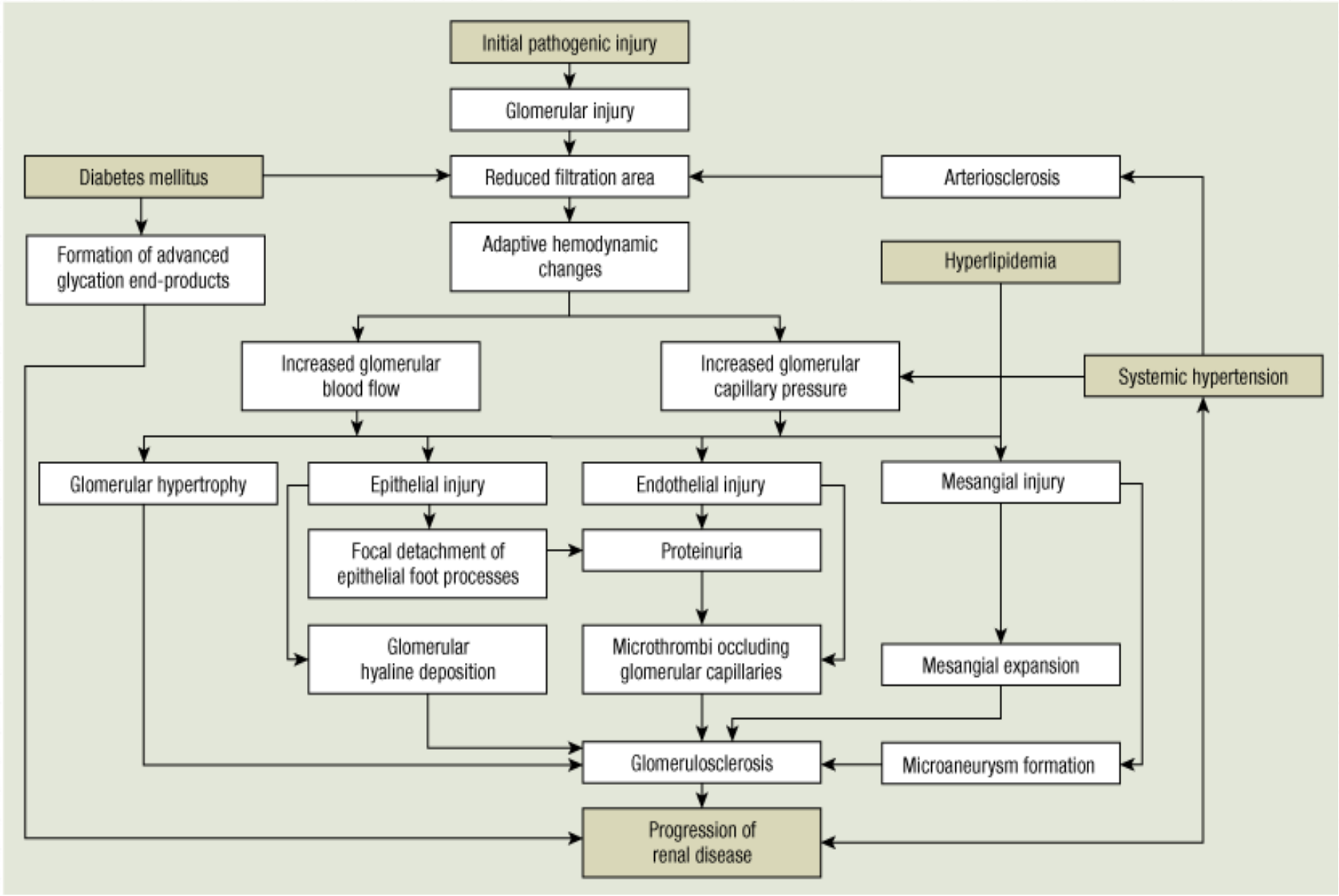
Progression of Chronic Renal Failure

Factors causing progression

- Sustaining primary disease
- Systemic hypertension
  - Intraglomerular hypertension
  - Proteinuria
  - Nephrocalcinosis
  - Dyslipidaemia
  - Imbalance between renal energy demands and supply

Principles of Treatment of CRF

Differentiate from ARF on CRF
Establish aetiology
Establish severity
Seek and treat reversible factors
Seek and treat complications
Lifestyle improvements
Seek and treat factors that promote progression



DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: *Pharmacotherapy: A pathophysiologic Approach,* 7th Edition: Http://www.accesspharmacy.com

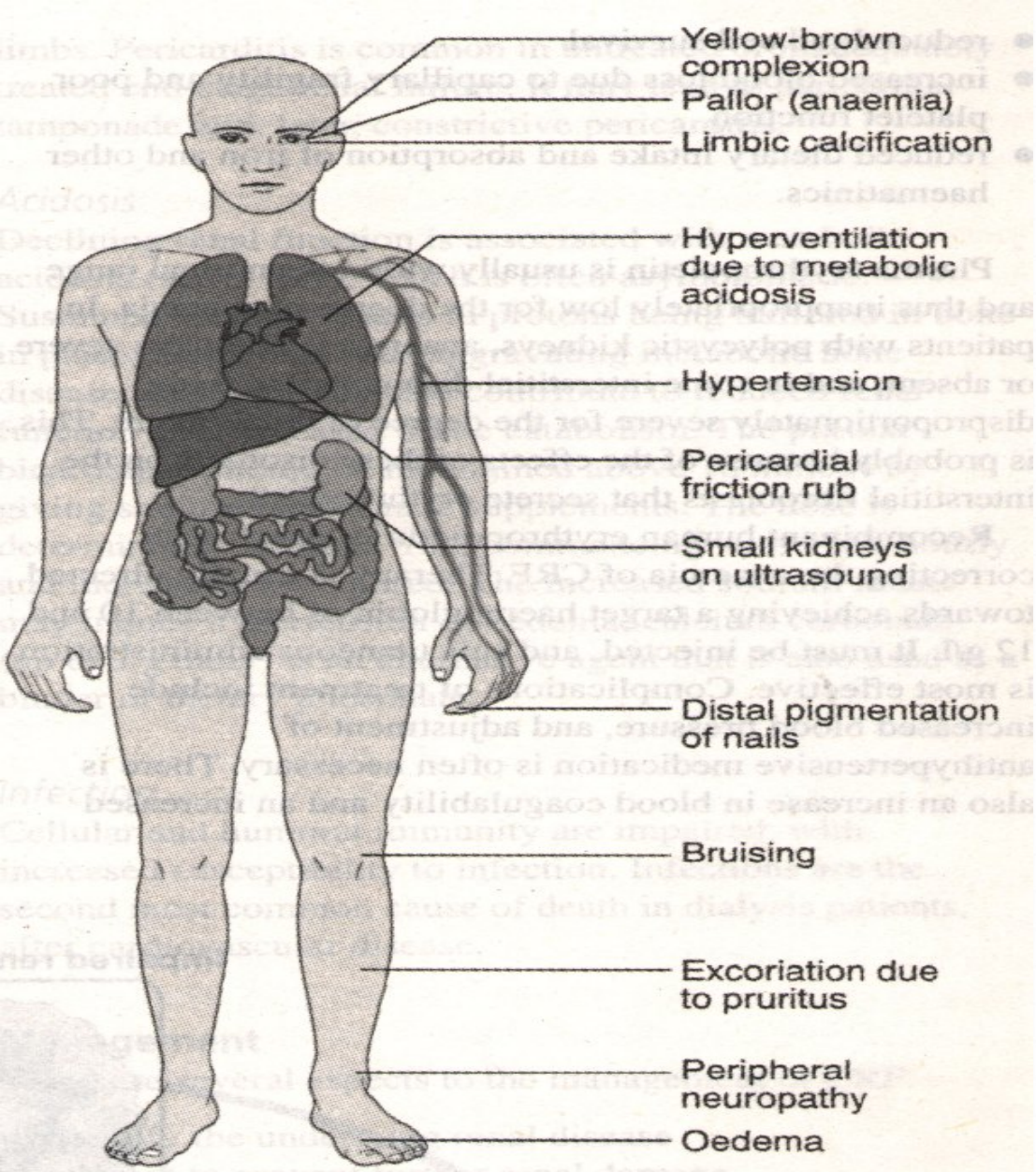


Fig. 6.14 Clinical features of advanced chronic renal failure.

Diet Therapy

Protein restriction (0.5-0.8mg/kg/d)

Adequte intake of calories(30-35kcal/kg/d)

Fluid intake:Urine volume +500ml

Low phosphate diet(600-1000mg/d)

Hyperphosphatemia

Due to decreased excretion in urine.

Control of hyperphosphatemia by dietary measures slow progression of CKD.

Hyperphosphatemia leads to pruritus, calcification in synovial membranes, blood vessels and even cardiac valves.

Therapy includes Phosphorus restriction to 800mg/day and use of phosphrous binders with food.

- Calcium Carbonate (TUMS), Ca-acetate (PHOSLO)
- Lanthanum
- Renagel

Differentiation ARF & CRF

Short History (ds-wks)

Normal Hb

Normal renal size

No osteodystrophy

Periph neuropathy -

Normal Ca and P

Normal PTH

Long history (mo-yrs)

Low Hb

Reduced renal size

Often osteodystrophy

Periph neuropathy +

Low Ca / elevated P

Increased PTH

Acute Versus Chronic

ARF

- Sudden onset
- Rapid reduction in urine output
- Usually reversible
- Tubular cell death and regeneration

CRF

- Progressive
- Not reversible
- Nephron loss

75% of function can be lost before its noticeable

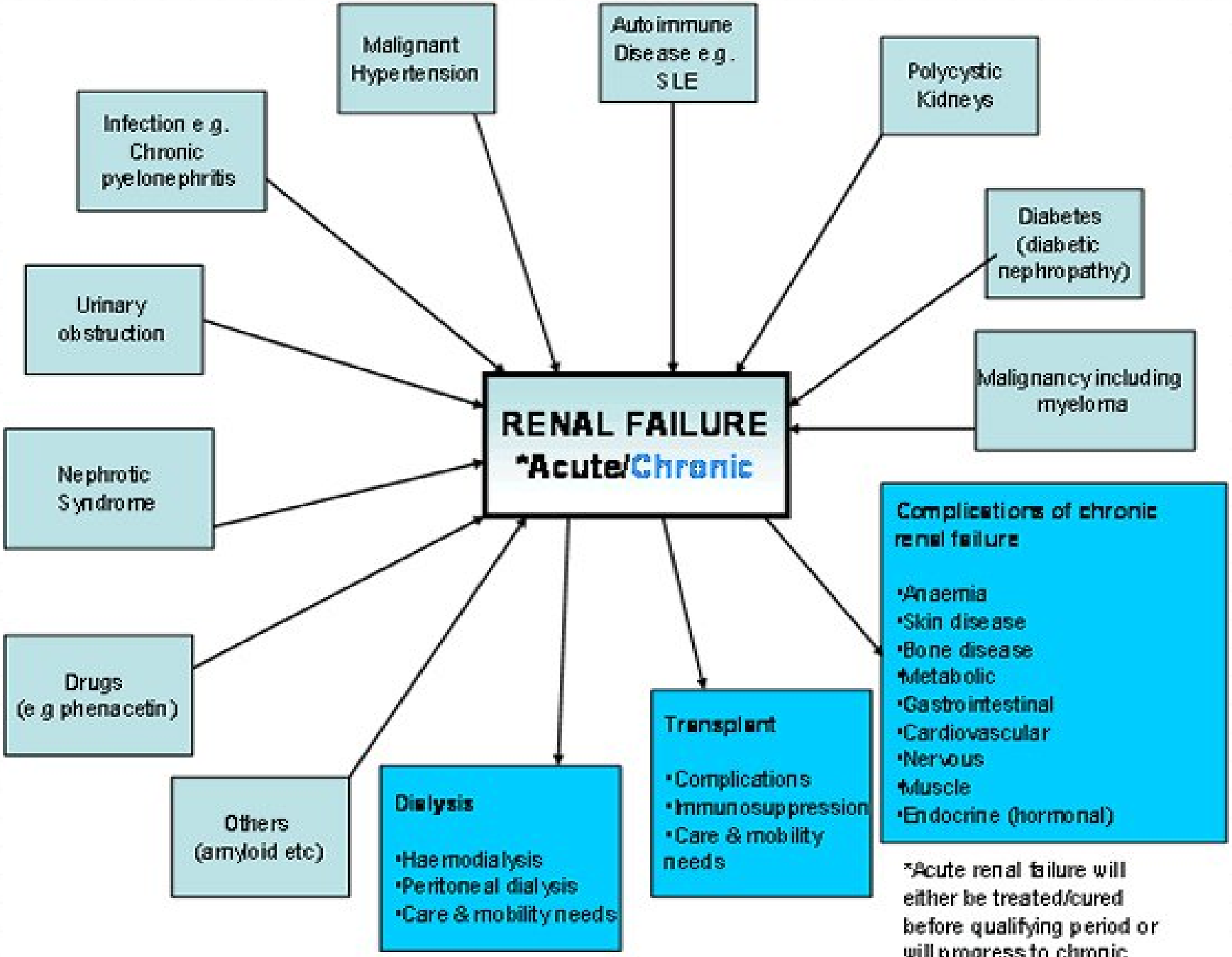
Acute on CRF

Recrudescence of primary disease
Complication of primary disease
Accelerated hypertension
Volume depletion
Cardiac failure
Sepsis
Nephrotoxins (radiocontrast, drugs)
Renal artery occlusion
Urinary tract obstruction
Dietary protein load

Prevent Decline of Renal Function

Interventions to slow progression of CKD:

- Proven benefit in RCTs:
  - BP Control (< 130/80)
  - **ACEI or ARBs**
  - BS control
- May be of benefit:
  - Protein restriction
  - Lipid control
  - Anemia control
  - HCO_3 supplementation
  - Control of 2° hyperparathyroidism
  - Vitamin D therapy


Malignant Hypertension
Autoimmune Disease e.g. SLE
Polycystic Kidneys
Infection e.g. Chronic pyelonephritis
Diabetes (diabetic nephropathy)
Urinary obstruction
Malignancy including myeloma
RENAL FAILURE
*Acute/Chronic
Nephrotic Syndrome
Complications of chronic renal failure
•Anaemia
•Skin disease
•Bone disease
•Metabolic
•Gastrointestinal
•Cardiovascular
•Nervous
•Muscle
•Endocrine (hormonal)
Drugs (e.g phenacetin)
Transplant
•Complications
•Immunosuppression
•Care & mobility needs
Others (amyloid etc)
Dialysis
•Haemodialysis
•Peritoneal dialysis
•Care & mobility needs
*Acute renal failure will either be treated/cured before qualifying period or will progress to chronic renal failure