Incidence and Outcomes

- **"Population incidence of AKI is 2000–3000 per million population."** *It's not a rare condition.*
- **"In ICU around 4–5% of patients will need RRT for AKI."** ⚠️ *Even if patients get dialysis, the chance of dying is still high — around half of them may not survive. This shows how serious AKI is in critical illness.*

🔷 **History of AKI Terminology**

- 🕰️ *Previously, doctors called it "acute renal failure," which means kidneys suddenly stopped working.*
- ❗ *Different studies defined it in different ways — by changes in creatinine, urea, urine output, or dialysis needs — so research results couldn't be easily compared.*
- ✅ *To do good research and compare results, doctors needed a clear, agreed-upon definition. That's why new criteria like RIFLE and AKIN were created.*

NOTE : as the cut off of creatinine decreases you will get more cases of AKI, and mortality rates would increase with AKI

🔷 **Benefits of a Consensus Definition**

🧠 Why define AKI clearly?

- Helps with **clinical research**
- Makes studies from different hospitals **comparable**
- Encourages **teamwork**
- Helps doctors **recognize AKI early** using fixed rules

🔷 **RIFLE Criteria (2004)**

💡 Developed by ADQI group.

- R = Risk
- I = Injury
- F = Failure
- L = Loss
- E = End-stage kidney disease

🧪 Based on two easy things to check:

- Serum **creatinine** (Cr)
- **Urine output** 👎 **Limitations:**
- Needs baseline creatinine (not always available)
- Doesn't consider timing (how fast AKI developed)
- No info about when to start dialysis

🔷 **AKIN Criteria (2004)**

👥 Joint work of top kidney and ICU groups: ADQI, ASN, ISN, NKF, ESICM

- Replaced "acute renal failure" with **"acute kidney injury"** ➡️ Reflects **different levels** of kidney damage (not just complete failure)

📊 **AKIN Staging:**

Stage	Creatinine	Urine Output
1	1.5–2x ↑ of baseline	< 0.5 mL/kg/hr for >6 hrs
2	2–3x ↑	< 0.5 mL/kg/hr for >12 hrs
3	>3x ↑ or dialysis needed	< 0.3 mL/kg/hr for >24 hrs or no urine >12 hrs

🔷 **AKIN vs RIFLE**

🧪 Studies show **no major advantage** of AKIN over RIFLE in predicting death or outcomes in ICU patients. We only use them for research → we depend on ↑ of 0.3 mg/dl in 24–48h.

🔷 Definition of AKI

📄 AKI = quick increase in creatinine over hours/days

- Oliguric = urine < 400 mL/day
- Non-oliguric = normal urine, but still kidney damage

🧠 *Patients can look okay on the outside but be retaining toxins internally.*

🔷 Causes of AKI

1. **Pre-renal** = problem before kidney (blood flow) **MCC**
2. **Renal** = kidney tissue itself is damaged
3. **Post-renal** = blockage after kidney (stones, enlarged prostate), increased back pressure and increase the GFR

🔷 Pre-renal Failure

📉 Caused by low blood flow to kidneys:

- Dehydration
- Heart failure
- Sepsis (low BP)
- Liver disease

🌊 *Kidney is not damaged yet **(NOOOO STRUCTRUAL DAMAGE)** — just not getting enough blood. If blood flow returns, function improves fast.*

RESPONSE ??

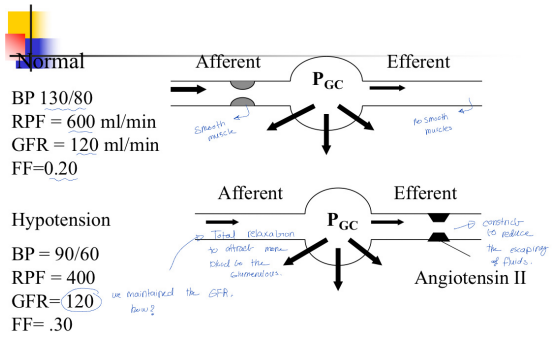
🔷 GFR Autoregulation

🩺 Kidneys try to keep GFR constant:

- **Dilate afferent arteriole** (more blood in), by increasing renal PG
- **Constrict efferent arteriole** (using angiotensin II)

⚠️ *Some drugs like NSAIDs, ACE inhibitors (THESE DRUGS INHIBIT THE ALDOSTERON) , and diseases like chronic hypertension can block these responses and worsen AKI.*

Effect of AII on GFR in Hypotension



🔶 Factors That Impair GFR Autoregulation

These conditions interfere with the kidney's ability to adjust blood flow and keep GFR stable:

Factor	Effect
Chronic renal failure	Afferent arteriole already fully dilated — no room to adjust
NSAIDs / COX-2 inhibitors	Block prostaglandins → no afferent dilation

ACE inhibitors / ARBs	Block angiotensin II → no efferent constriction
Chronic vascular disease	Stiff vessels (from age, HTN) can't respond well to pressure changes

🔶 **Causes of Prerenal AKI**

Anything that reduces blood flow to the kidneys:

🔷 **1. Low Blood Pressure (BP)**

- **Volume depletion**: dehydration, vomiting, diarrhea, bleeding
- **Cardiogenic shock**: weak heart pump
- **Vasodilation**: in **sepsis** or **liver disease**

🔷 **2. Renal Vasoconstrictors**

- Tacrolimus, cyclosporine
- Catecholamines, cocaine
- Amphotericin
- Hypercalcemia (vasoconstriction)

🧠 These reduce renal perfusion by narrowing vessels.

🔶 **Diagnosing Prerenal AKI**

What tells you it's prerenal?

Test/Observation	What You Expect
History	Fluid loss, drug use, hypotension (anything that suggest loss of volume)
Physical exam	↑HR, ↓BP (lying to standing) (rule out positional changes), dry mucosa, flat neck veins
Urinalysis	***Bland* (no casts or blood) _ WE HAVE NO STRUCTURAL CHANGES (WE CALL IT POOR MAN BIOSPY)**
Urine Sodium or Chloride	Low (<20 mmol/L) → kidneys trying to conserve salt (IF THE PATIENT IS OLIGO , IF POLY WE WILL GET FALSE POSITIVE)
Oliguria	May be present, but kidneys still intact
Responds to fluids	Yes — this confirms prerenal, not structural damage (REVERSIBLE)

🔶 **Intrinsic (Renal) AKI — By Location think about the 4 main parts : glomerular/ vascular/ tubular/ interstitial**

Part of Kidney	Example Diseases
Vascular	TMA, renal artery occlusion
Glomerular	RPGN (ONLY THE RAPID PROGRESSIVE TYPE) (e.g., lupus, ANCA, post-infection)
Tubules	Ischemic ATN, Toxic ATN
Interstitial	AIN (allergic)
Tubular Lumen	Crystals (uric acid, oxalate)

🔶 **Renal AKI — By Frequency**

Most to least common:

1. Ischemic ATN
2. Toxic ATN
3. RPGN
4. AIN

5. TMA
6. Crystals

🔶 **Ischemic Acute Tubular Necrosis (ATN)**

- **YOU need to have hypovolemia/ drop in BP / low perfusion to kidney in order for structural damage to happen (affecting mainly the tubules)**
- **Same causes as pre renal**

💥 Happens when kidneys don't get enough blood (or oxygen) → especially in:

- **Proximal tubule S3 segment**
- **Thick ascending limb**

💊 Aggravated by:

- Sepsis
- Obstructive jaundice
- Radiocontrast
- Hemoglobin or myoglobin (rhabdomyolysis)

🔶 **Tubular Injury Mechanism**

Stage	What Happens
Loss of polarity	Transport proteins (e.g., Na/K ATPase) move to wrong side
Loss of brush border	Decreases reabsorption
Loss of ICAMs	Cells detach and shed into tubules
Cell death	Necrosis or apoptosis follows hypoxia

🔶 **Hypoxic Cell Damage – Biochemical Events**

🔥 **Hypoxia** leads to:

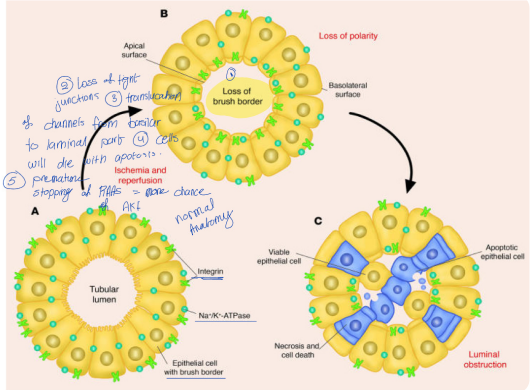
- ↓ ATP
- ↑ Cytosolic calcium
- Activation of damaging enzymes:
- Proteases
- Lipases
- Caspases
- ↑ Reactive Oxygen Species → more damage

🔶 **Structural Changes**

- Breakdown of anchoring proteins (ankyrin, spectrin)
- Cytoskeleton collapses
- Loss of microvilli
- **Na/K ATPase and integrins move to the wrong cell surface**

🔶 **Tubular Obstruction & Backflow**

- Dead cells + proteins → form **casts**
- Casts block the tubule → pressure builds upstream
- Tight junctions break → **filtrate leaks** out into blood
- GFR decreases



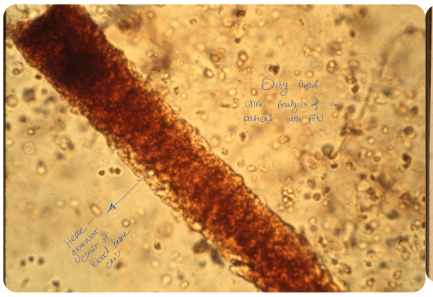
🔶 **Tubuloglomerular Feedback**

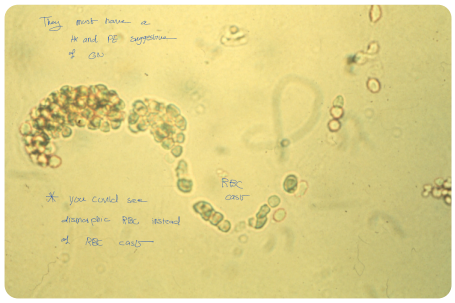
🧠 Too much sodium reaches distal tubule → macula densa senses it → causes:

- Afferent arteriole **constriction**
- **RAAS is suppressed**
- GFR drops further

🔶 **Diagnosing ATN**

Clue	Explanation
History	Ischemia, toxins, shock, sepsis
Urinalysis	Granular ("muddy brown") casts, blood, debris
No response to fluids	Kidney is structurally damaged
Creatinine rises quickly	Within hours to days
Oliguria or anuria	Often present





🔶 **Toxic ATN – Common Causes**

Toxin	Source
Aminoglycosides	Antibiotics
Radiocontrast dye	Imaging
Hemoglobin/myoglobin	Rhabdomyolysis, hemolysis
Ethylene glycol	Antifreeze poisoning
Amphotericin / Cisplatin	Antifungal / Chemotherapy drugs

🧪 These may cause **polyuria or normal output**, not always oliguric.

Allergic Interstitial Nephritis

Usually prolonged exposure to drug n Penicillins, Allopurinol, Cipro, NSAID's, sulphonamides, May be rash, fever, eosinophils in blood, urine, ALWAYS: pyuria, WBC casts

🔶 **RPGN (Rapidly Progressive GN)**

Autoimmune causes of fast kidney injury:

- **Anti-GBM antibodies** → Goodpasture's
- **Immune complex** → SLE, post-infection, IgA nephritis
- **ANCA-positive (pauci-immune)** → Wegener's, Microscopic polyangiitis

🔶 **Thrombotic Microangiopathy (TMA)**

Small-vessel clotting causes AKI + anemia + low platelets:

- Hemolytic uremic syndrome (E. coli)
- Malignant hypertension
- Scleroderma renal crisis
- Preeclampsia/Toxemia
- Cyclosporine
- Bone marrow transplant

🩸 Diagnosis: AKI + hemolytic anemia + fragmented RBCs + thrombocytopenia

🔶 **Dialysis Indications in AKI**

🩺 Start dialysis if:

- **Hyperkalemia** > 5.5 not improving with meds
- **Volume overload** not improving
- **Pulmonary edema** with O_2 need or CXR findings
- **Uremia symptoms**: confusion, pericarditis, nausea
- **Fast rise in creatinine** especially with:
- Oliguria
- Multi-organ failure

📌 ICU patients may start dialysis earlier — even at Cr 200–400 µmol/L.

🔶 **Biomarkers – Old vs. New**

🔷 **Traditional (Not Great)**

- **Creatinine**: slow to rise, not sensitive, influenced by age, sex, muscle
- **Urea**: not specific

📉 Problems with creatinine:

- Delayed rise after injury
- Depends on steady state
- Influenced by many non-kidney factors

🔶 **Ideal Biomarker Characteristics**

A good AKI biomarker should be:

- Noninvasive (urine/blood)
- Cheap and fast
- Early and accurate
- Sensitive and specific

- Work well in clinical studies
- Able to **stratify risk** (mild vs. severe cases)

🔶 **Emerging Biomarkers**

Biomarker	Use
NGAL	Rises early after surgery — predicts AKI
Cystatin C	Alternative to creatinine, rises earlier
KIM-1	Specific to **ischemic ATN**

AKI Types, Causes, Features

Type	Common Causes	Key Features
Pre-renal	Dehydration, heart failure, sepsis, liver disease	↓ perfusion, no structural damage, responds to fluids
Intrinsic (Renal)	Ischemia, toxins, AIN, RPGN, TMA	Tubule/glomerular/interstitial damage, doesn't respond to fluids
Post-renal	Stones, BPH, tumors	Obstruction, hydronephrosis

✅ **2. RIFLE vs. AKIN Summary (Simplified)**

Criteria	Risk/Stage 1	Injury/Stage 2	Failure/Stage 3
RIFLE	↑Cr ×1.5 or ↓UO	↑Cr ×2 or ↓UO	↑Cr ×3 or ↓UO or dialysis
AKIN	↑Cr ≥0.3 in 48h or ×1.5	×2	×3 or dialysis
🧠 *RIFLE includes "Loss" and "ESRD" stages. AKIN is more focused on early detection.*			

✅ **3. Mnemonics**

- **Causes of AKI** – *"POP RINT"* → **P**rerenal, **O**bstruction, **P**ostrenal, **R**enal – **I**schemia, **N**ephritis, **T**oxins
- **ATN Toxic Causes** – *"A Really Hard Core Poison List"* → **A**minoglycosides, **R**adiocontrast, **H**emoglobin/myoglobin, **C**isplatin, **P**oisons (ethylene glycol), **L**iposomal amphotericin
- **AIN Classic Triad** – *"Rash, Fever, Eosinophils"*