
Namaste
مرحبا
Willkommen
Bem Vindo
Selamat Datang
Welcome
Bienvenidos
Benvenuti
Welkom
Bienvenue
Croeso
أهلا وسهلا
Bienvenidos
Selamat Datang
Welcome
Willkommen
добре дошъл
Καλώς ήλθατε
Benvenuti

Proteinuria

4mg/m2/hr

- **100mg/m2/day**
- **150mg/24h**

0.2mg/mg creatinine spot/24h

- **200mg/g**
- **20mg/mmol**

Dipstick screening

- Single +ve ➔ 5-15%
- Repeat 3x ➔ 0.1%

Persistent first morning

Dipstick screening

- Detects mainly albumin

➔ Underestimate (others & degraded alb.)

- Trace may not be significant
- +1 frequently miss microalbuminuria

Dipstick screening

- AAP no longer recommends non-selective screening of healthy children for kidney disease using urinalysis at any age

Microalbuminuria

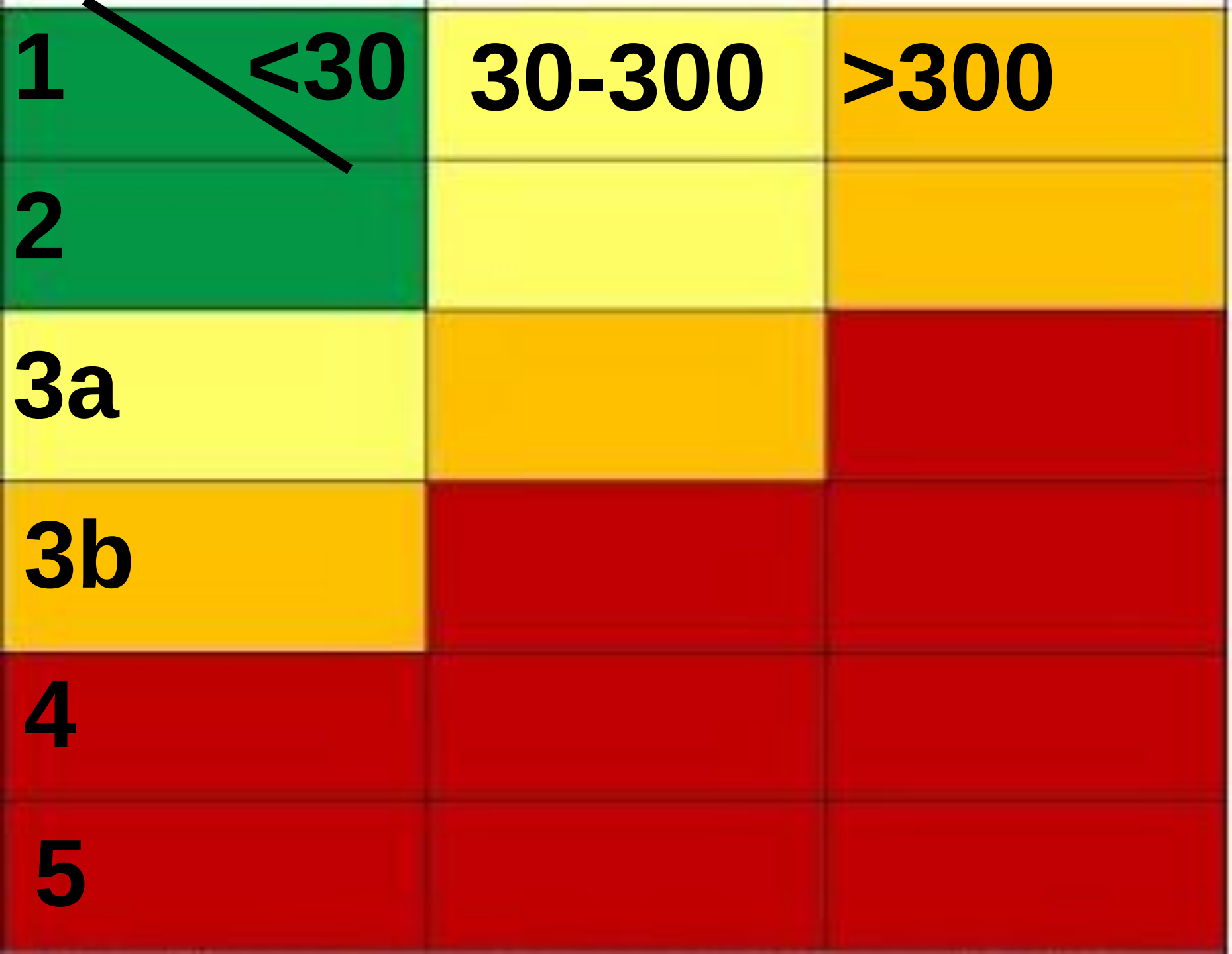
30-300 mg/g creatinine

Prognosis of CKD by GFR and Albuminuria Categories

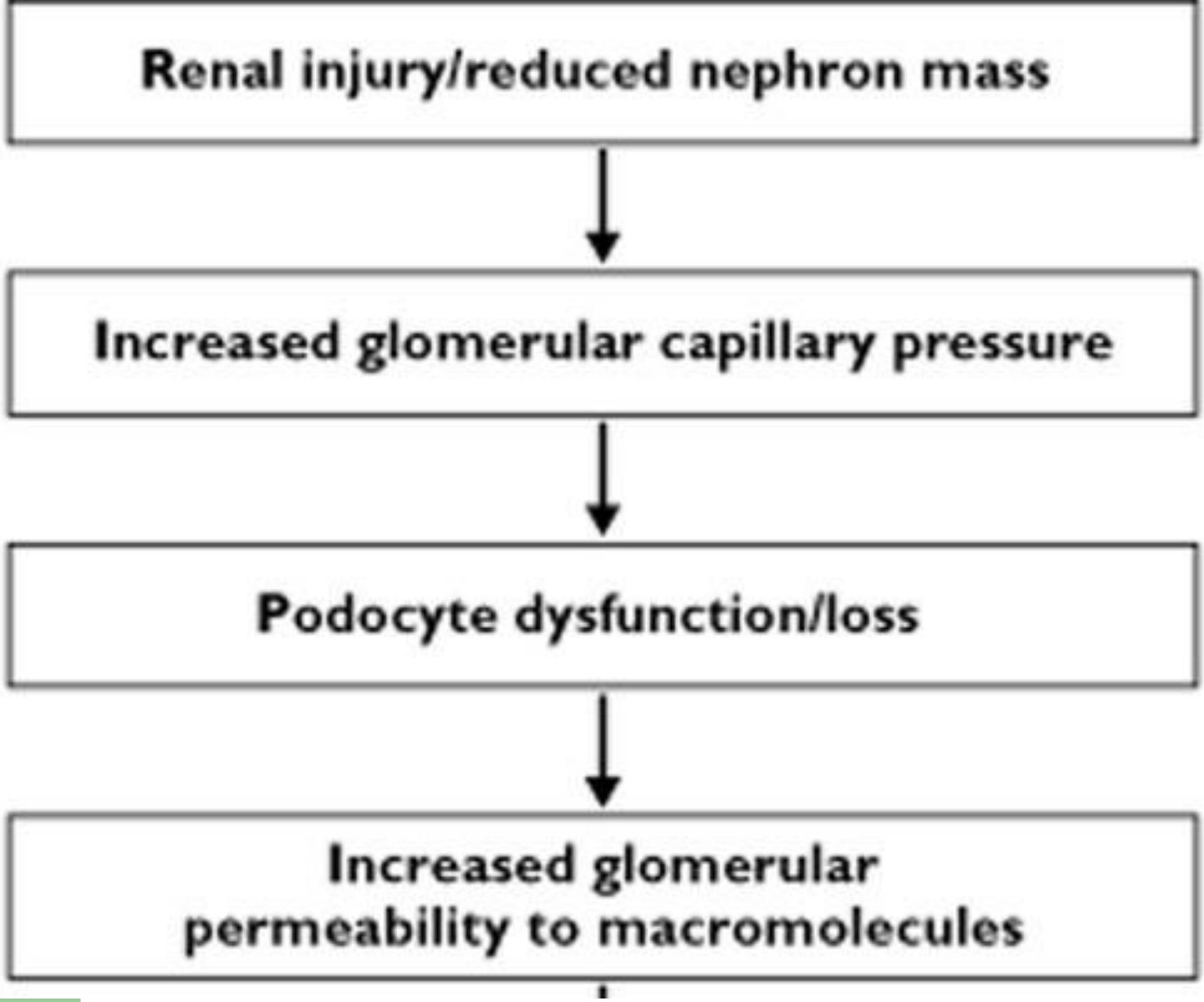
KDIGO, 2012

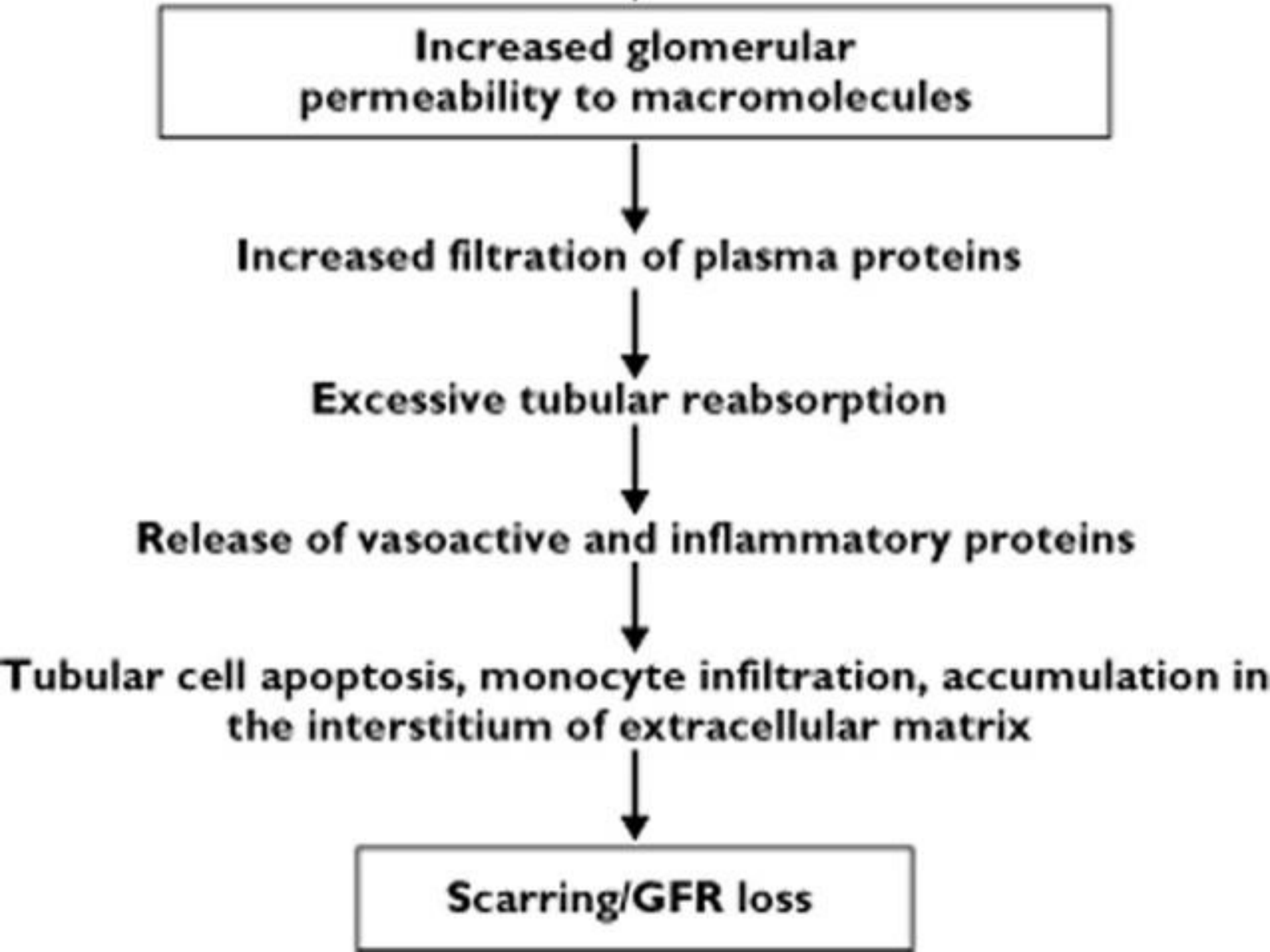
GFR categories (ml/min/1.73 m²) Description and range				Albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.
KDIGO 2012


1
<30
30-300
>300
2
3a
3b
4
5

- **Proteinuria accelerates CKD progression**


Renal injury/reduced nephron mass
Increased glomerular capillary pressure
Podocyte dysfunction/loss
Increased glomerular permeability to macromolecules


Increased glomerular permeability to macromolecules
Increased filtration of plasma proteins
Excessive tubular reabsorption
Release of vasoactive and inflammatory proteins
Tubular cell apoptosis, monocyte infiltration, accumulation in the interstitium of extracellular matrix
Scarring/GFR loss

Hyperfiltration

Tubular Ptn load

Pro-inflammatory

Profibrotic

↑ filtered PCT protein content

- PI Protein exposure
- Excess PCT cell protein (receptor) handling

➔proinflammatory & profibrotic mediators

↑ filtered PCT protein content

➔ NF-kB dependent & independent pathways ➔ upregulated chemotactic & adhesion molecules

↑ tubular chemokine expression, complement activation & macrophage infiltration

➔ ↑ interstitial infl. & fibrogenesis

Proteinuria accelerates CKD progression

- Loss of selectivity & filtration of larger proteins, Ig, C, etc
- Mesangial stretch ➔ ↑ TGF-B

Proteinuria accelerates CKD progression

- Antigenic effects of albumin degradation products
- Promote excr. of bound toxins/ mediators
- Protein binding of protective molecules
  Retinol binding ➔ ↓podocyte regeneration ↑oxidative damage

- **Effect of albumin infusions on proteinuric patients with saturated albumin handling**

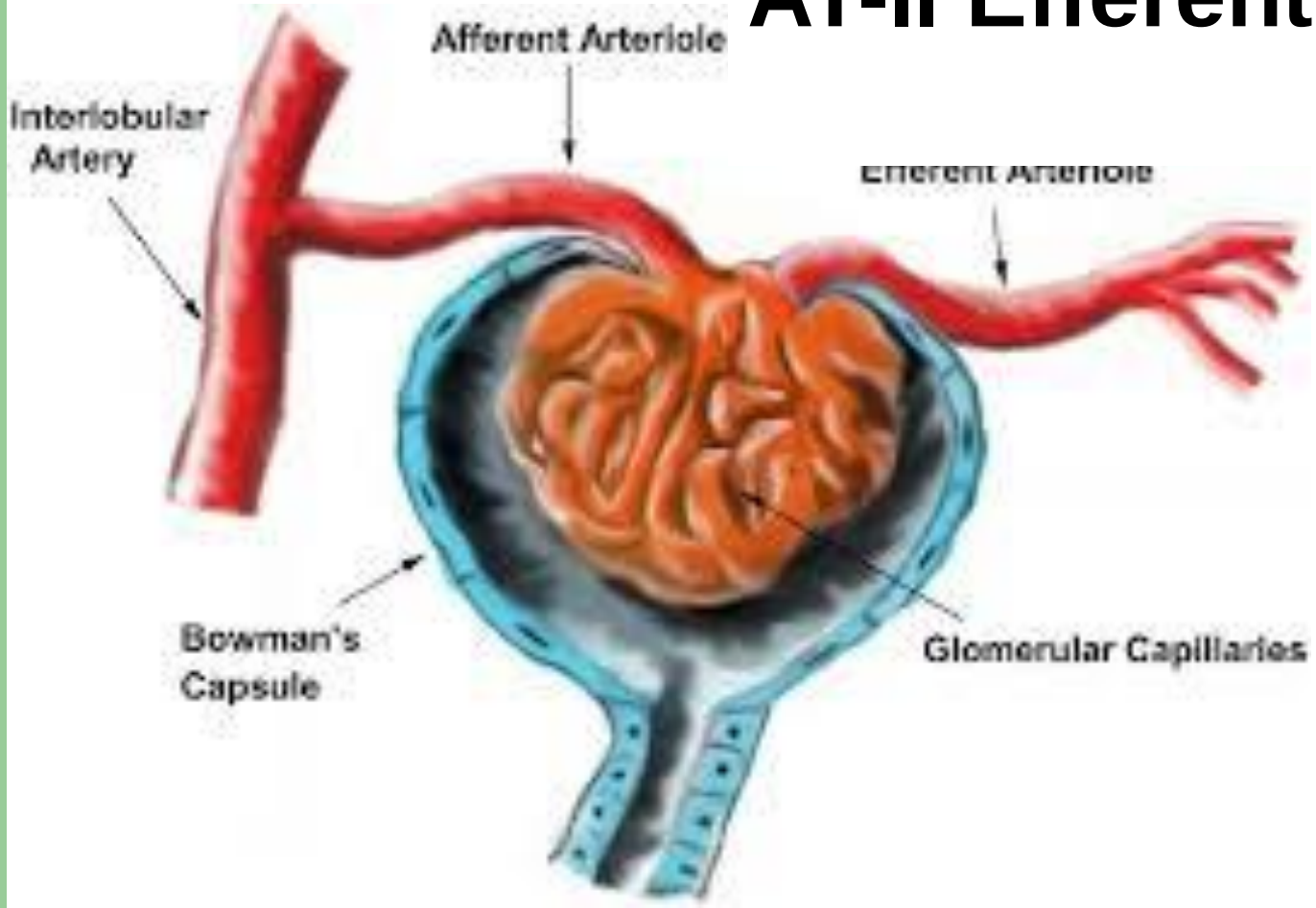
➔**Essentially 100% recovered in urine**

↓ proteinura consistently shown to be renoprotective

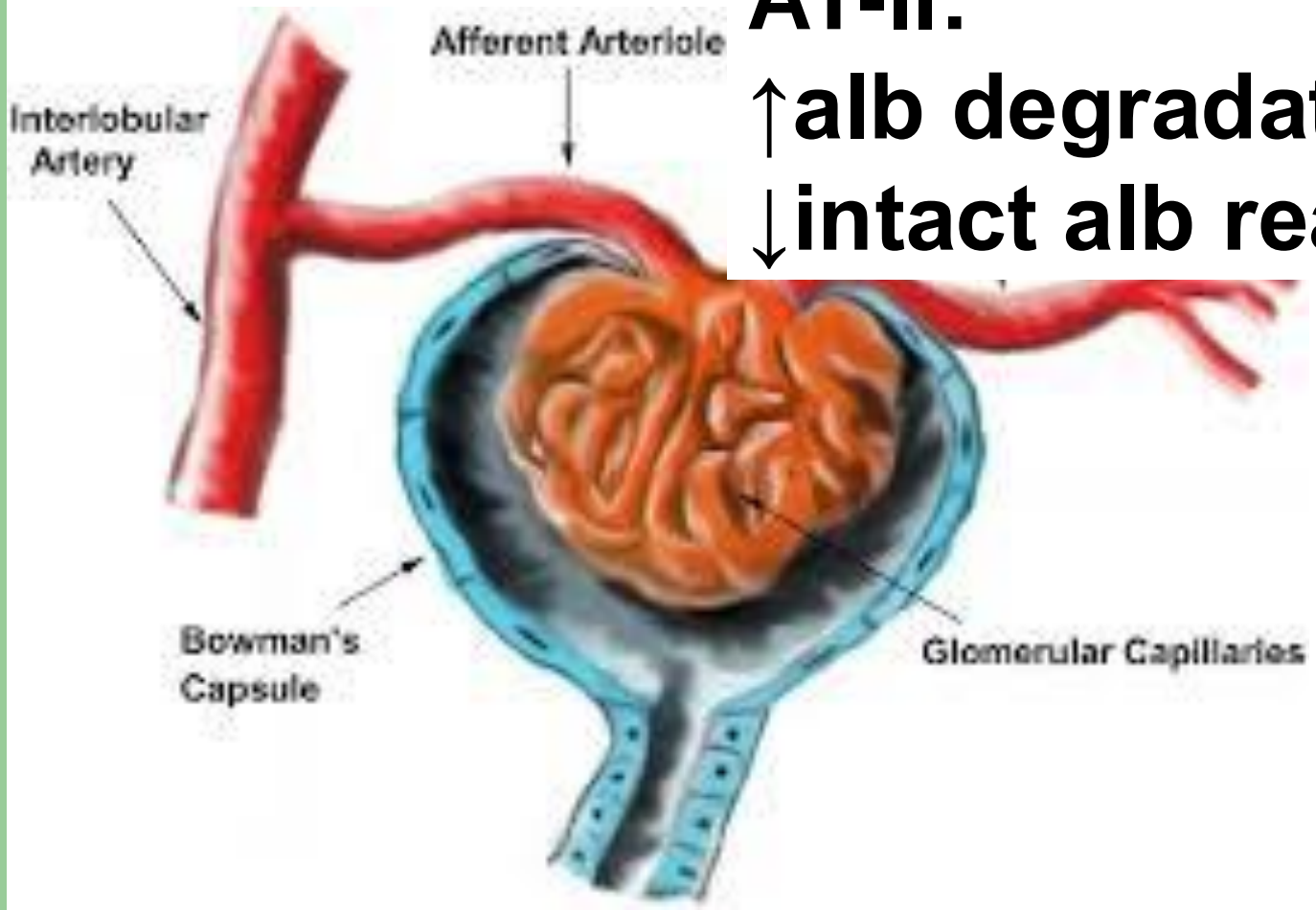
- Renoprotection associated with BP lowering dependent on initial proteinuria
- Independent of CKD progression, proteinuria ↑ CV risk (adult—based evidence)

RAAS blockade in AKI?
RAAS blockade & Nephroprotection

AT-II Efferent VC



RAAS blockade in AKI?
RAAS blockade & Nephroprotection



AT-II:

↑alb degradation

↓intact alb reabsorp.

RAAS blockade

- Hemodynamic effect

  (BP, glomerular P & SA)
- ↓ AT II shift alb degradation➔ reabsorption
- ↓ inflammation
- ↓ salt & water retention

RAAS blockade

- Associated with better renal protection despite similar BP control

➔ 1st line in proteinuric CKD

RAAS blockade

- Ramipril/ARB (non-kid. metabolism)
- Combination not supported
- Check change in proteinuria & aim for max. approved/ tolerated dose
- Caution in CKD4, avoid/ stop if volume depletion, AKI, hyper-K
- Teratogenic effect

SGLTi

- Empagliflozin
- Dapagliflozin
- Canagliflozin

Delay CKD progression & ↓CV risk in diabetic kidney disease

SGLT2 Inhibitors

- Diuretic effect
- Glycosuria
- Nephroprotection
- Erythropioetin increase

- Decreased left ventricular mass
- Improved diastolic function

- Reduced vascular stiffness
- Improved endothelial function

- Increased utilization of ketone bodies
- Improved energy processes

SGLT

AFFERENT
VD ➔

↑ filtration, glom P & permeability

PCT ➔

Na—glucose reabsorption

EFFERENT
↓ Adenosine

↓ distal Na

&Tubuloglom. feedback

Na—H exchanger colocalizes

SGLTi

AFFERENT
VD ➔

↑ filtration, glom P & permeability

PCT ➔

Na—glucose reabsorption

EFFERENT
↓ Adenosine

VD synergic RAASi

↓ distal Na **RESTORE**

&Tubuloglom. feedback

Na—H exchanger colocalizes **Natriuresis**

SGLTi

+Protect podocytes & ↑podocyte autophagy

+Inhibit pro-inflammatory & pro—oxidant pathways

SGLTi; Based on Diabetic Kidney Disease

Adult non-diabetic proteinuric CKD

- Encouraging signals from RCTs
- Available evidence clearly supports down to GFR 20
- Benefit in non-proteinuric needs further/ longer studies
- Pediatric use still experimental or off-label

Mineralocorticoid antagonist

- **Spironolactone & Finerenone (Non—steroidal mineralocorticoid antagonist)**

Mineralocorticoid antagonist

↑ mineralocorticoid activity:

- Pro-inflammatory
- Profibrotic

Protective

- BM changes & podocyte injury
- Mesangial proliferation
- Endothelial dysfunction

Direct anti Proteinuric

Diuretics

- Thiazides shown to ↓ proteinuria by >35% in several studies
- Effect ↑ by low-salt

➔BP & vol control & glomerular hyperfiltration

Diuretics

- Thiazide-like drugs as indapamide: same effect
- Others less explored but possible:

  Loop- acetazolamide-- amiloride

ET-1 R antagonist

Short-term atrasentan can ↓proteinuria

Long-term effect uncertain

- **↓ glomerular hyperfiltration**
- **↓ inflammation & tubular protective**
- **Na, water retention**

Non-dihydropyridine CCB

- Verapamail
- Diltiazem

Corticosteroids & CNIs

Complement inhibitor

- **Iptacoban**

FB in PNH

FDA 2024 for adult IgAN after RAASi

- Proteinuria accelerates CKD progression
- Several mechanisms lead to damage, infl. & fibrosis
- Decreasing proteinuria renopotective
- RAAS blockade 1st line in proteinuric CKD
- SGLTi proven in diabetic kidney disease. Promising in others
- Mineralocorticoid antagonists, diuretics esp thiazides & ET-1 antagonist
- Control of underlying process

THANK YOU