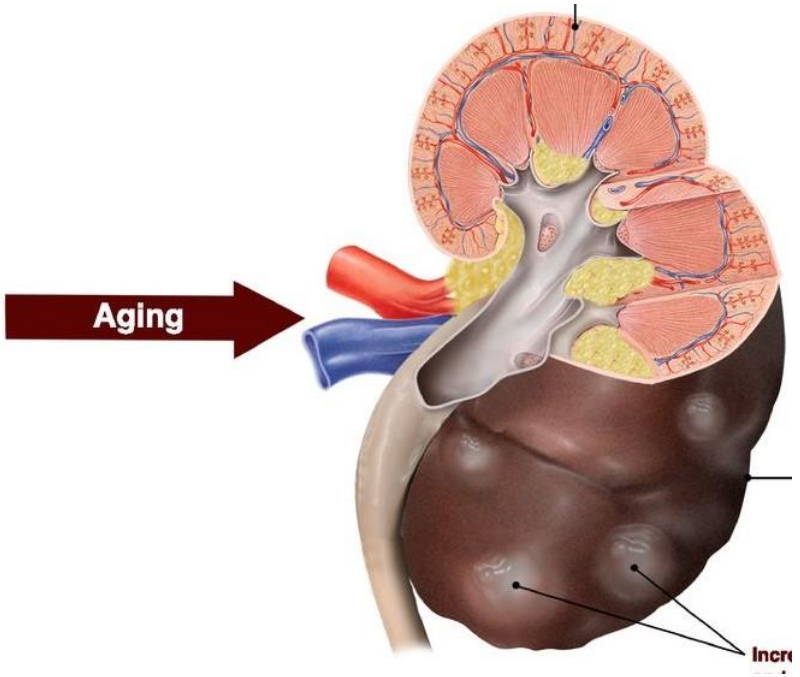
Physiology of CKD & AKI in elderly people



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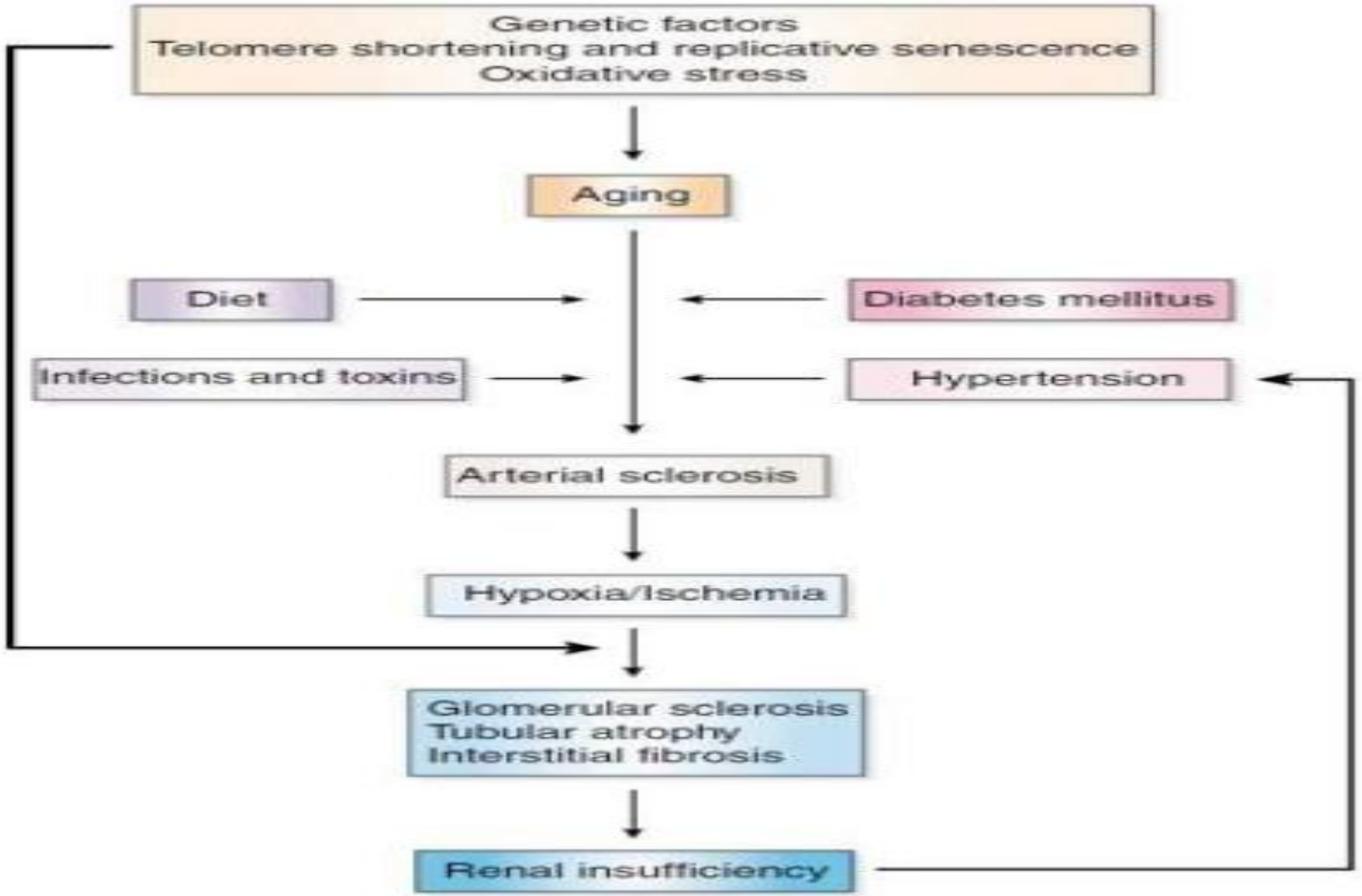
Physiology of CKD in elderly people

- The kidneys are affected by the aging process, which results in numerous effects on the renal system .
- Renal mass decreases between the ages of 30 and 80 years , with the steepest decline observed after age 50 .

- Fat and fibrosis scarring, which may replace some parenchymal tissue, occurs primarily in the renal cortex and scarring (5-37% between the ages of 40 and 90 years) affects the nephrons that are important for **maximal urine concentration**.
- The results from aging studies in animals and humans suggest that diverse factors contribute to the scarring process, such as:

Tissue ischemia, injury, hypertension,metabolic defects and obesity.

Physiology of CKD in elderly people

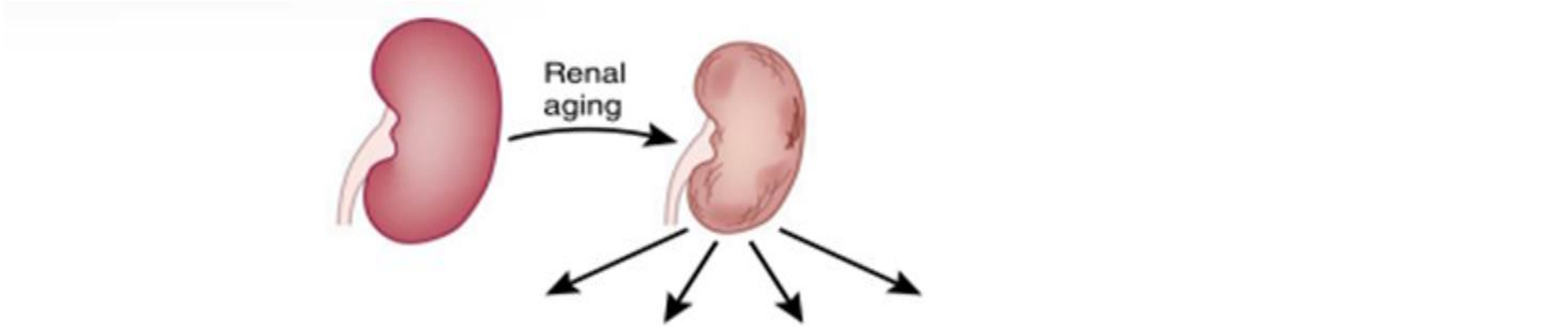


Physiology of CKD in elderly people

Table 1. Structural and functional findings in the kidney with healthy aging

Category	Age-related finding
Microstructural changes	Arteriosclerosis
	Arteriolosclerosis
	Ischemic-appearing glomeruli (global deflation)
	Global glomerulosclerosis and obsolescence
	Interstitial fibrosis
	Tubular atrophy
	Decrease in nephron number
	Hypertrophy of remaining tubules
	Stable glomerular volume
Macrostructural changes	Renal artery atherosclerosis and fibromuscular dysplasia
	Decrease in cortical volume
	Increase in medullary volume until age 50 yr
	Increase in kidney surface roughness
	Increase in number of cysts
	Increase in size of cysts
Functional changes	Decrease in total kidney GFR
	Stable snGFR
	Stable single-nephron glomerular filtration capacity
	Stable and minimal urine albumin excretion (urine albumin-to-creatinine ratio will misleadingly increase from sarcopenia of aging)

Physiology of CKD in elderly people



Clinical changes	Microscopic changes	Macroscopic changes	Functional changes
Progression of new CKD	Glomerulosclerosis	Mass (20–25% between age 30 to 80)	GFR (in most patients)
Function and survival after T_x	Interstitial fibrosis	Weight (10% per decade)	Sodium resorption
Functional renal reserve	Pericapsular fibrosis	Length (0.5 cm per decade >40)	Transtubular K+ gradient
Susceptibility to AKI	GBM thickness	Parenchyma (10% per decade)	Urinary concentration
	Arteriosclerosis		Renal vascular resistance
	Tubular atrophy		Plasma flow

Physiology of CKD in elderly people

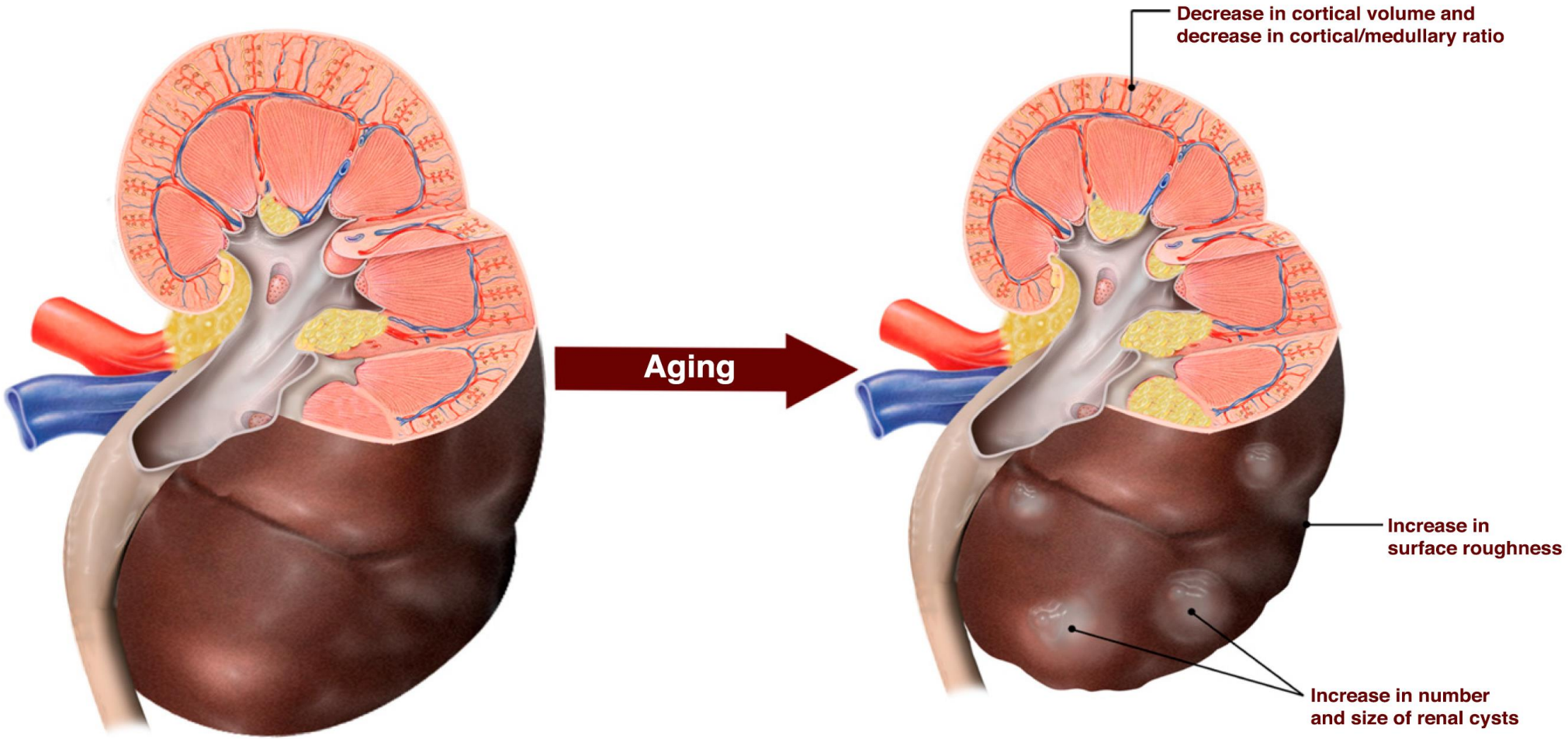
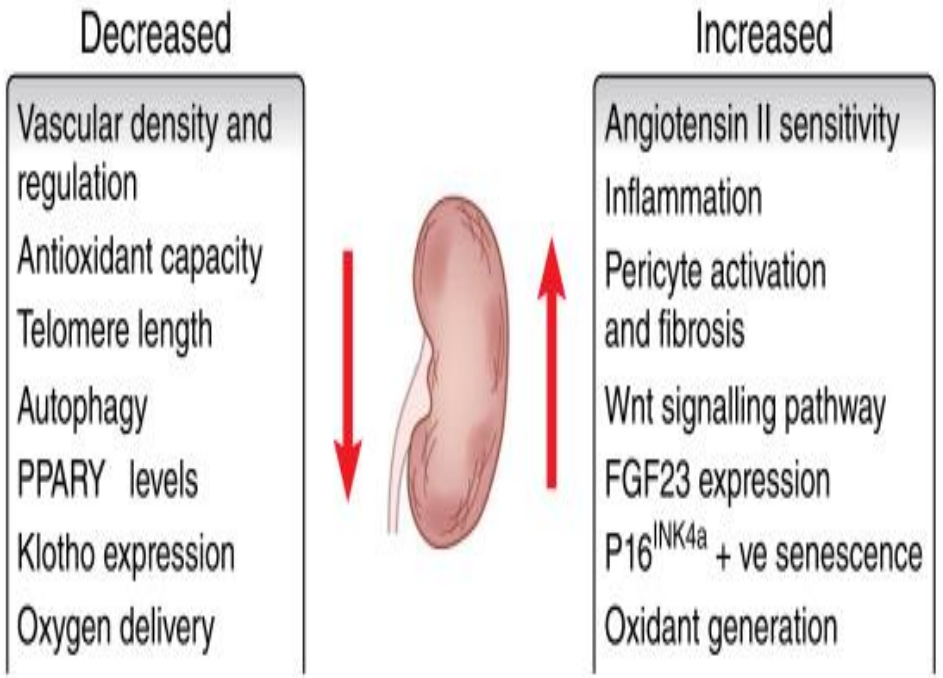


Figure 2. There are degenerative macro-structural changes that occur in the human kidney with even healthy aging. There is cortical volume loss, some increase in medullary volume (not shown), increase in surface roughness, increased sinus fat, and an increase in renal cysts. These findings can be attributed to underlying nephrosclerosis with nephron loss, hypertrophy of remaining tubules, and tubular diverticuli.

Physiology of CKD in elderly people



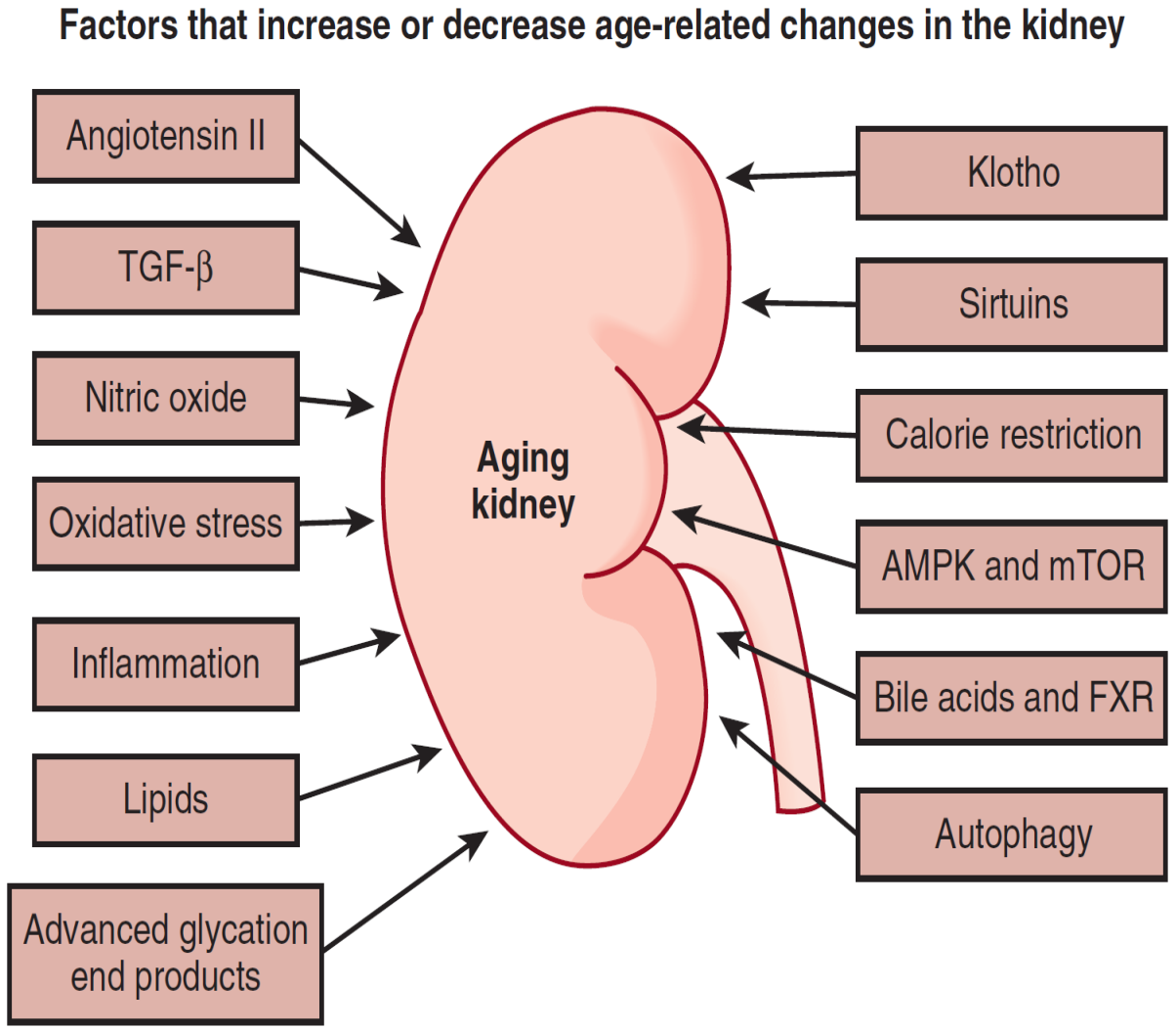
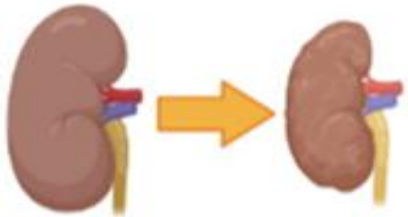


Figure Factors that increase and decrease age-related renal glomerulosclerosis and tubulointerstitial fibrosis. AMPK, Adenosine monophosphate–activated protein kinase; FXR, farnesoid X receptor; mTOR, mammalian target of rapamycin; TGF-β, transforming growth factor-β.

Physiology of CKD in elderly people

RENAL AGING



CKD IN ELDERLY PEOPLE

Structural changes

- Lost of renal parenchyma
- Decreased nephron numbers
- Glomerular basal lamina thickening
- Glomerulosclerosis

Functional changes

- Decreased capacity of urine concentration: Less Na reabsorption
- Vasoconstriction: Less production of NO and other renal vasodilators
- Decreased levels of Klotho

Chronic inflammation

+

Comorbilities

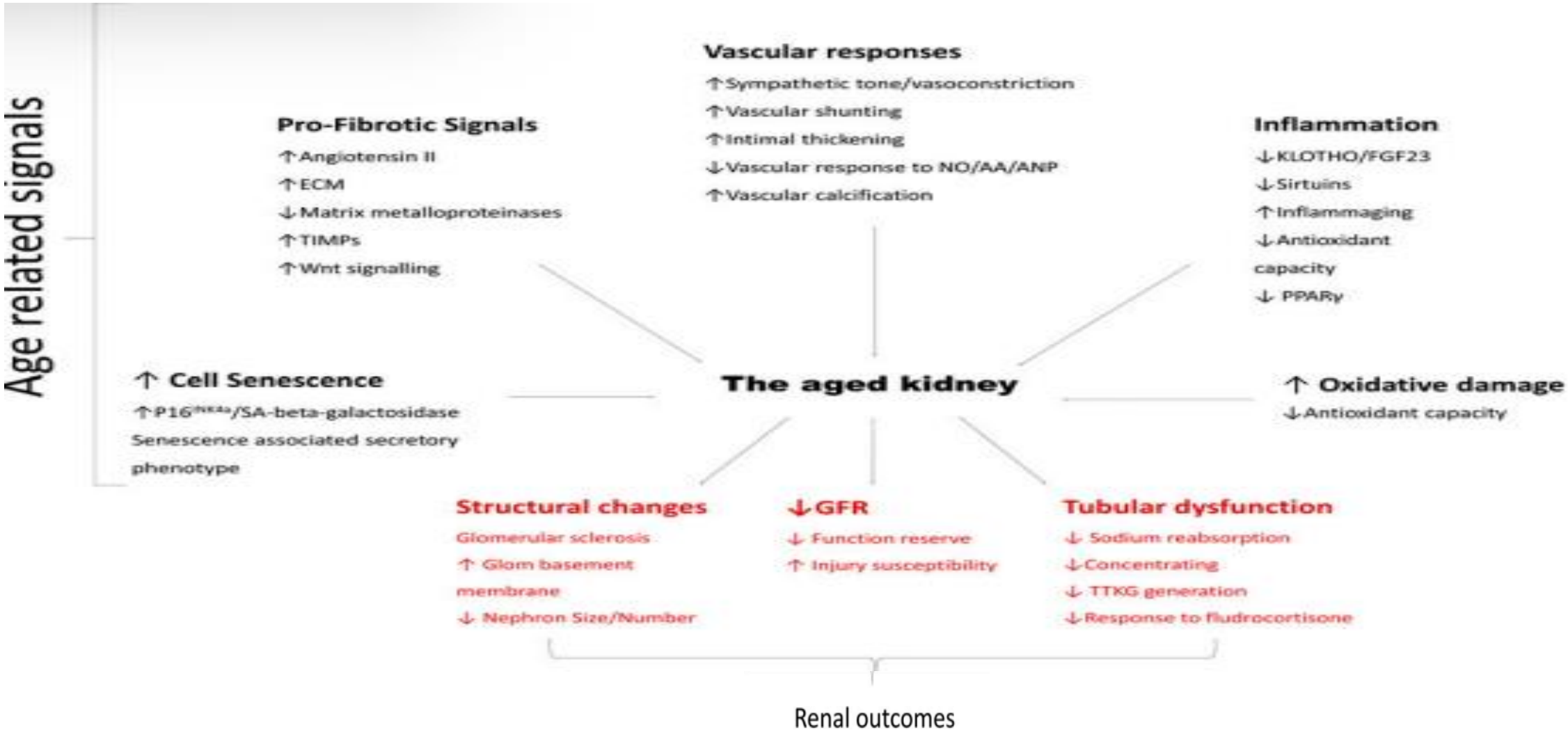
+

Aging

↓

Higher mortality risk

Physiology of CKD in elderly people



eGFR Calculate

1. Cockcroft-Gault Equation (mL/min)	$CCr = \frac{(140 - age) \times LBW\ [kg]}{Cr\ [mg/dL] \times 72}$ *For women Multiply by 0.85*
2. MDRD study equation (mL/min/1.73 m²)	$GFR = 186.3 \times (SCr)^{-1.154} \times (Age)^{-0.203}$ *Multiply by 0.742 for women* *Multiply by 1.21 for African ancestry*
3. CKD-EPI equation	$GFR = 141 \times \min(SCr/\kappa)^{\alpha} \times \max(SCr/\kappa)^{-1.209} \times 0.993^{age}$ *Multiply by 1.018 for women* *Multiply by 1.159 for African ancestry* **κ** is 0.7 for females and 0.9 for males, **α** is –0.329 for females and –0.411 for males, **min** indicates the minimum of SCr/κ or 1, & **max** indicates the maximum of SCr/κ or 1

eGFR Calculate in elderly people

- The values for normal estimated glomerular filtration rate (eGFR) in aging population have important implications for the diagnosis of CKD in the elderly.

- However, the MDRD equation underestimates mean eGFR by 25% and the CKD-EPI equation underestimates mean GFR by 16%.

- Estimates of renal function from serum creatinine levels alone may be inadequate in the elderly, given the changes in muscle mass with age.

Classification of CKD

GFR category	GFR (ml/min)	Terms
G1	>90	Normal or high
G2	60-89	Mildly decreased*
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Severely decreased

ACR category	ACR (mg/mmol)	Terms
A1	<3	Normal to mildly increased
A2	3-30	Moderately increased
A3	>30	Severely increased

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m^2) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	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.

CKD in elderly people

- CKD increases in prevalence with age and heralds a poor outcome.

Recognized as a global public health problem.

- CKD with eGFR less than 60 mL/min/1.73 m2 is present in approximately 38% of U.S. adults 70 years and older.

CKD in elderly people

- Proteinuria significantly increased the risk of ESRD with advancing age.

- In addition , prolonged use of analgesics, frequently seen in the elderly , may be associated with papillary necrosis and progression to CKD.

CKD in elderly people

- Calorie restriction and Klotho deficiency may be a candidate therapeutic target for attenuating kidney aging.

- CKD patients exhibit remarkable declines in the kidney expression of Klotho, which is associated with resistance to FGF23 , hyperphosphatemia and vascular calcification, muscle and skin atrophy, and early death symptoms similar to those of Klotho-deficient mice .

Complications CKD in elderly people

- CKD in the elderly is associated with a greater risk of kidney failure and CVD, including ischemic stroke and death.

- Frailty is also more prevalent among older patients with CKD than among those with normal renal function.

- cognitive impairment increases in older CKD patients independently of Other confounding factors.

Complications CKD in elderly people

- **Frailty**

a common issue in older adults with ESRD, is commonly defined as a physiologic state of increased vulnerability to stressors due to a decreased physiologic reserve.
Frailty was defined as a clinical syndrome where **three or more** of the following findings were present:
unintentional weight loss, self reported exhaustion , weak grip strength, slow gait speed, or low physical activity.

The frailty phenotype was more common with increasing age and independently predicted **incident falls , worsening physical function, hospitalization**, and **death.**

RRT in elderly people

The decision to initiate RRT in the elderly is complicated by more challenges than in younger patients.

Beyond geriatric syndromes, elderly patients more likely face problems
with nonmedical barriers, including limited transportation, family support, and income, furthermore, the elderly also have more frequently cardiovascular and overall comorbid conditions as well as reduced life expectancy compared with younger patients.

RRT in elderly people

In aretrospective analysis of patient survival among those older than 75 years who had stage 5 CKD,
the 1- and 2year survival rates were 84% and 76%, respectively, in the group receiving dialysis compared with 68% and 47%, respectively, in the group treated conservatively.

This survival advantage was lost in patients with multiple comorbid conditions, particularly in those with ischemic heart disease.

RRT in elderly people

Timing of dialysis initiation must be considered.

The IDEAL (Initiating Dialysis Early and Late) study found no benefit for early initiation , and another study suggested that in the elderly it may even be associated with harm, perhaps because of accelerated loss of residual renal function .

Early vs. Late Initiation Dialysis
Cooper, et al. NEJM 2010

- Australia
- Randomized trial
  - 828 patients CKD-5
  - Early initiation
    - eGFR 10-14 ml/min
  - Late initiation
    - eGFR 5-7 ml/min
- Primary outcome
  - Death

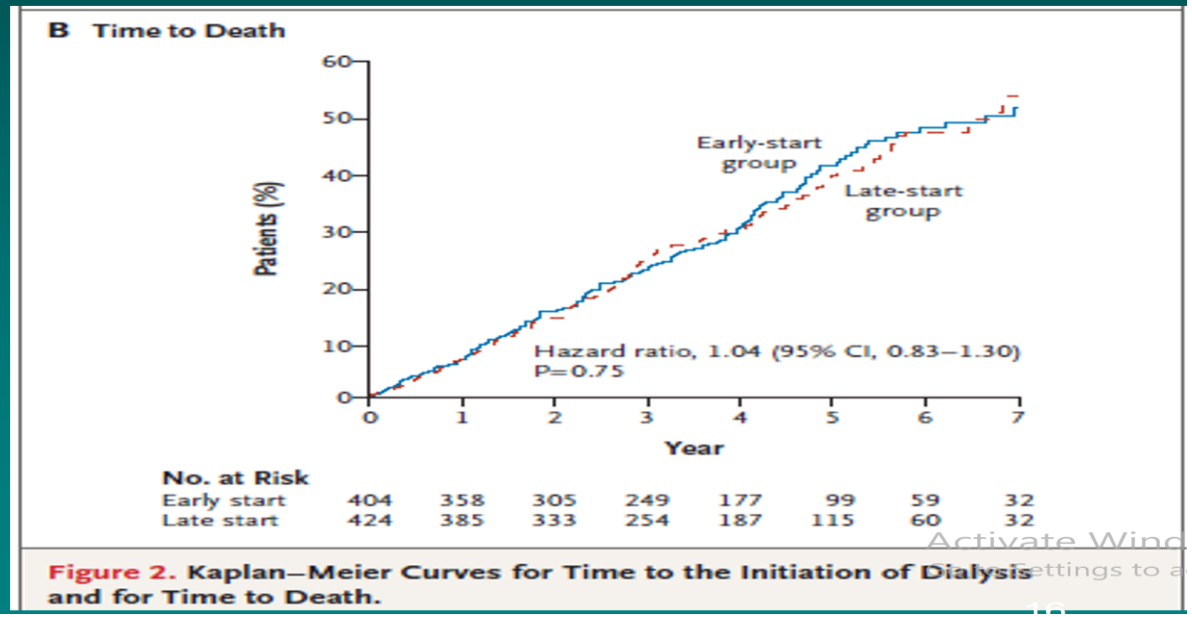


Figure 2. Kaplan–Meier Curves for Time to the Initiation of Dialysis and for Time to Death.

RRT in elderly people

- For maintenance hemodialysis, an arteriovenous fistula(AVF) is the preferred access, particularly in the elderly , because it is associated with a lower incidence of Infectious complications.
- Concern for fistula maturation is not unique to older patients, and thus age should not be a limiting factor in AVF creation given the equivalent procedural and fistula survival rates in younger and older patients.

- Factors limiting fistula creation such as significant vascular disease and cardiovascular instability may be more prevalent in the elderly.

RRT in elderly people

- peritoneal dialysis may be an option for elderly patients who experience hemodynamic instability during hemodialysis.

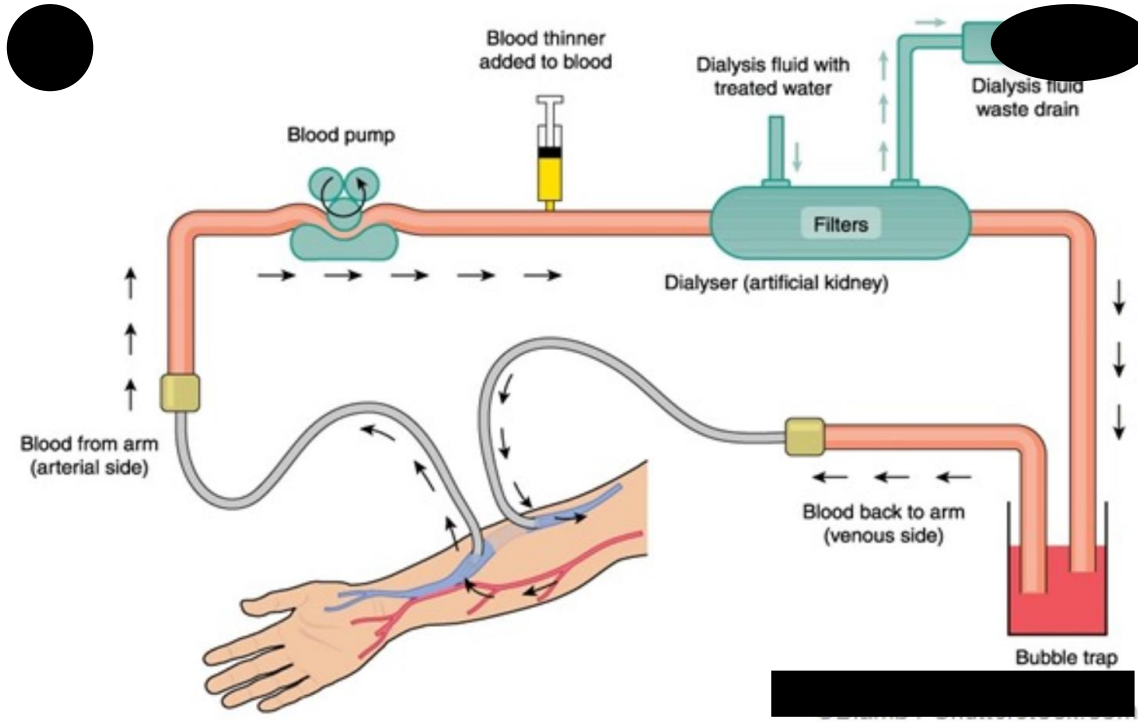
- There is little difference between older and younger patients in the likelihood of technique failure, number of peritonitis episodes, and types of infections, and fewer peritoneal catheter replacements are actually required in older patients.

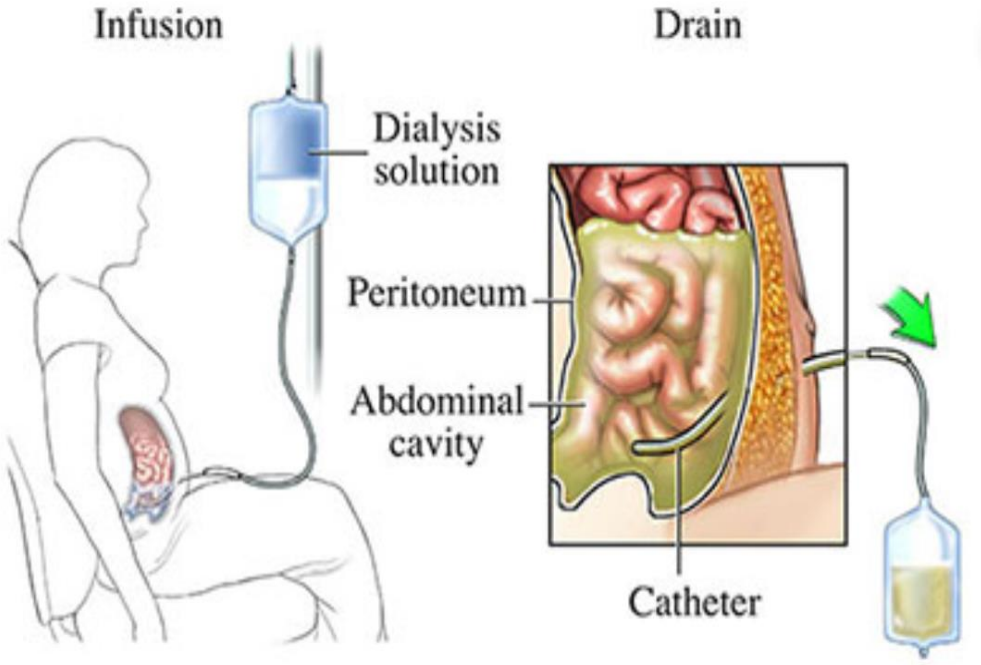
RRT in elderly people

No difference in survival on HD compared to PD

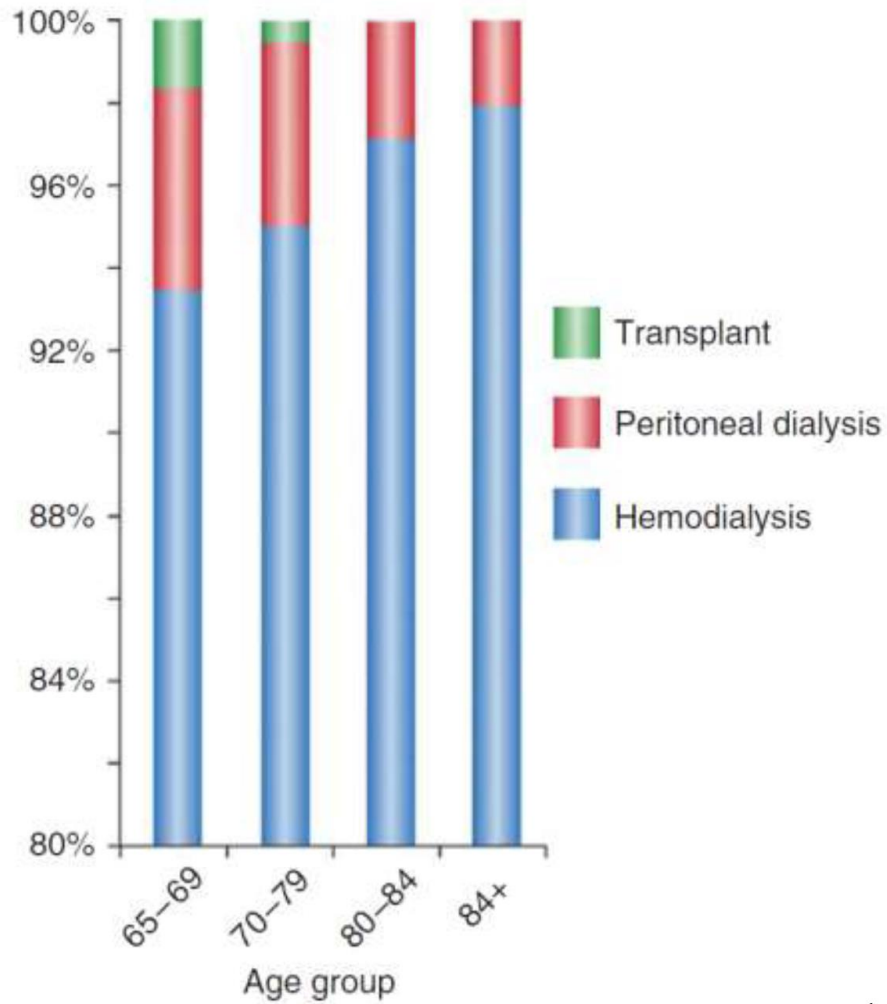
• Decision should therefore be made with patient dependent on patient goals, lifestyle and medical concerns

• Availability of assistance enables older patients to have dialysis at home-assisted PD





Choice of Initial Dialysis Modality



HD or PD in elderly: patient perspective

HAEMODIALYSIS

- Hospital based treatment
  - Not dependent on patient ability
  - Can provide social structure for frail elderly
  - Transport (journey and waiting time) needs to be added into treatment time
  - Often feel washed out for hours after HD session
- Interferes with social and family life
- Increased hospitalisation for vascular access problems
- Difficult to travel for holidays or visiting family

PERITONEAL DIALYSIS

- Home based treatment
  - Patient independence
  - Fits in with work and social activities
  - Can be done by carer (paid assistant or family)
- Less visits to hospital
- Flexibility of manual exchanges (3-4/day) or automated cycling machine over night
- Treatment burden related to daily and repetitive nature of performing exchanges
- Easier to travel to go on holiday or visit family nationally or overseas

RRT in elderly people

- Medical conditions which are a **relative contraindication to peritoneal dialysis** include: **severe pulmonary disease ; significant scarring from previous abdominal surgery; uncorrectable hernias; active inflammatory bowel disease;** and **colostomy, ileostomy,** or **gastric tubes .**

RRT in elderly people

- Elderly patients undergoing dialysis may be more prone to hypoglycemia because of prolonged insulin clearance, poor intake, and decreased sympathetic response due to Other medications.

Therefore, close monitoring of medications and careful attention to detect subtle changes in the clinical condition of the elderly patient undergoing dialysis are essential.

RRT in elderly people

- Age alone does not necessarily preclude candidacy for renal transplantation for those medically eligible.

- As the subset of older patients with ESRD grows, there is a shift toward older renal transplant candidates while kidney allocation remains skewed toward younger recipients.

RRT in elderly people

The 2013 Scientific Registry of Transplant Recipients reports that approximately 40% of all candidates waiting for transplant are between 50and 64 years old and 18% are 65 years or older.

The proportion of older patients receiving kidney transplants in relation to the number of older patients wait listed to receive transplants are similar to the proportion of younger recipients of kidney transplants compared with younger waitlisted patients.

RRT in elderly people

Older patients undergoing transplantation have a significant survival advantage over those remaining on dialysis.

The overall risk of death is 41% lower for older kidney transplant recipients than for waitlisted candidates, with survival advantage also noted for recipients of extended criteria donor (ECD) kidneys at 3months, 1 year, and 5 years.

RRT in elderly people

Table 24.1 Adjusted Patient and Allograft Survival Rates for Transplant Recipients 65 Years of Age and Older

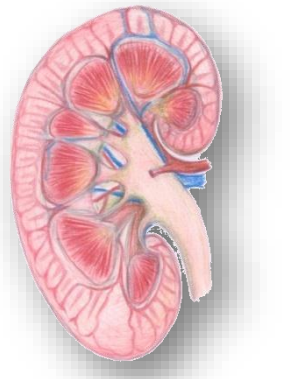
	3 Months		1 Year		5 Years	
	Patient Survival (%)	Allograft Survival (%)	Patient Survival (%)	Allograft Survival (%)	Patient Survival (%)	Allograft Survival (%)
Living donor	99.2	98	96.9	95.4	79.2	73.9
Deceased non–extended criteria donor	97.5	95.2	93.3	89.4	69.6	61.6
Deceased extended criteria donor	95.5	90.3	90.1	83.2	61.3	52.5

Data from U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: 2009 annual report. *Available at http://optn.transplant.hrsa.gov/ar2009/survival rates.htm. Accessed April 2011.*

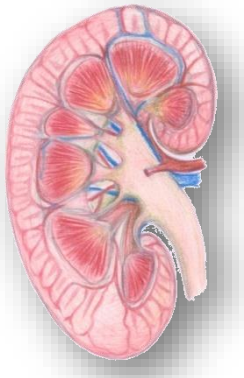
RRT in elderly people

Although risk of acute rejection can be lower in older recipients, the impact of acute rejection on overall longterm allograft function may be more significant.

Nevertheless, transplant graft loss in older recipients occurs primarily from patient death secondary to infection and CVD.



Acute kidney Injury in elderly people



Definition of AKI

2.1.1:

Acute kidney injury (AKI) is defined as any of the following (Not Graded):

- Increase in SCr by ≥ 0.3 mg/dl (≥ 26.5 µmol/l) **within 48 hours;**

OR

- Increase in SCr to ≥ 1.5 times baseline, which is **known or presumed to have occurred within prior 7 days**

OR

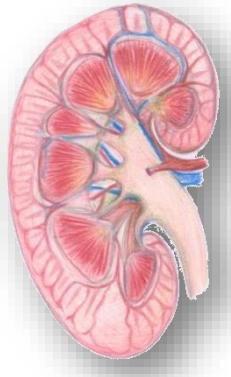
- Urine volume <0.5 ml/kg/h **for 6 hours**

Staging of AKI

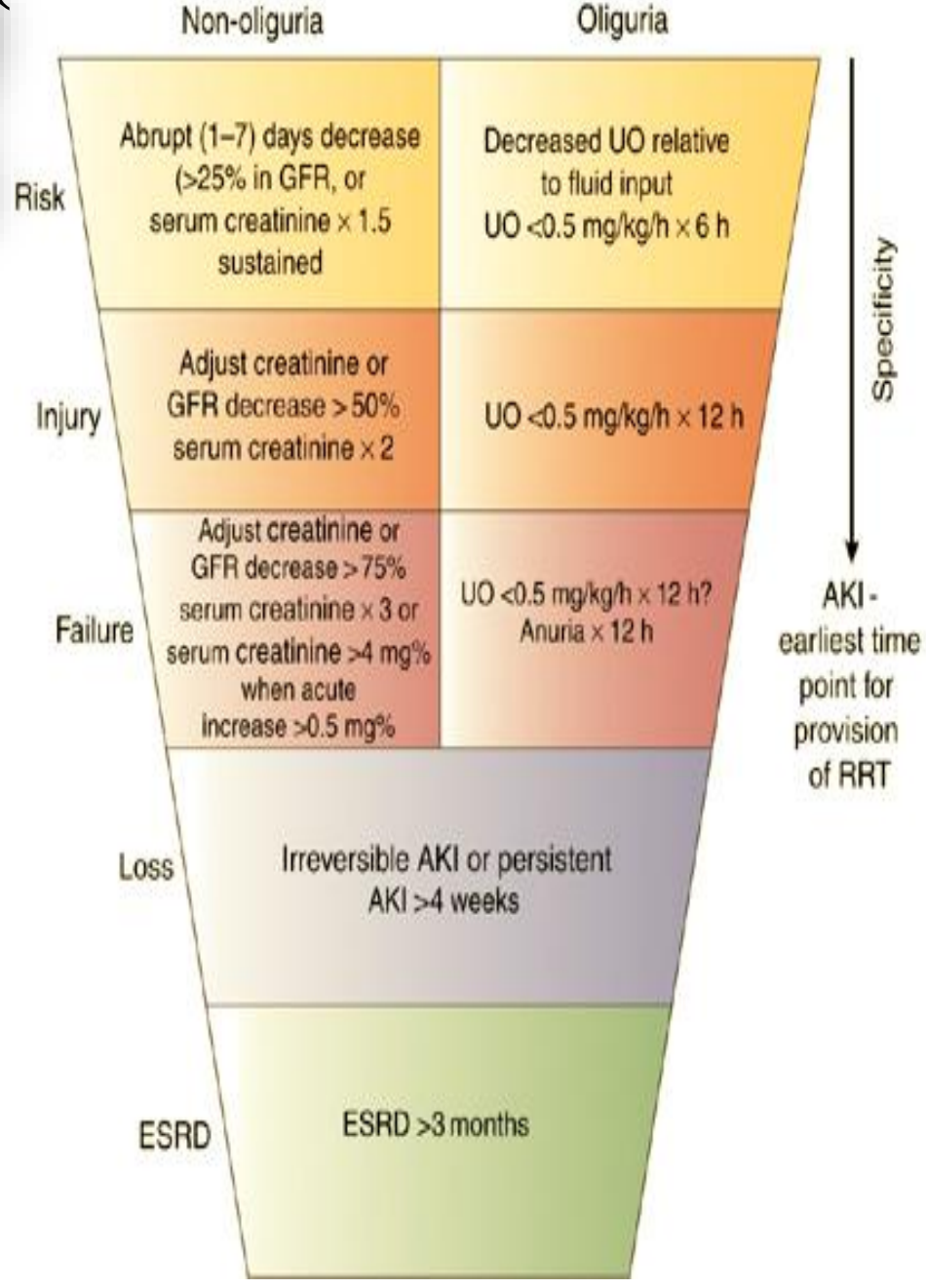
2.1.2:

AKI is staged for severity according to the following criteria (below). (Not Graded)

Stage	Serum Creatinine	Urine Output
1	1.5-1.9 times baseline OR ≥0.3 mg/dl (≥ 26.5 µmol/l) increase	<0.5 ml/kg/h for 6-12 hours
2	2.0-2.9 times baseline	<0.5 ml/kg/h for ≥12 hours
3	3.0 times baseline **OR increase in serum creatinine to ≥4.0 mg/dl (≥ 353.6 µmol/l) OR initiation of renal replacement therapy OR**, in patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ≥ 24 hours OR Anuria for ≥ 12 hours



(RIFLE) classification of ARF



AKI in elderly people

- Susceptibility to both ischemic and nephrotoxic acute kidney injury (AKI), as well as time for recovery from injury , increases with age.
- Acute kidney injury is **3.5 times** more prevalent in those **older than 70 years** and is associated with greater morbidity and mortality in older hospitalized patients.
- An estimated **28% of those older than 65 years** are unlikely to recover kidney function after AKI.

AKI in elderly people

- Reduced antioxidant potential and increased oxidative stress predisposed older rats to more severe reperfusion injury.
- Expression of candidate genes, including claudin-7 (Cldn7),

  Kidney injury molecule-1 (Kim1), and matrix metalloproteinase(MMP7),

  was increased during ischemic injury in slices of kidney from older rats in comparison with younger rats;

  interestingly, gene expression was attenuated in calorie restricted older rats.

Ischemia-Associated AKI

Pathophysiology of Ischemic Acute Renal Failure

$\downarrow O_2$

MICROVASCULAR

Glomerular Medullary

- ↑ Vasoconstriction *in response to*: endothelin, adenosine, angiotensin II, thromboxane A2, leukotrienes, sympathetic nerve activity
- ↓ Vasodilation *in response to*: nitric oxide, PGE_2, acetylcholine, bradykinin
- ↑ Endothelial and vascular smooth muscle cell structural damage
- ↑ Leukocyte-endothelial adhesion, vascular obstruction, leukocyte activation, and inflammation

Inflammatory and vasoactive mediators

TUBULAR

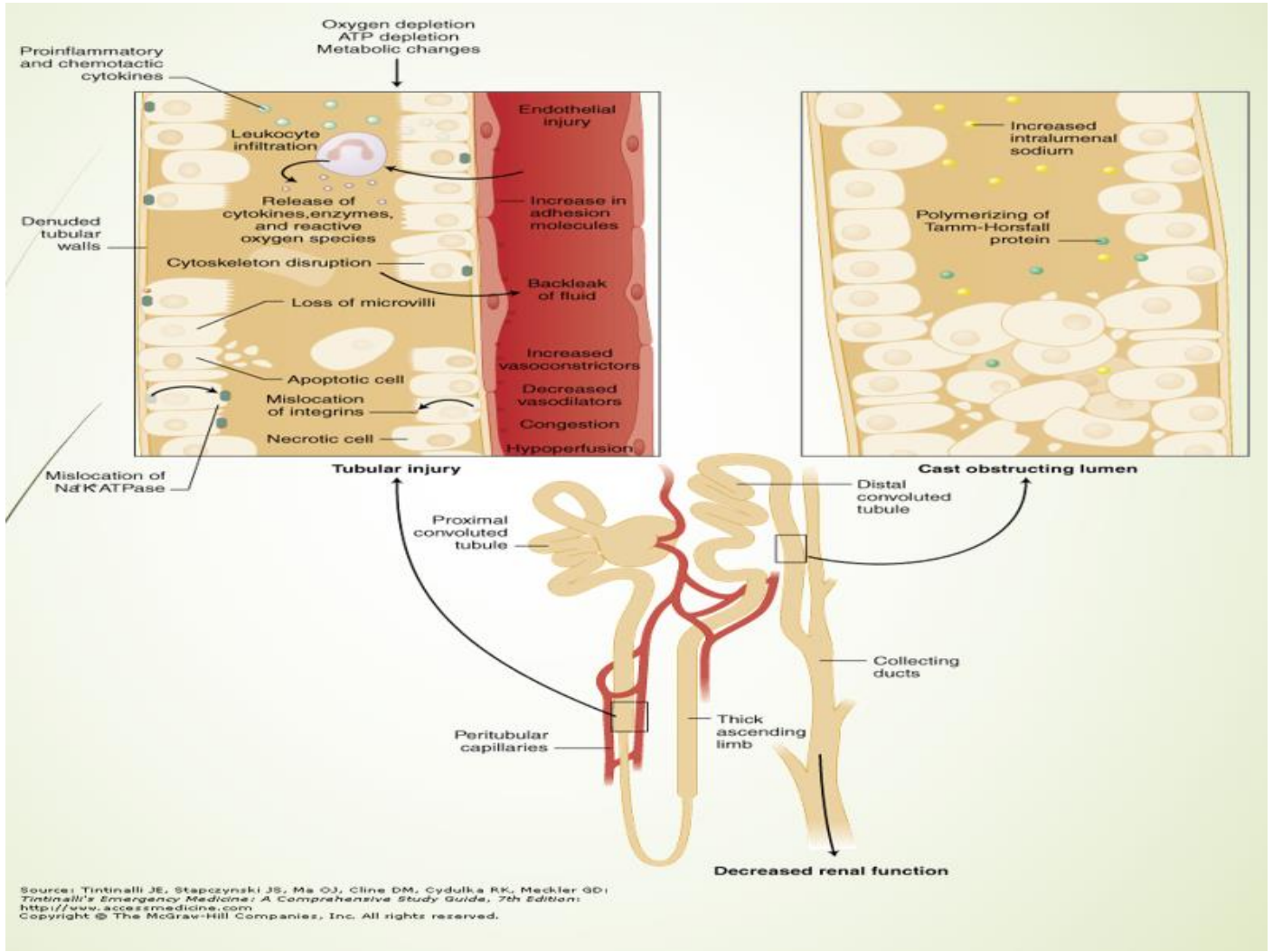
- Cytoskeletal breakdown
- Loss of polarity
- Apoptosis and necrosis
- Desquamation of viable and necrotic cells
- Tubular obstruction
- Backleak

Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

Pathophysiologic mechanisms of ischemic tubular necrosis

Other contributors to low GFR include :

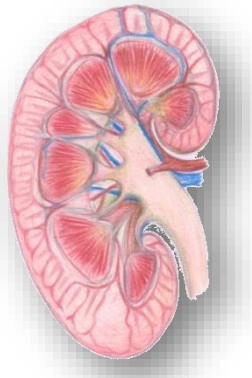
- Back leak of filtrate across damaged denuded tubular epithelium
- mechanical obstruction of tubules from necrotic debris



AKI in elderly people

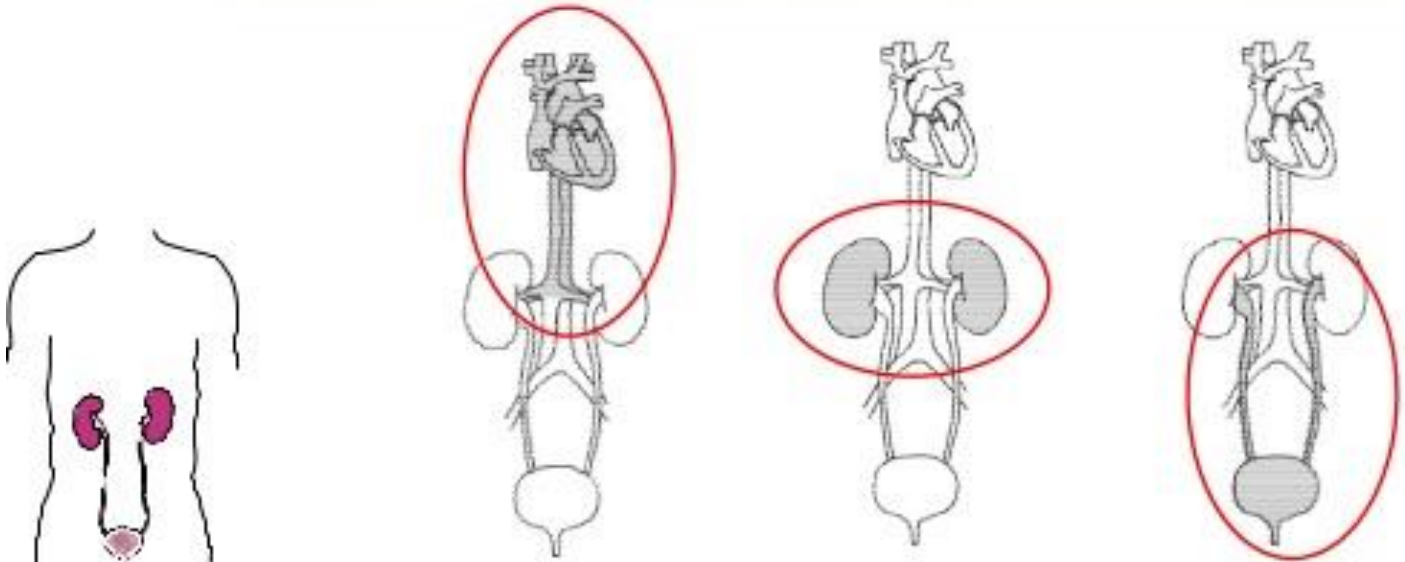
- Multifactorial and iatrogenic insults, whether prerenal , intrinsic, or postrenal, that lead to AKI are poorly tolerated as age increase and renal reserve decreases.

- The common presence of comorbid **diabetes, hypertension, heart failure , liver disease, or malignancies** in older individuals adds to the poor tolerability of an acute renal insult.

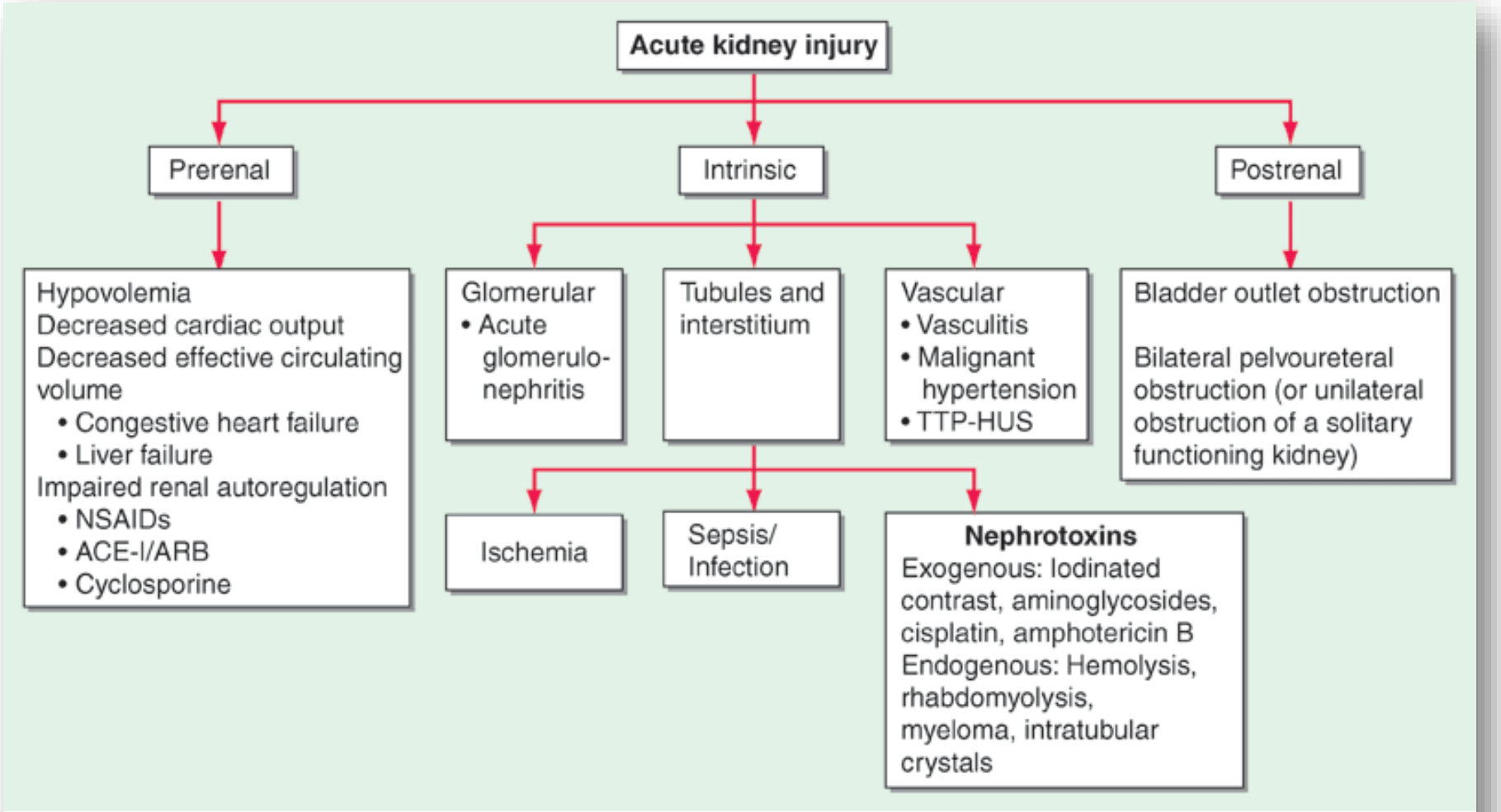


Traditional classification of ARF

The causes of ARF are traditionally divided into three categories. Although this division is useful for classification, all three categories may occur simultaneously in a given patient. ARF is a complication that can occur following any medical condition. It can result from pre-renal causes, intrinsic renal causes or post-renal causes.



Classification of the major causes of acute kidney injury



Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J:
Harrison's Principles of Internal Medicine, 18th Edition: www.accessmedicine.com

Major Disease Categories Causing AKI

Disease Category	**Incidence**
Prerenal azotemia caused by acute renal hypoperfusion	55-60%
Intrinsic renal azotemia caused by acute diseases of renal parenchyma: -Large renal vessels dis. -Small renal vessels and glomerular dis. -ATN (ischemic and toxic) -Tubulo-interestitial dis. -Intratubular obstruccttion	35-40% ***>90%***
Postrenal azotemia caused by acute obstruction of the urinary tract	<5%

AKI in elderly people

Approximately half of the AKI events in the elderly result from prerenal processes.

Vomiting, **diarrhea**, **bleeding**, and **use of excessive diuretics** are common causes of dehydration and volume depletion in this population.

- Impaired thirst,decreased urinary concentration ability, and diminished sodium conservation capacity predispose to these processes.

- Blunted autoregulation, decreased RPF, and reduced renal reserve in the older kidney allow volume changes to be less well tolerated.

AKI in elderly people

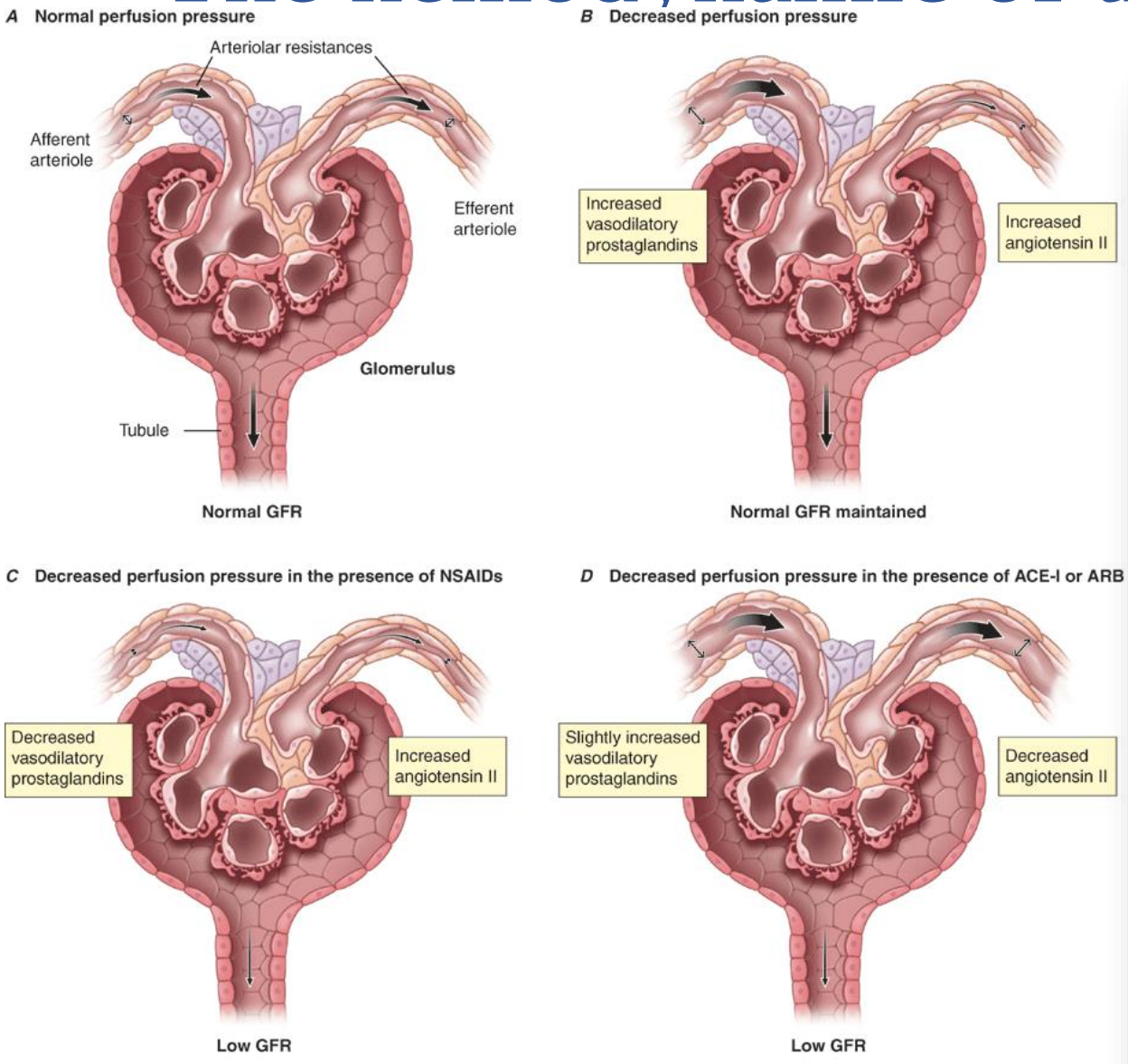
Renal hypoperfusion from decreased cardiac output, sepsis, and use of medications that interfere with renal autoregulatory mechanisms,

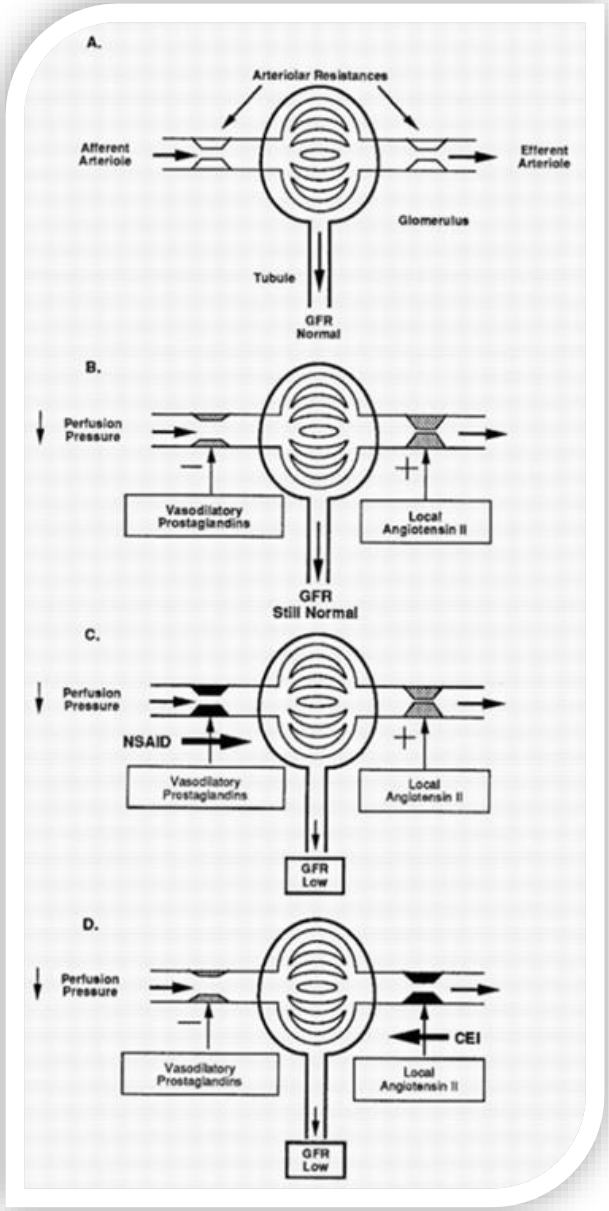
such as angiotensin antagonists (ACEIs, ARBs) and prostaglandin inhibitors(NSAIDs),

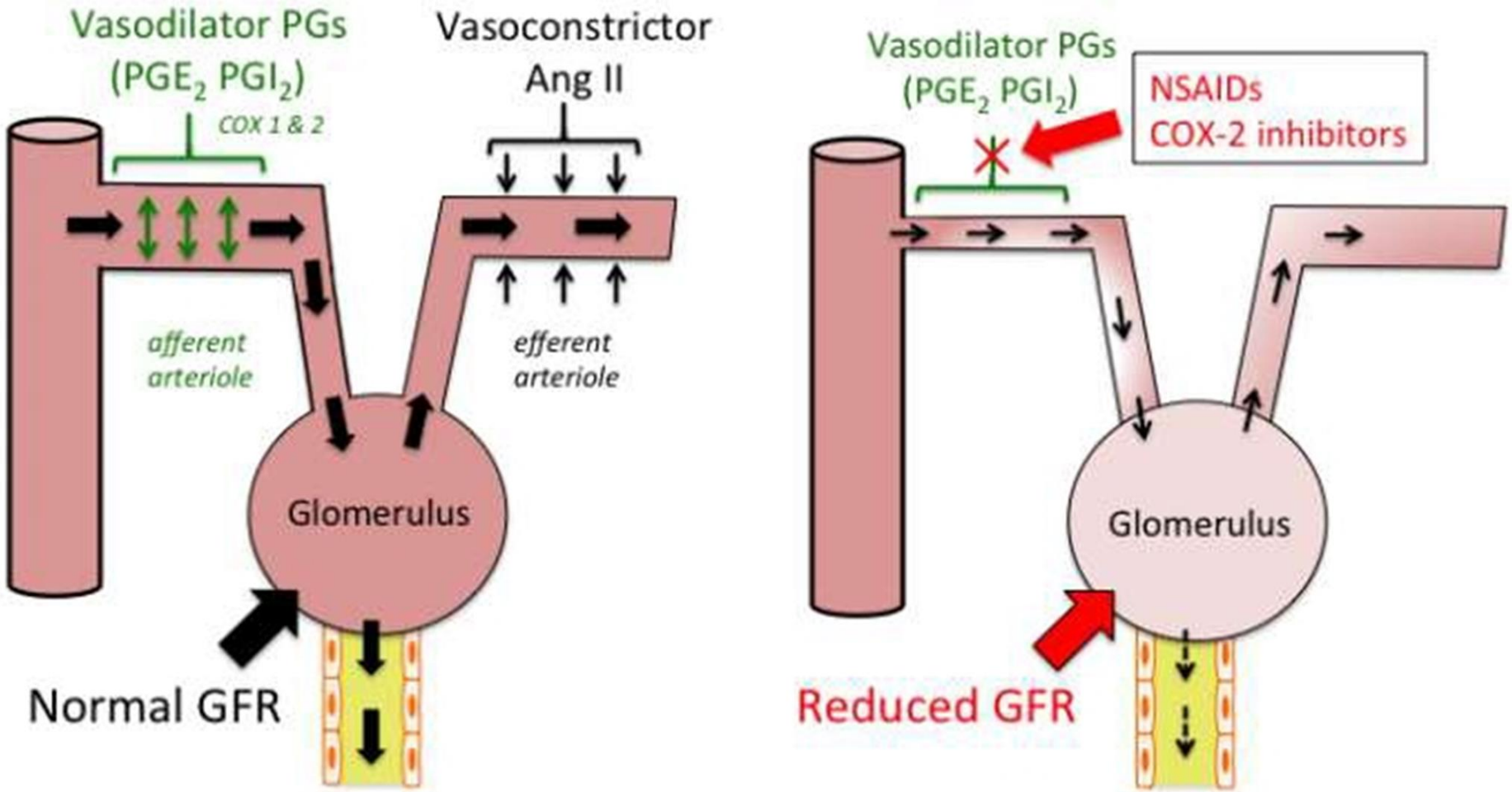
can cause and exacerbate prerenal processes , leading to AKI in older adults.

NSAID use increases the risk of AKI in those 65 years and older by 58%.

The hemodynamic of the kidney






Vasodilator PGs
(PGE2 PGI2)
COX 1 & 2
Vasoconstrictor
Ang II
afferent
arteriole
efferent
arteriole
Glomerulus
Normal GFR
Vasodilator PGs
(PGE2 PGI2)
NSAIDs
COX-2 inhibitors
Glomerulus
Reduced GFR

AKI in elderly people

Lower levels of the NO substrate, l-arginine , in the elderly are associated with decreased NO synthesis in aging vasculature and higher ADMA levels, impairing vasodilation and predisposing older kidneys to ischemia.

LABORATORY FINDINGS IN ACUTE RENAL FAILURE

Index	Prerenal Azotemia	Oliguric Acute Renal Failure
BUN/P_{Cr} ratio	>20:1	10–15:1
Urine sodium U_{Na}, meq/L	<20	>40
Urine osmolality, mosmol/L H_2O	>500	<350
Fractional excretion of sodium[a]	<1%	>2%
Urine/plasma creatinine U_{Cr}/P_{Cr}	>40	<20
Urinalysis (casts)	None or hyaline/ granular	Muddy brown

[a] $FE_{Na} = \frac{U_{Na} \times P_{Cr} \times 100}{P_{Na} \times U_{Cr}}$

Abbreviations: BUN, blood urea nitrogen; P_{Cr}, plasma creatinine concentration; P_{Na}, plasma sodium concentration; U_{Cr}, urine creatinine concentration; U_{Na}, urine sodium concentration.

AKI in elderly people

Because tubular defects in older individuals may lead to a higher urine sodium excretion despite underlying hypoperfusion.

➢the usual renal indices used to differentiate prerenal from intrinsic causes:

urine sodium excretion, **fractional sodium excretion**, and **urine osmolality**

need careful interpretation in the elderly.

AKI in elderly people

Although prerenal processes are often reversible with :

careful volume management,

discontinuation of the exacerbating factor,

or improvement in cardiac output,

the evolution from prerenal azotemia to acute tubular necrosis (ATN) occurs

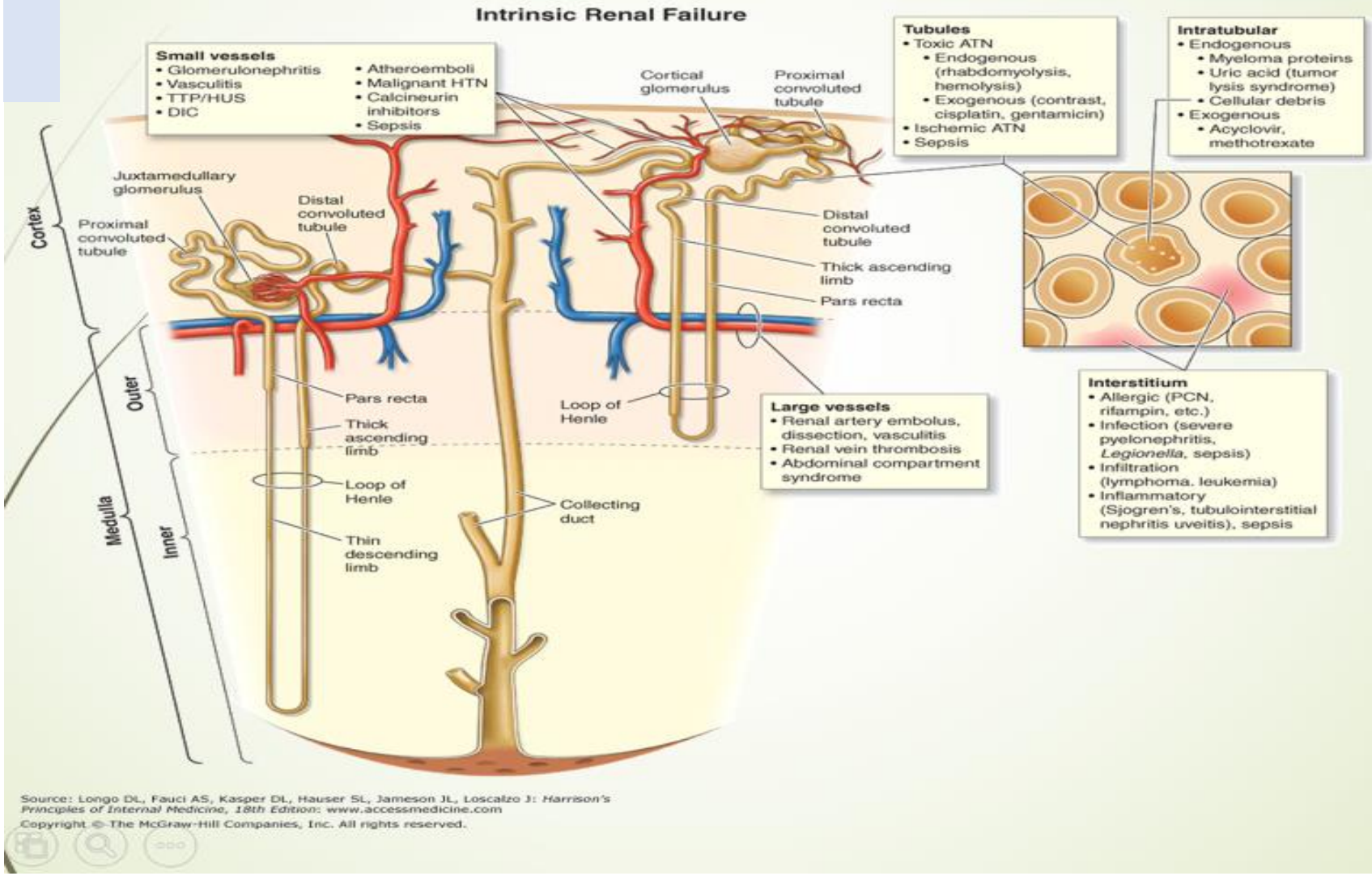
more commonly in older(23%) than younger (15%) patients

AKI in elderly people

Intrinsic AKI results in acute structural insults that prolong recovery of renal clearance In the elderly.

ATN from ischemic and nephrotoxic tubular injury Affects approximately 50% of hospitalized older patients with intrinsic AKI.

Intrinsic AKI



AKI in elderly people

Hypotension, either before or after surgery, sepsis, and nephrotoxins are poorly tolerated by aging kidneys and are major culprits in hospital-acquired AKI in the elderly.

A prospective evaluation of all patients admitted to one hospital over a 12-month period, of whom 4176 were older than 60 years, noted that the incidence of treatment-related in hospital AKI in the elderly was 1.4%.

AKI in elderly people

Nephrotoxins contributed to AKI in **66%** of the elderly patients,
sepsis and hypotension in **45.7%**,
contrast induced nephropathy in **16.9%**,
and postoperative renal failure in **25.4%**, with various combinations of these factors leading to AKI.

Sepsis, oliguria, and **hypotension** were independent predictors of poor outcome in this older population.

Acute tubular necrosis

ischemia (50% of cases)
nephrotoxins(35%ofcases).

- **Nephrotoxic drugs**
  - Aminoglycoside antibiotics
  - Amphotericin B
  - Pentamidine
  - Foscarnet
  - Acyclovir
  - Indinavir
  - Antineoplastic agents (e.g., cisplatin)
  - Radiocontrast dye
  - Organic solvents (e.g., carbon tetrachloride)
  - Ethylene glycol (antifreeze)
  - Anesthetics (enflurane)
  - Oral sodium phosphosoda

Endogenous toxins

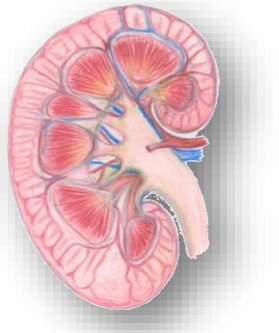
Myoglobin (e.g., rhabdomyolysis)

Hemoglobin (e.g., incompatible blood transfusion, acute falciparum malaria)

Uric acid (e.g., acute uric acid nephropathy)

Aminoglycoside nephrotoxicity

- AKI occurs in up to 20% of patients on aminoglycosides, even with careful dosing and therapeutic plasma levels
- correlates better with total cumulative dose than with plasma levels(usually after 5-7days)
- Predisposing factors :
  - old age, preexisting renal disease, volume depletion, and combination with other agents (e.g., diuretics, cephalosporins, vancomycin)
- Early findings are isosthenuria caused by nephrogenic diabetes insipidus
- Later findings include azotemia
- Recovery of renal function after drug discontinuation is often delayed and may require **weeks or months** to be complete.
- AKI from aminoglycosides is typically **nonoliguric**



AKI in elderly people

The number of cationic groups on the molecules determines the facility with which these drugs are transported across the cell membrane and is an important determinant of toxicity.

- **Neomycin** is associated with the most nephrotoxicity
- gentamicin, tobramycinand amikacin are intermediate;
- **streptomycin** is the least nephrotoxic.

AKI in elderly people

➢Therefore careful estimation of renal clearance is crucial in the elderly prior to antibiotic and chemotherapy dosing with continued close monitoring and drug dose adjustment as necessary.

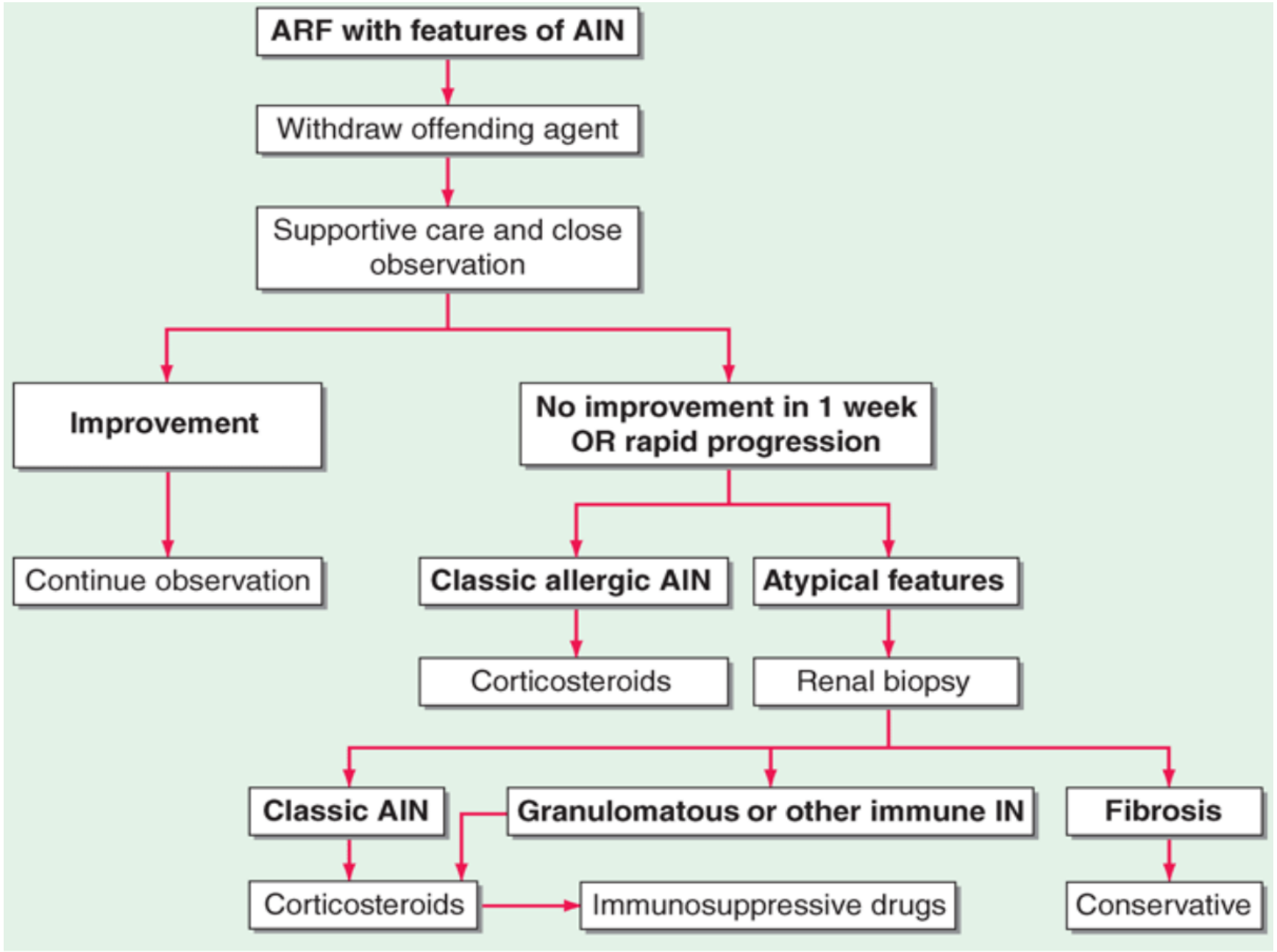
Drug-induced AIN

Drug induced interstitial nephritis is more common in the elderly, particularly with commonly used drugs such as penicillins and proton pump inhibitors.

- More than 100 drugs have been implicated in drug- induced AIN.
- Some of the drugs most commonly associated with AIN are:
  - Antibiotics (e.g., methicillin, cephalosporins, rifampicin, sulfonamides, erythromycin, and ciprofloxacin)
  - Diuretics (e.g., furosemide, thiazides, chlorthalidone)
  - NSAIDs
  - Anticonvulsant drugs (e.g., phenytoin, carbamazepine)
  - Allopurinol

Diagnosis

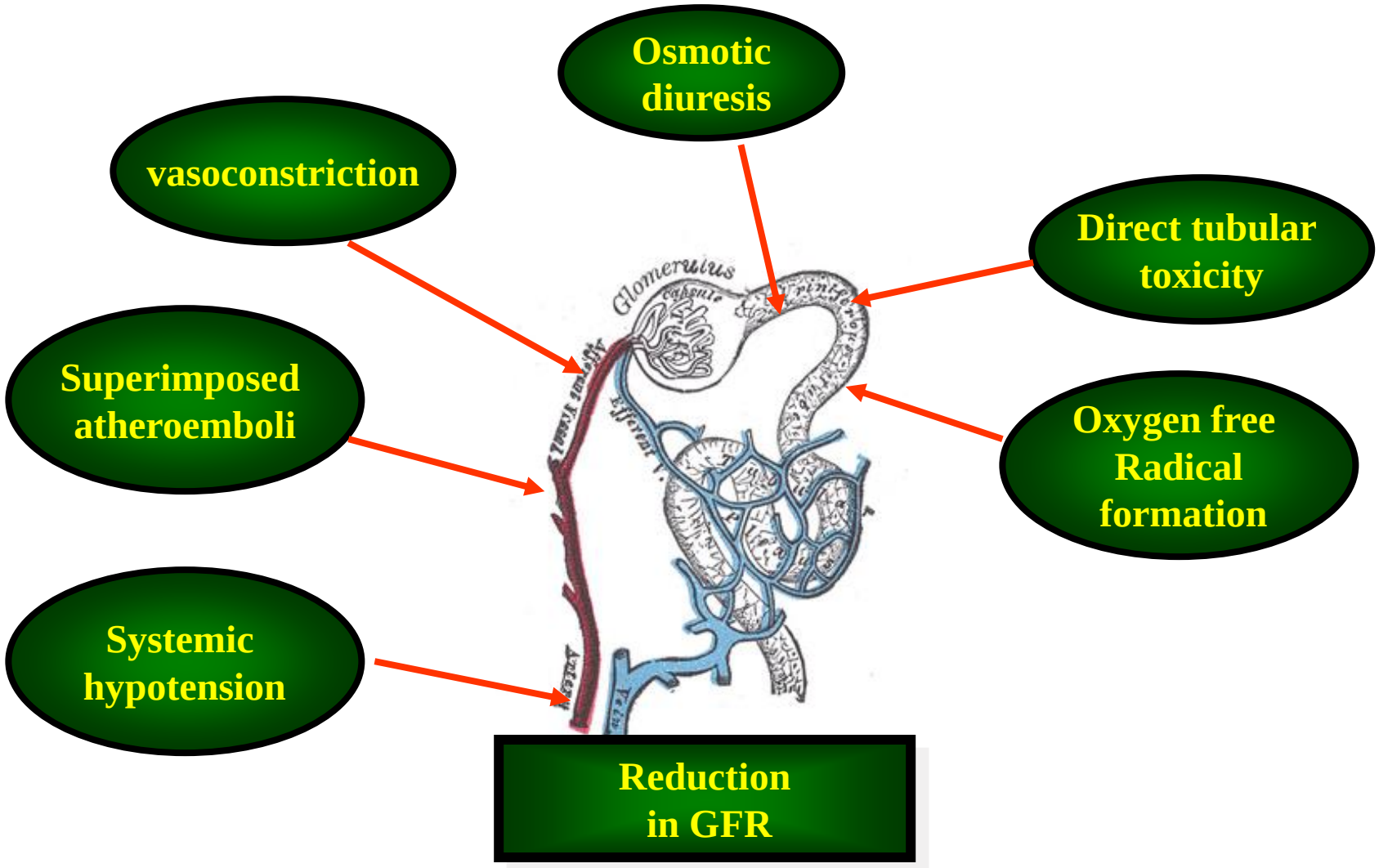
- unexplained renal failure with or without oliguria and exposure to a potentially offending agent
- Peripheral blood eosinophilia adds supporting evidence
- Urinalysis reveals pyuria with white blood cell casts and hematuria
- Urinary eosinophils are neither sensitive nor specific for AIN
- Renal biopsy is generally not required for diagnosis

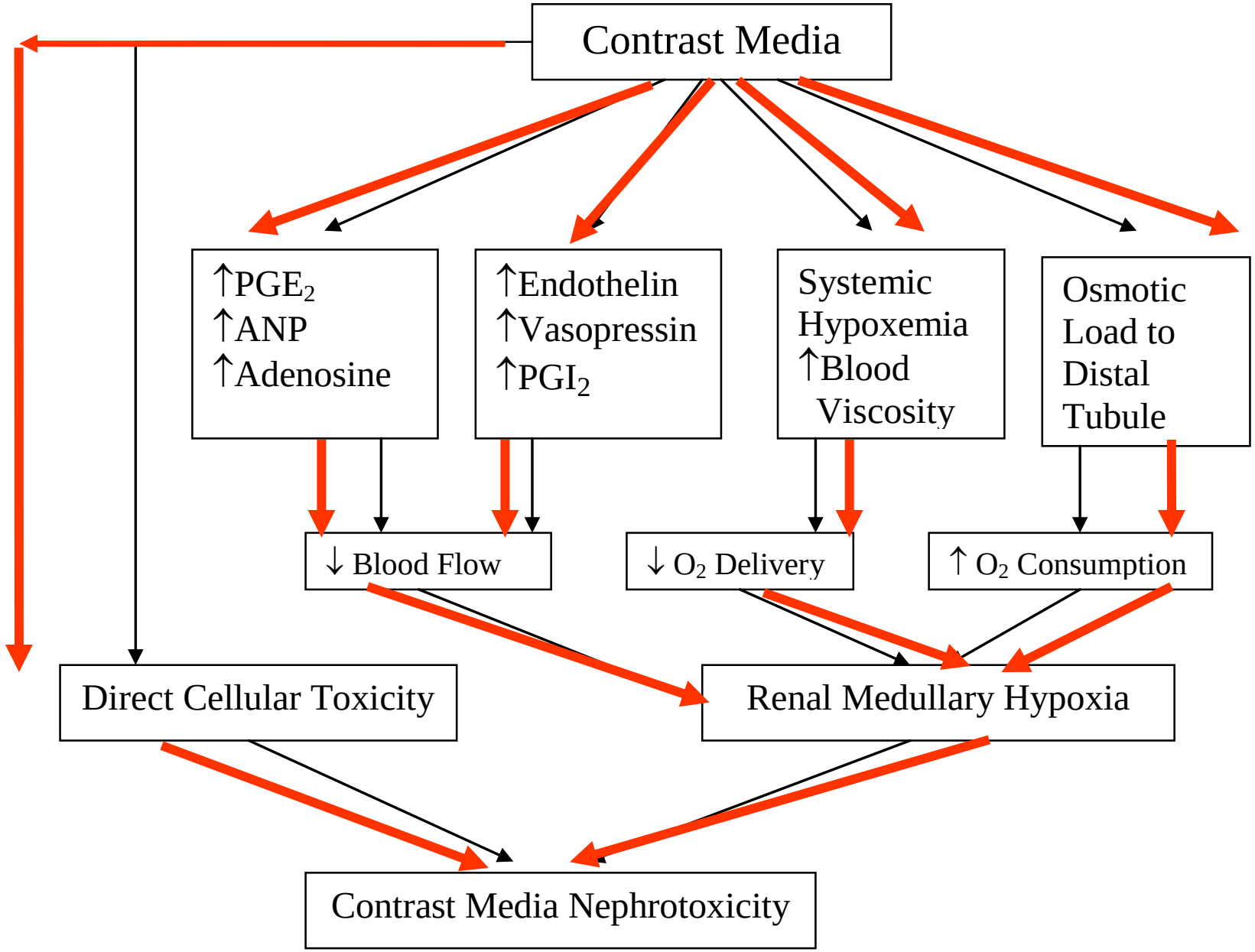

ARF with features of AIN
Withdraw offending agent
Supportive care and close observation
Improvement
No improvement in 1 week OR rapid progression
Continue observation
Classic allergic AIN
Atypical features
Corticosteroids
Renal biopsy
Classic AIN
Granulomatous or other immune IN
Fibrosis
Corticosteroids
Immunosuppressive drugs
Conservative

Contrast-Induced Acute Kidney Injury (CI-AKI)

The definition of iodinated contrast-induced renal injury varies from series to series, typically ranging from an increase in serum creatinine of 25–50% or an absolute increase Of>0.5 mg/dl (44 umol/l) occurring within 24 or 48 h. Serum creatinine typically peaks at 3 to 5 days and returns to baseline after about a week.

Renal effect of intravascular contrast agents:

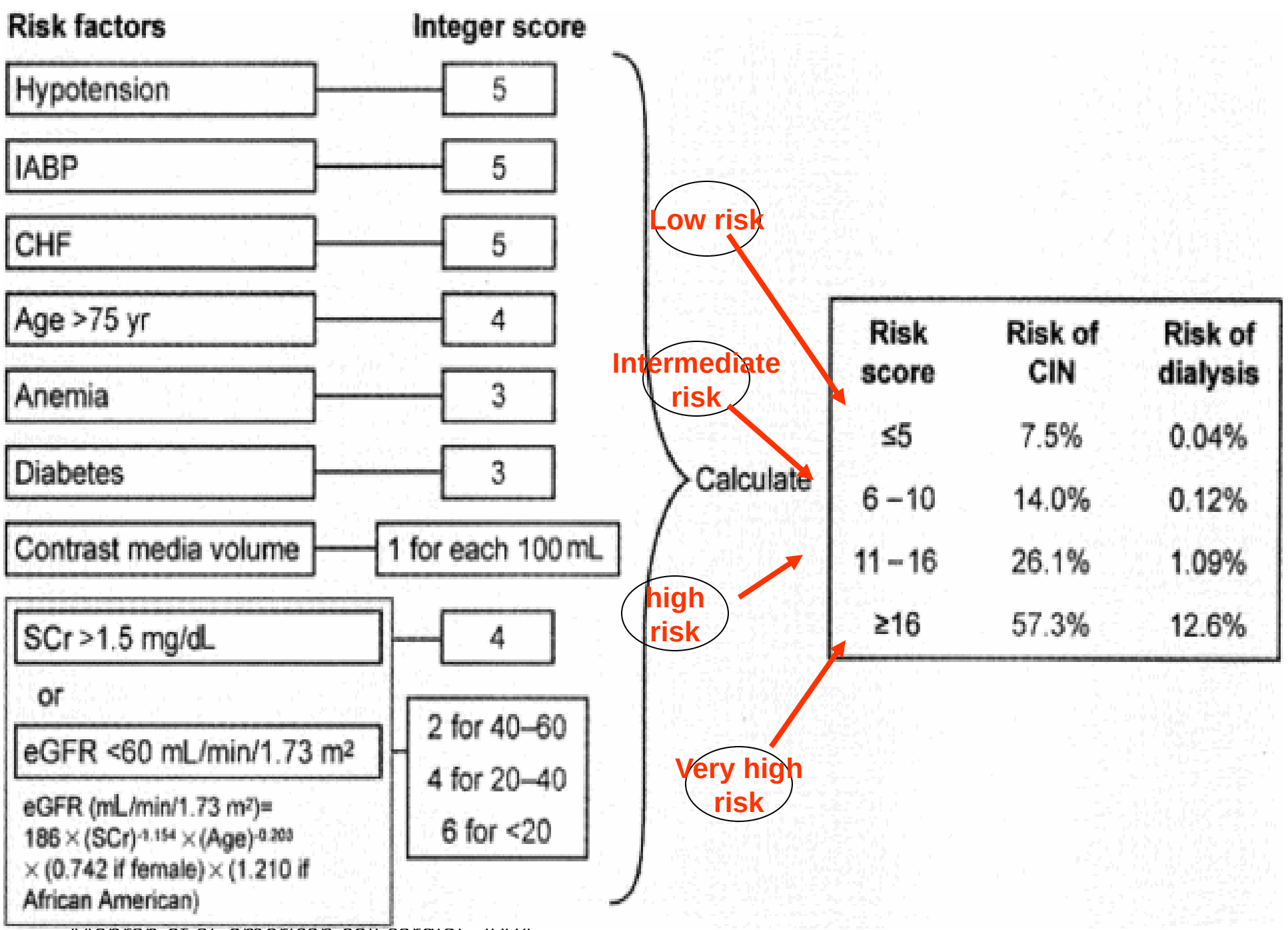




From Rudnick et al, Am J of Kidney Disease, 1994

The frequency of contrast nephropathy is increased in:

- Hypotension
- Heart failure
- Advanced age
- Renal failure
- Diabetes mellitus
- Anemia
- Volume depletion
- Large volume of contrast
- Frequent contrast enhancement studies
- Ionic and hyper-osmolar contrast agents
- Concomitant use of nephrotoxic drugs
- Cirrhosis
- Proteinuria



Mehran et al, american coll cardiol, 2004

AKI in elderly people

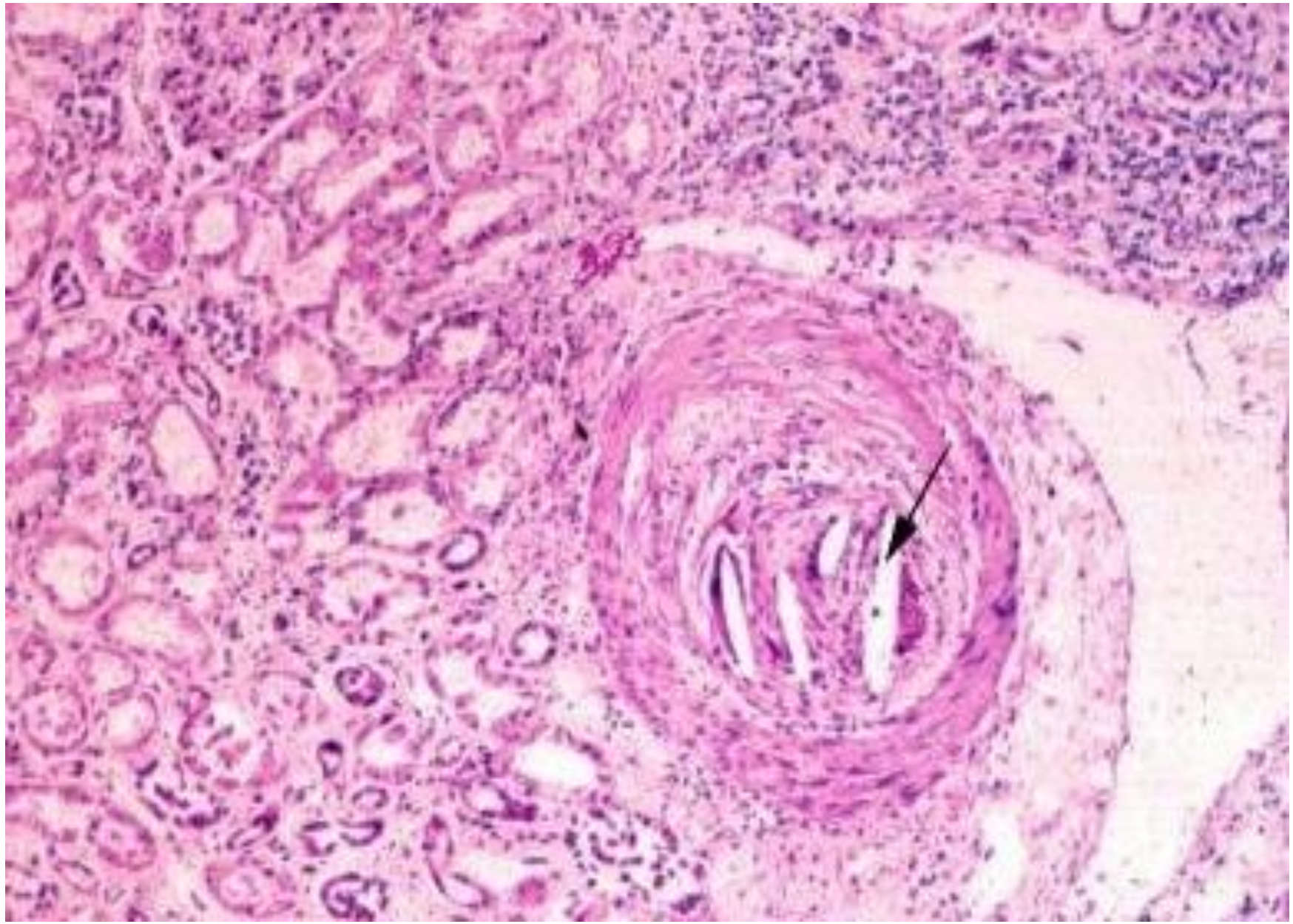
- Use of concurrent medications such as NSAIDs,ACEIs, and ARBs as well as metformin for underlying comorbidities in the elderly should be carefully evaluated and appropriately discontinued before an intravenous injection of a contrast agent.

- never possible, diuretic also be discontinued several days prior to contrast agent injection in the elderly to prevent an added prerenal process.

AKI in elderly people

Atheroembolic AKI is of greater risk in elderly patients who have generalized atherosclerosis, particularly with intra arterial cannulation and the use of anticoagulation.

In one study, approximately 7.1% of renal biopsy specimens obtained for acute kidney failure in patients older than 60 years were found to have atheroemboli.



AKI in elderly people

Aging patients with clinical complications from atherosclerosis sometimes shower cholesterol crystals into the circulation either:

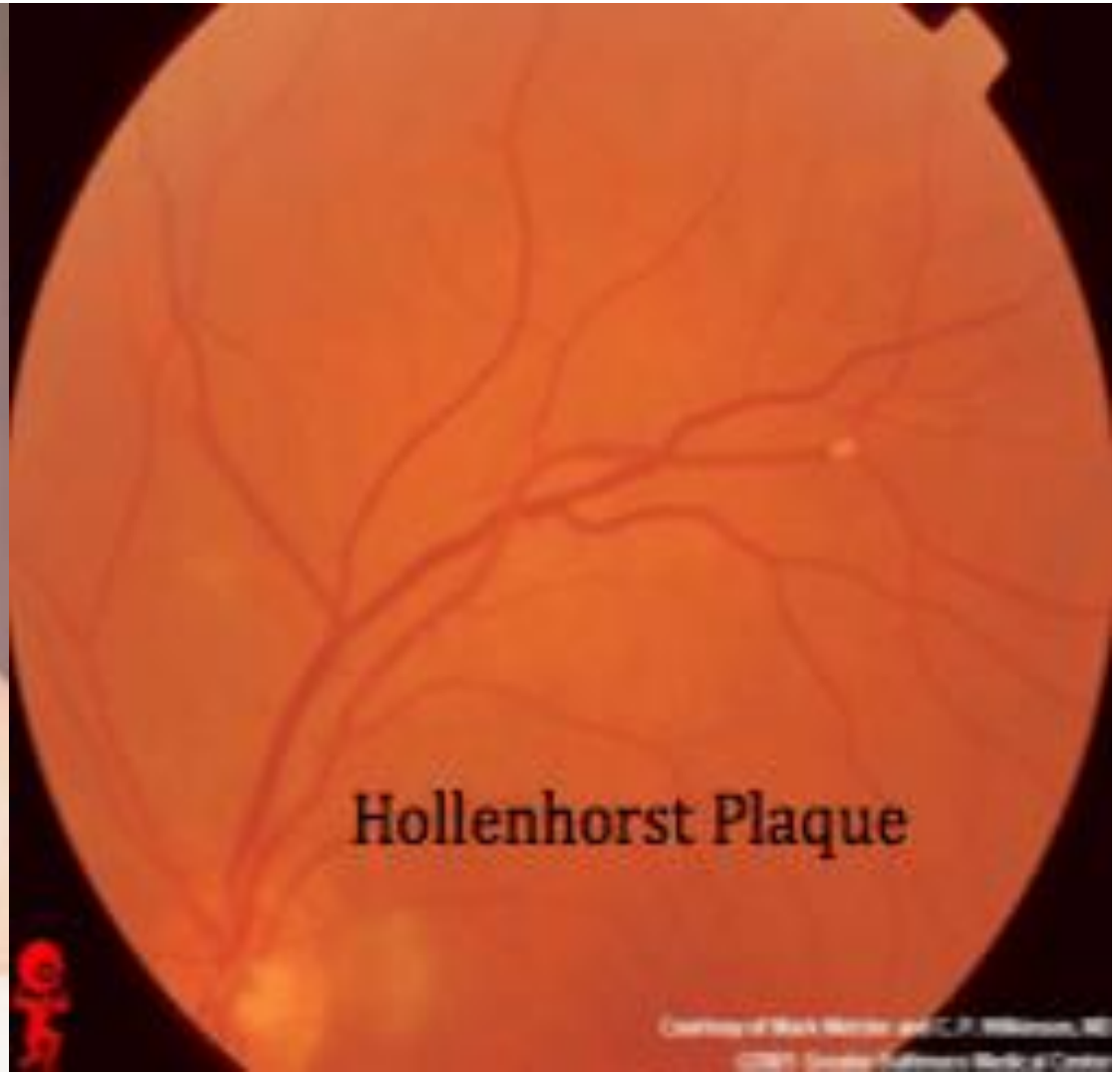
1. **spontaneously**
2. more commonly, following an **endovascular procedure** with manipulation of the aorta or with use of systemic anticoagulation.

Spontaneous emboli may shower acutely or shower sub acutely and somewhat more silently.

AKI in elderly people

Depending on the location of the atherosclerotic plaques releasing these cholesterol fragments, one may see:

- cerebral transient ischemic attacks
- livedo reticularis in the lower extremities
- Hollenhorst plaques in the retina with visual field cuts
- necrosis of the toes
- acute glomerular capillary injury


Hollenhorst Plaque

GLOMERULAR DISEASE

- Renal biopsy findings in the elderly suggest that acute and chronic glomerular disease is common in this patient population. As in younger patients, AKI and/or nephrotic syndrome often is the reason for renal biopsy in the elderly.

GN in elderly people

- Primary glomerular diseases appear to be more prevalent in the elderly than secondary diseases, although diabetic glomerulopathy may be under represented because biopsies often are not performed in cases of presumed diabetic renal disease.

- Relative frequencies of various glomerular diseases are different in older and younger patients.

Table 1. Diseases commonly affected the aging kidney

Diseases commonly affected the aging kidney	
Systemic diseases	Diabetes mellitus
	Dyslipidemia
	Atherosclerosis
	Myeloma cast nephropathy
	Amyloidosis
	Light-chain deposition disease
	Vasculitides
Glomerular diseases	Membranous nephropathy
	Mesangial proliferative GN
	ANCA-associated GN
	Minimal change disease
	Focal segmental glomerulosclerosis
Interstitial nephritis	-
Other causes of kidney diseases	Inflammatory renal diseases
	Drug-induced nephropathy
Urinary tract infection	-
Obstructive uropathy	Neurogenic bladder
	Renal stones
	Obstructive pyelonephritis/papillary necrosis
	Cancers of prostate and bladder
	Retroperitoneal tumors

ANCA, ani-neutrophil cytoplasmic antibody; GN, glomerulonephritis

GN in elderly people

- Membranous nephropathy is the most common histologic finding in numerous case series, with 36% of 317 renal biopsy specimens from patients older than 60 years showing nephrotic syndrome.

- Anti-PLA2R antibodies may be detected by ELISA in 75% of patients with idiopathic membranous nephropathy with higher levels associated with both greater chance of partial or complete remission as well as greater risk for decreased renal function on follow-up.

GN in elderly people

- Nephrotic syndrome can coexist with or precede malignancy in up to 30% of elderly diagnosed with malignancy.
- An immune response to tumor antigens is considered the possible pathologic cause.
- Solid tumors of the **lung,breast, colon** or **rectum, kidney**, and **stomach** have been commonly reported in association with membranous lesions in renal biopsy specimens, with resolution of the nephrosis after tumor treatment .

GN in elderly people

- Minimal change disease (11%) and amyloidosis (10.7%)also were noted and were more frequent than other diagnoses in this large series.

- In addition, minimal change disease can manifest as AKI in the elderly with significant Proteinuria and hypertension.

- Minimal change lesions in renal biopsy specimens have also been noted in conjunction with Hodgkin's and non-Hodgkin's lymphoma in the elderly.

GN in elderly people

- Although treatment with steroids and cytotoxic agents may lead to partial or complete remission, individual risk/benefit assessment is important given the high risk of infection in the elderly.
- Case series of minimal change lesions in the elderly suggest that such lesions may respond to steroid use alone; however,the response to both steroids and cytotoxic agents is less than for younger patients.
- Older patients with minimal change disease seem to experience relapse less frequently and have more stable remissions after cyclophosphamide Treatment.

GN in elderly people

➢ In the very elderly (≥80 years),focal sclerosis from hypertension and hypertensive nephrosclerosis seemed to be more prevalent, followed by immunoglobulin A and membranous nephropathy.

GN in elderly people

- Several small case series suggest that pauciimmune glomerulonephritis(GN) is more common in older adults more than 60 years of age.

- Greater age is associated with increased risk of death from therapy as well as from all causes in older patients with pauci-immune GN.

GN in elderly people

- Although the incidence of postinfectious or poststreptococcal diffuse proliferative GN has decreased in most developed nations, the disease is becoming more evident in the elderly in underdeveloped regions and in those elderly living in poor socioeconomic or debilitating conditions.

- Therefore a careful history should be taken to identify possible exposure, and a history and/or physical examination findings suggesting the possibility of infection should prompt early diagnosis and supportive treatment in the elderly.

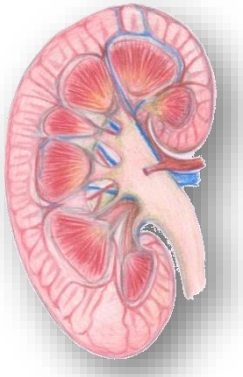
GN in elderly people

- Paraproteinemia, particularly multiple myeloma, can also manifest as AKI in the elderly with or without overt hypercalcemia.

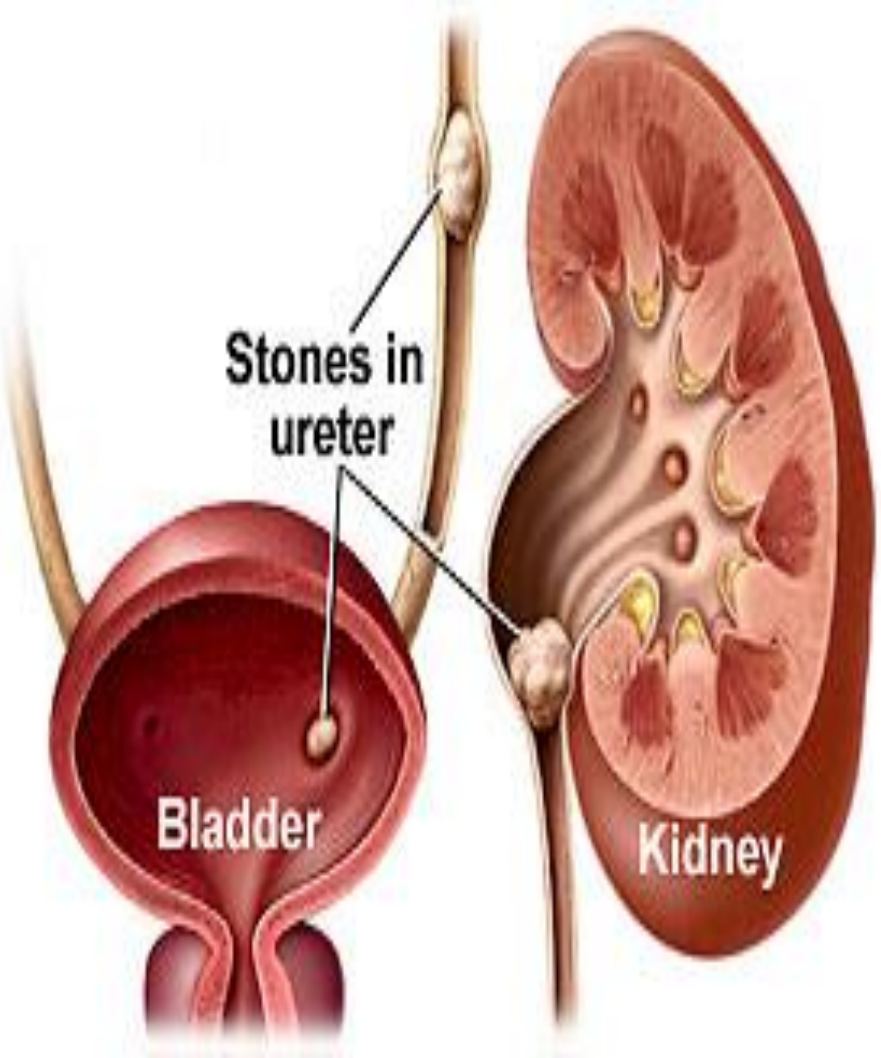
Thus quantification of urine protein, serum free monoclonal light chain analysis immunoelectrophoresis , and immunofixation can be important early on, particularly if the cause of AKI remains unclear.

GN in elderly people

- Evaluation for primary and secondary amyloidosis should be included in the elderly patient presenting with nephrotic syndrome; Congo red staining of renal or other tissue signifies the presence of amyloid fibrils, confirming the diagnosis.



Post-renal AKI



urinary tract obstruction

Subtle increases in blood urea nitrogen and creatinine with or without complaints of dysuria, hesitancy, or dribbling should prompt an evaluation for underlying urinary tract obstruction.

Postrenal AKI

1. Bilateral ureteral obstruction or unilateral obstruction in a solitary kidney (upper urinary tract obstruction)

a. Intraureteral

- a Stones
- a Blood clots
- a Pyogenic debris or sloughed papillae
- a Edema following retrograde pyelography
- a Transitional cell carcinoma

b. Extraureteral

- a Pelvic or abdominal malignancy
- a Retroperitoneal fibrosis
- a Accidental ureteral ligation or trauma during pelvic surgery

c. Bladder neck/urethral obstruction (lower urinary tract obstruction) a Prostatic hypertrophy

- a Prostatic and bladder carcinoma
- a Autonomic neuropathy or anticholinergic agents causing urinary retention a Urethral stricture
- a Bladder stones
- a Fungal infection (e.g., fungus balls)
- a Blood clots

urinary tract obstruction

Careful investigation for:

urogenital tumors, pelvic prolapse, and papillary sloughing, as well as medication review for anticholinergic drugs, sedatives and hypnotics narcotic and opioid analgesics, antipsychotics, and histamine1 receptor antagonists, should be considered , with prompt urologic intervention as necessary.

AKI in elderly people

- AKI also increases the risk of ESRD in the elderly.

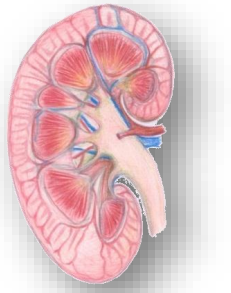
In acohort of nearly 234,000 Medicare beneficiaries 67 years and older discharged from the hospital,

The incidence of AKI was 3.1%, and ESRD developed in 5.3 per 1000.

AKI in elderly people

➢Therefore **early recognition of a greater susceptibility** of elderly patients to AKI is crucial,with the aim of preventing the disease by **avoiding nephrotoxic medications** and **interventions** that increase the risk.

➢Early nephrology referral and management are prudent if these exposures cannot be avoided.



Acute Renal Failure
Management

- Early recognition
- Treatment of the cause
- Prevention of acute renal failure
- Conservative measures
- Fluid balance
- Electrolytes and acid-base balance
- Nutritional support
- Drugs
- Treatment of hyperkalemia
- Dialysis

AKI in elderly people

Response to dialysis therapy for AKI in the elderly is frequently good, providing relief of uremic symptoms and complications such as :
volume overload, bleeding , disorientation, catabolic state, and **electrolyte disturbances.**

Therefore, as in any patient, it is important to consider the overall assessment of the elderly patient in the decision about renal replacement therapy (RRT), including:
Illness severity, comorbidities, and **projected cognitive and/or physical recovery** in addition to **patient and family wishes.**

Thank you