Diuretics, Kidney Diseases Urine R&M

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Clinical Significance of Proteinuria

- Early detection of renal disease in at-risk patients
  - hypertension: hypertensive renal disease
  - diabetes: diabetic nephropathy
  - pregnancy: gestational proteinuric hypertension (pre-eclampsia)
  - annual "check-up": renal disease can be silent
- Assessment and monitoring of known renal disease

Measurement of Urinary Protein Excretion

Standard urinary dipstick

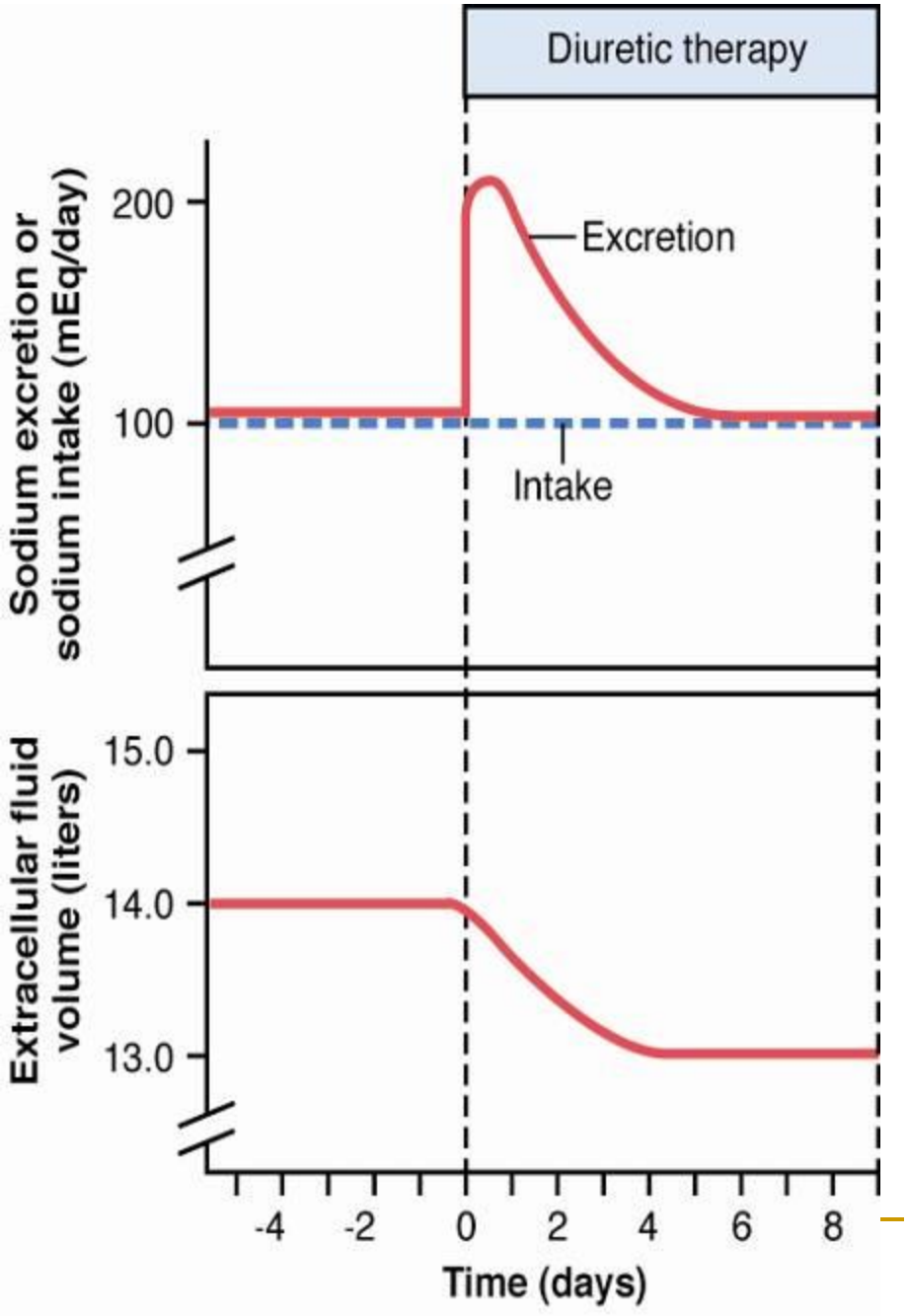
- Negative
- Trace — between 15 and 30 mg/dL
- 1+ — between 30 and 100 mg/dL
- 2+ — between 100 and 300 mg/dL
- 3+ — between 300 and 1000 mg/dL
- 4+ — >1000 mg/dL

Dipstick protein tests may not be very accurate: "trace" results can be normal & positives must be confirmed by quantitative laboratory test.

Microalbuminuria

- Definition: urine excretion of > 30 but < 150 mg albumin per day
- Causes: early diabetes, hypertension, glomerular hyperfiltration
- Prognostic Value: diabetic patients with microalbuminuria are 10-20 fold more likely to develop persistent proteinuria

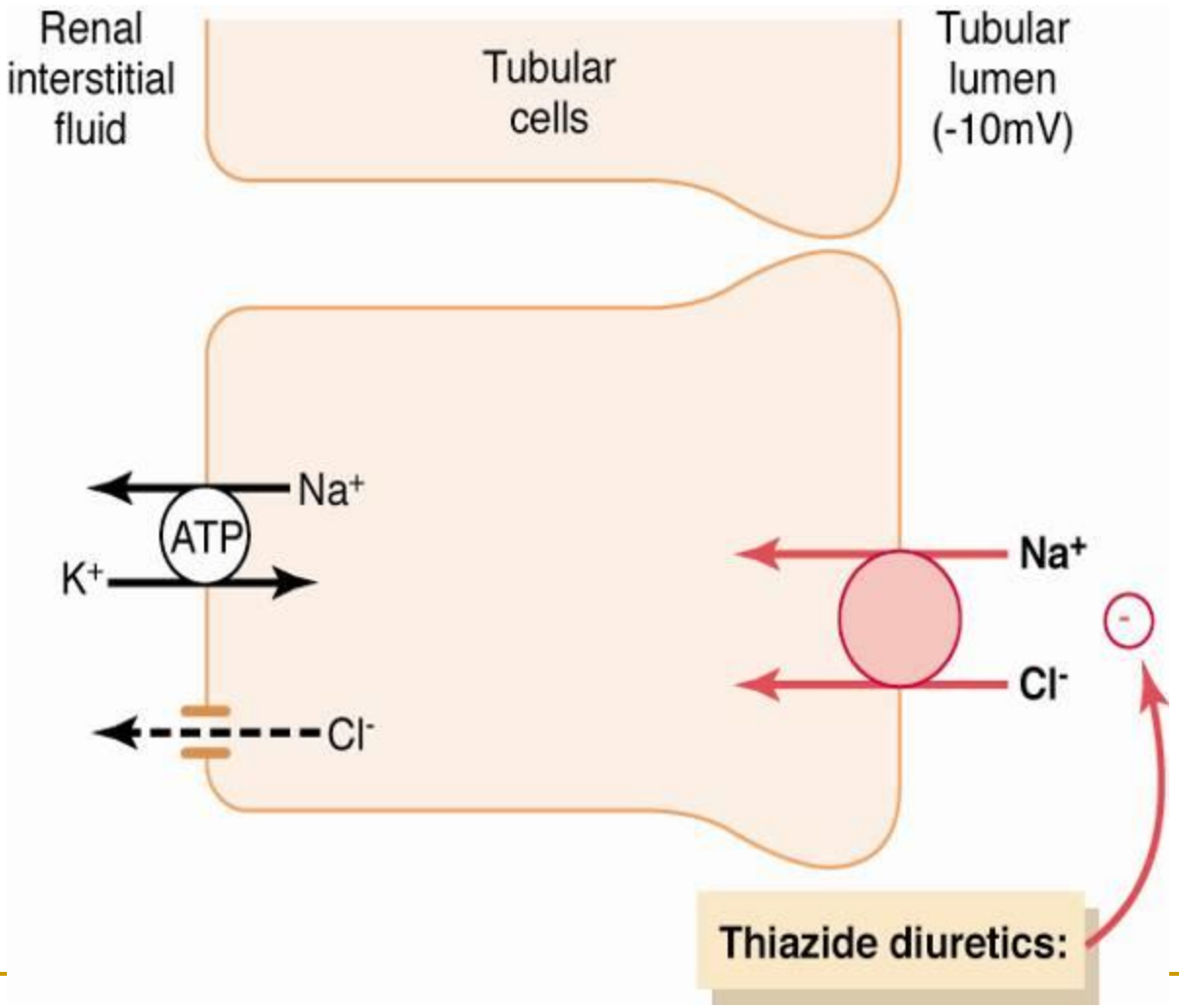
Sodium excretion and extracellular fluid volume during diuretic administration



Thiazide Diuretics

Used to treat:

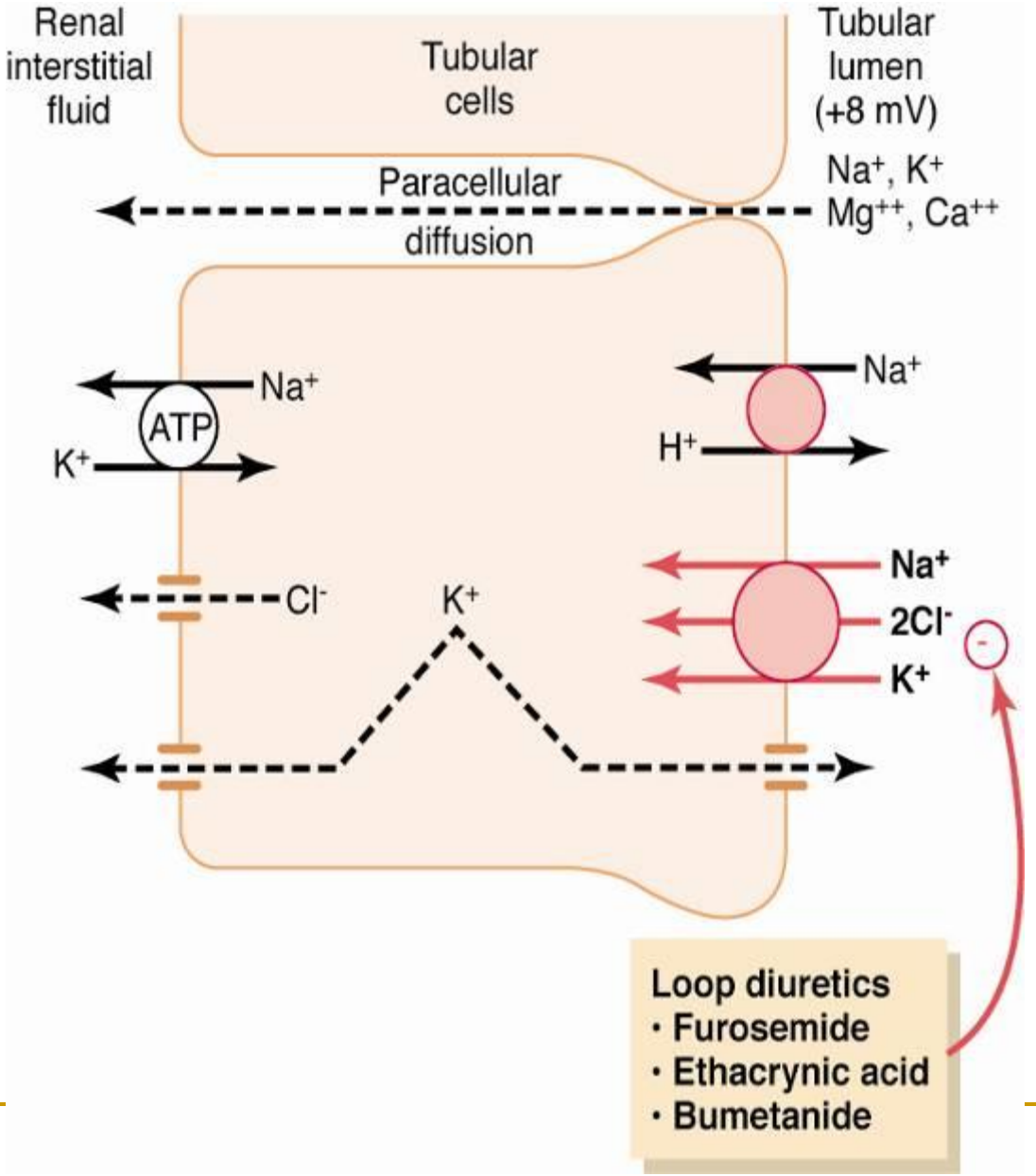
- hypertension
- edema
- renal stones (nephrolithiasis)



Loop Diuretics

Used to treat:

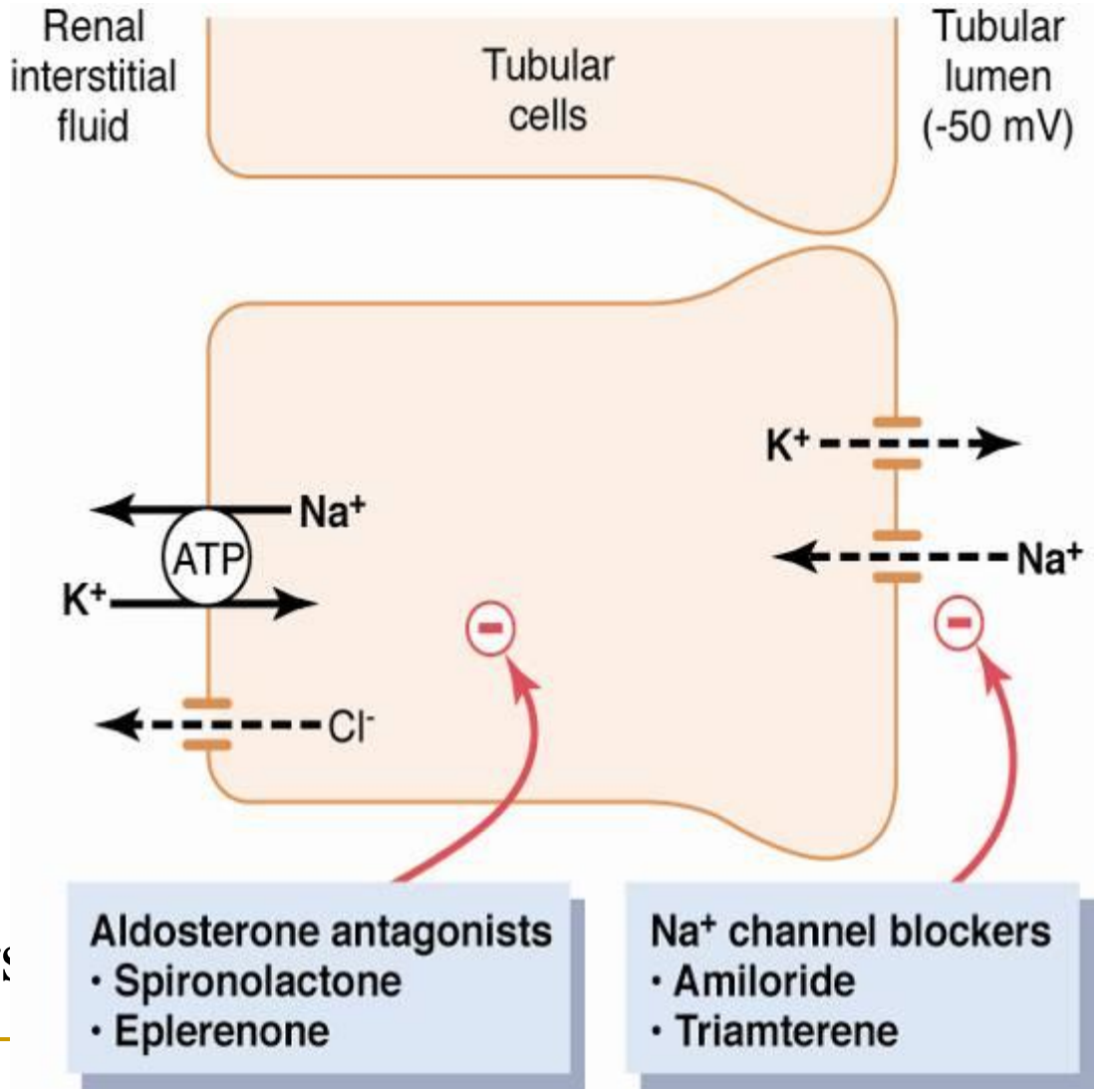
- pulmonary edema
- cirrhosis
- acute renal failure



K^+ sparing diuretics – Mineralocorticoid Receptor Antagonists and Na^+ channel inhibitors

Used to treat:

- primary aldosteronism
- secondary aldosteronism
- "resistant" hypertension
- heart failure
- hypertension (Na^+ channel blockers



Renal Failure

- Acute renal failure: kidney function abruptly decreases (GFR declines) over days to weeks, but may recover

- Chronic renal failure: kidney function (GFR) declines progressively over months to years, and is usually irreversible, but can be slowed or perhaps arrested with effective treatment

Epidemiology og AKI (acute kidney injury):

- 0.1% population
- 3-7% hospitalized
- 25-30% ICU patient

Classification:

- Acute kidney injury is diagnosed on the basis of clinical history and laboratory data.
- A diagnosis is made when there is rapid reduction in kidney function, as measured by serum creatinine, or based on a rapid reduction in urine output, termed oligurea.

- **Staging**
- The *RIFLE criteria* (Risk, Injury, Failure, Loss, End-stag), proposed by the acute dialysis quality initiative (ADQI) group, aid in the staging of patients with AKI.

- Risk: GFR decrease >25%, serum creatinine increased 1.5 times or urine production of < 0.5 ml/kg/h for 6 hours.

- Injury: GFR decrease > 50%, doubling of creatinine or urine production < 0.5 ml/kg/h for 12 hours.

- Failure: GFR decrease > 75%, tripling of creatinine (> 4 mg/dl) OR urine output below 0.3 ml/kg/h for 24 hours or anuria for 12 hours.
- Loss: persistent AKI or complete loss of kidney function for more than 4 weeks
- End stage renal disease: need for renal replacement therapy (RRT) for more than 3 months

Acute Renal Failure (ARF)

- Prerenal ARF- caused by decreased blood flow to kidneys (~ 50-55% of cases are prerenal causes). Pre-renal can be converted to intra-renal damage
  - volume depletion (hemorrhage, dehydration)
  - heart failure
  - hypotensive shock, anesthesia
  - renal artery stenosis
  - thrombosis, atheroma emboli
  - transplanted kidney (stenosis, rejection)

Acute Renal Failure (ARF)

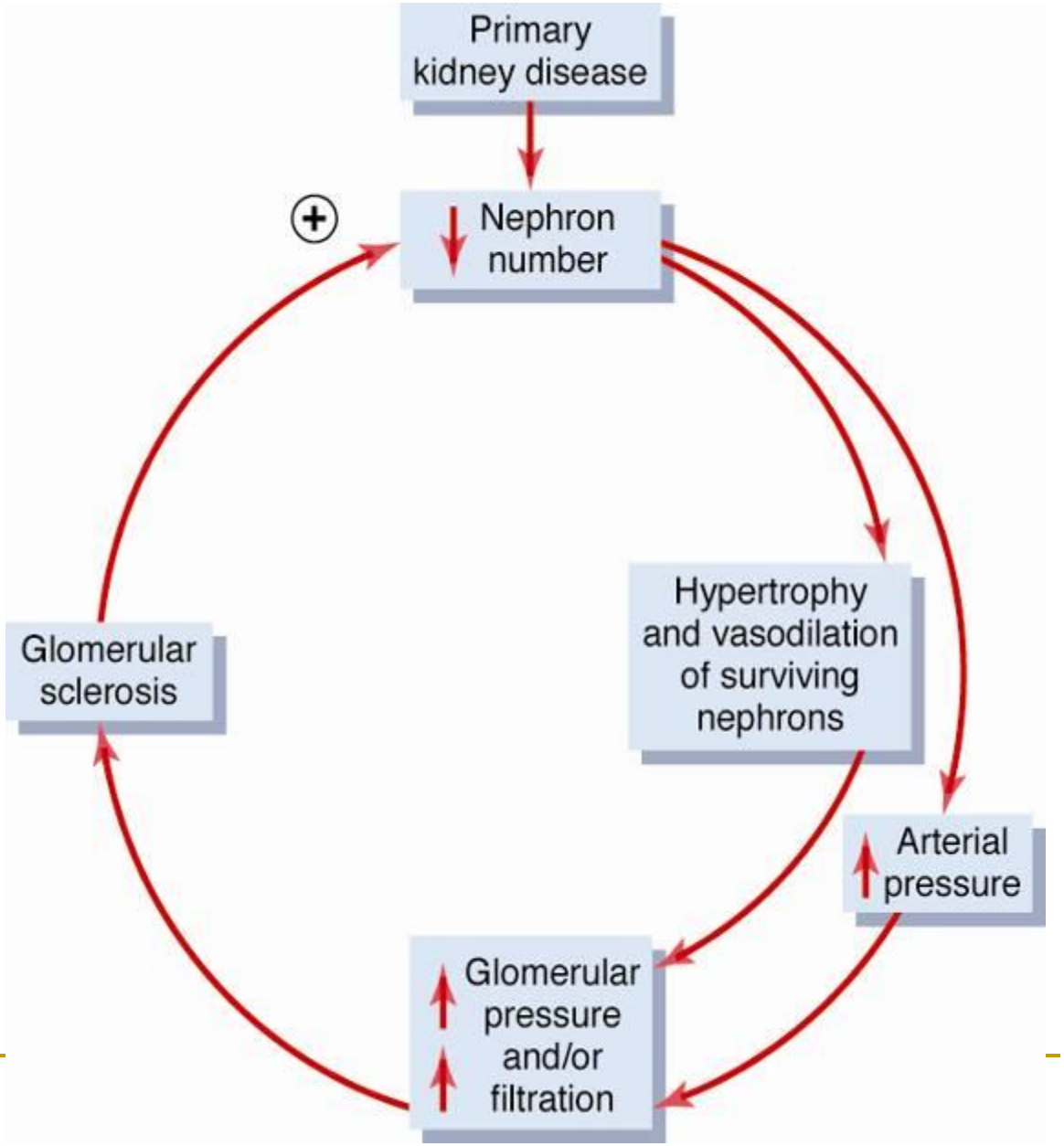
- Intrarenal ARF- caused by abnormalities within the kidneys (~ 35-40% of ARF)
  - small vessel or glomerular injury (vasculitis, acute glomerulonephritis, etc)
  - renal tubular injury (tubular necrosis – ischemia, toxins, heavy metals, CCl_4, etc.)
  - renal interstitial injury (acute pyelonephritis, interstitial nephritis)
  - renal ischemia due to pre-renal ARF

Acute Renal Failure (ARF)

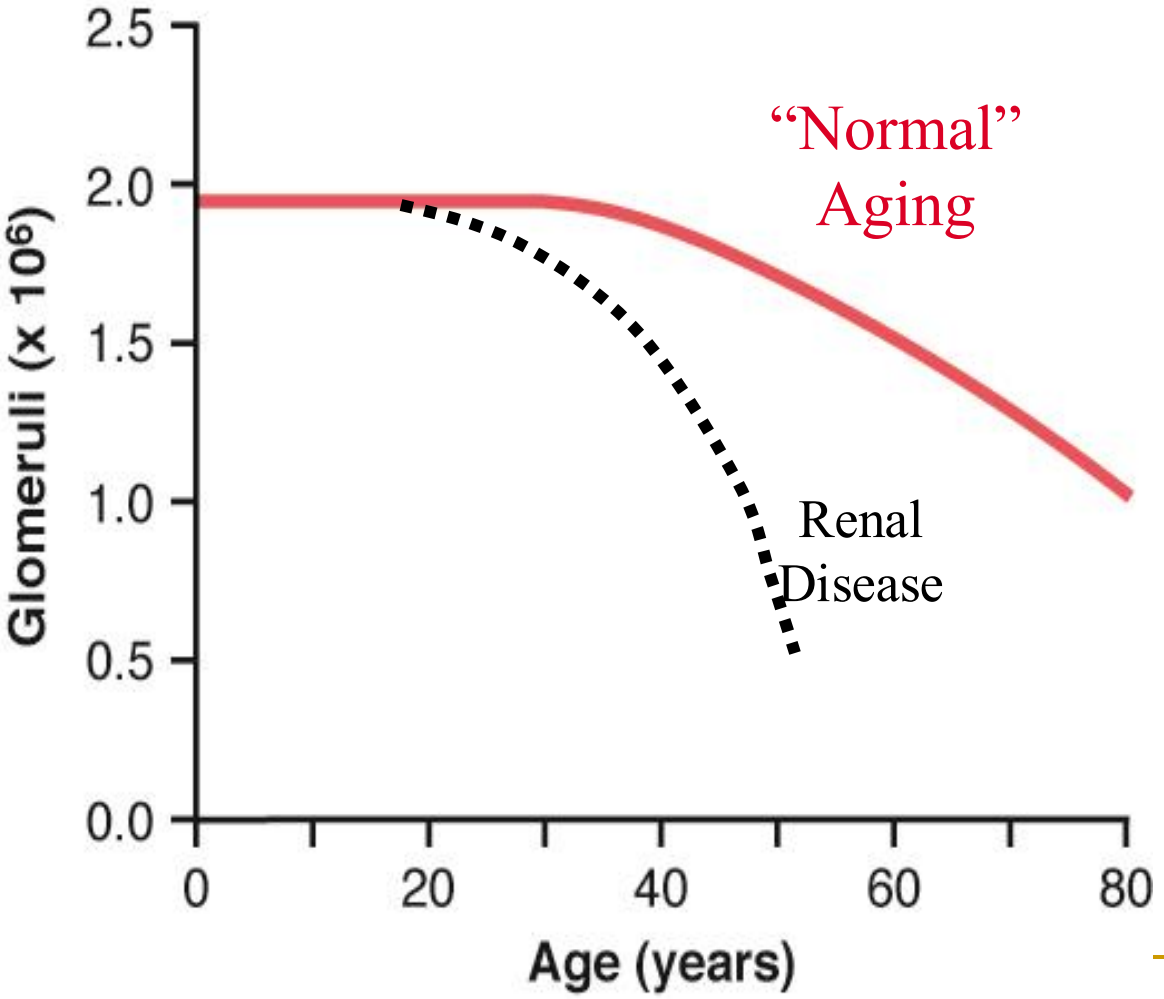
- Postrenal ARF- caused by abnormalities in the lower urinary tract (~ 5% of ARF)

  - kidney stones
  - prostatic hypertrophy
  - bladder cancer

Chronic renal disease: a slowly developing vicious cycle ?



Aging, Renal Disease and Nephron Loss



Total Renal Excretion and Excretion Per Nephron in Chronic Renal Failure

	Normal	75 % loss of nephrons
Number of nephrons	2,000,000	500,000
Total GFR (ml/min	125	40
GFR per nephron (nl/min)	62.5	80
Urine flow rate (ml/min)	1.5	1.5
Volume excreted per nephron (nl/min)	0.75	3.0

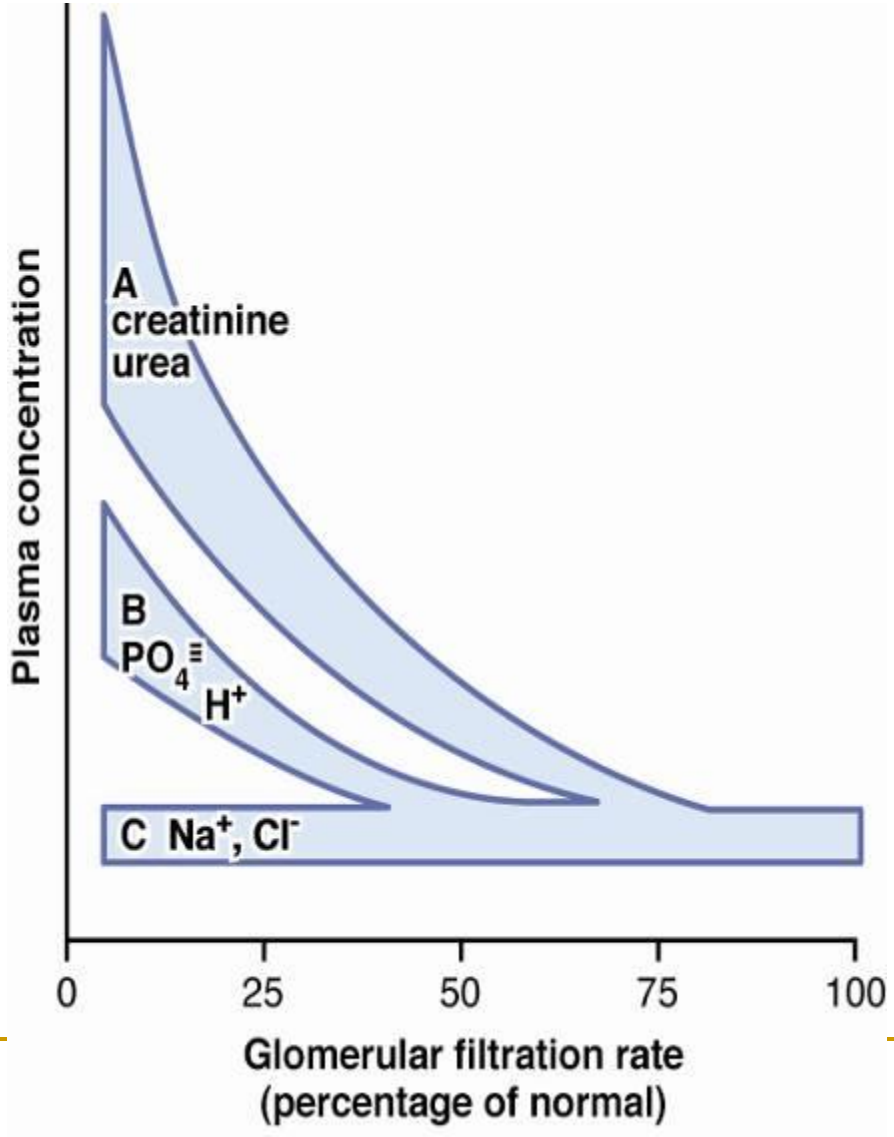
Increase glomerular pressure

Question

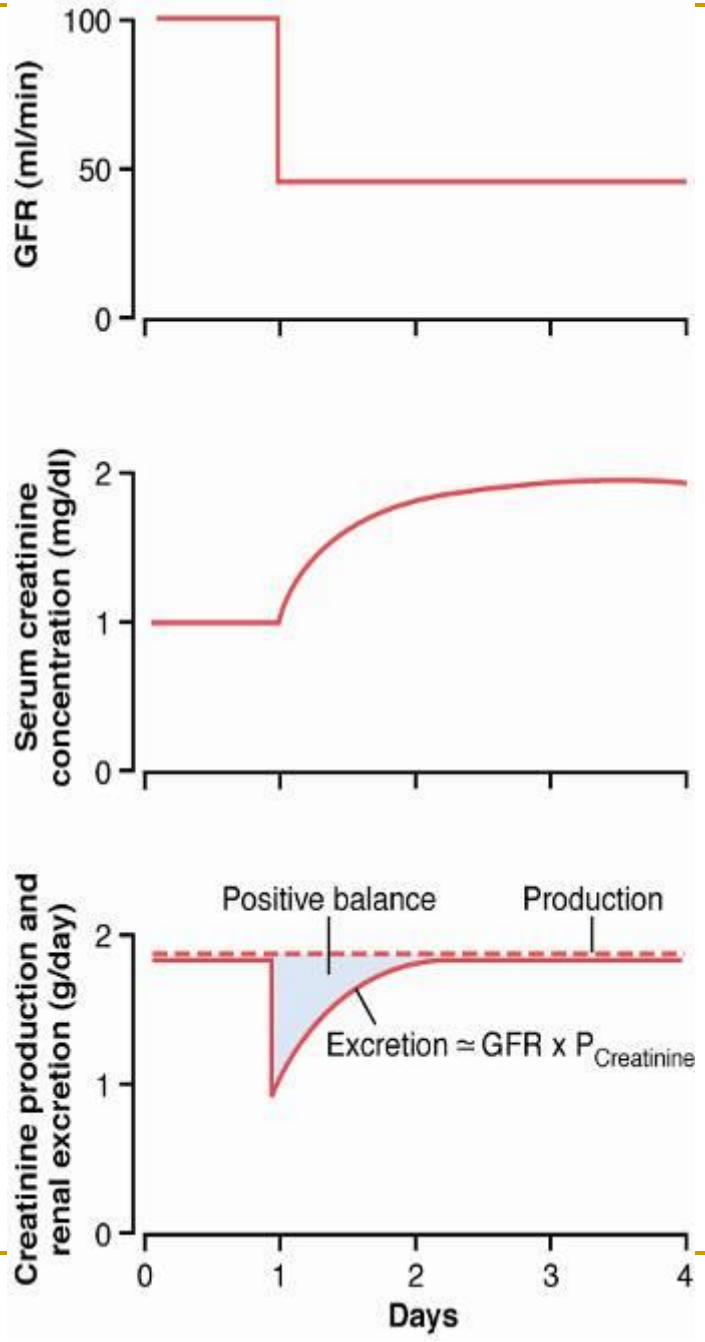
A 26-year-old man develops glomerulonephritis and his GFR decreases by 50% and remains at that level. For which of the following substances do you expect to find the greatest increase in plasma concentration?

1. Creatinine
2. K^+
3. Glucose
4. Na^+
5. Phosphate
6. H^+

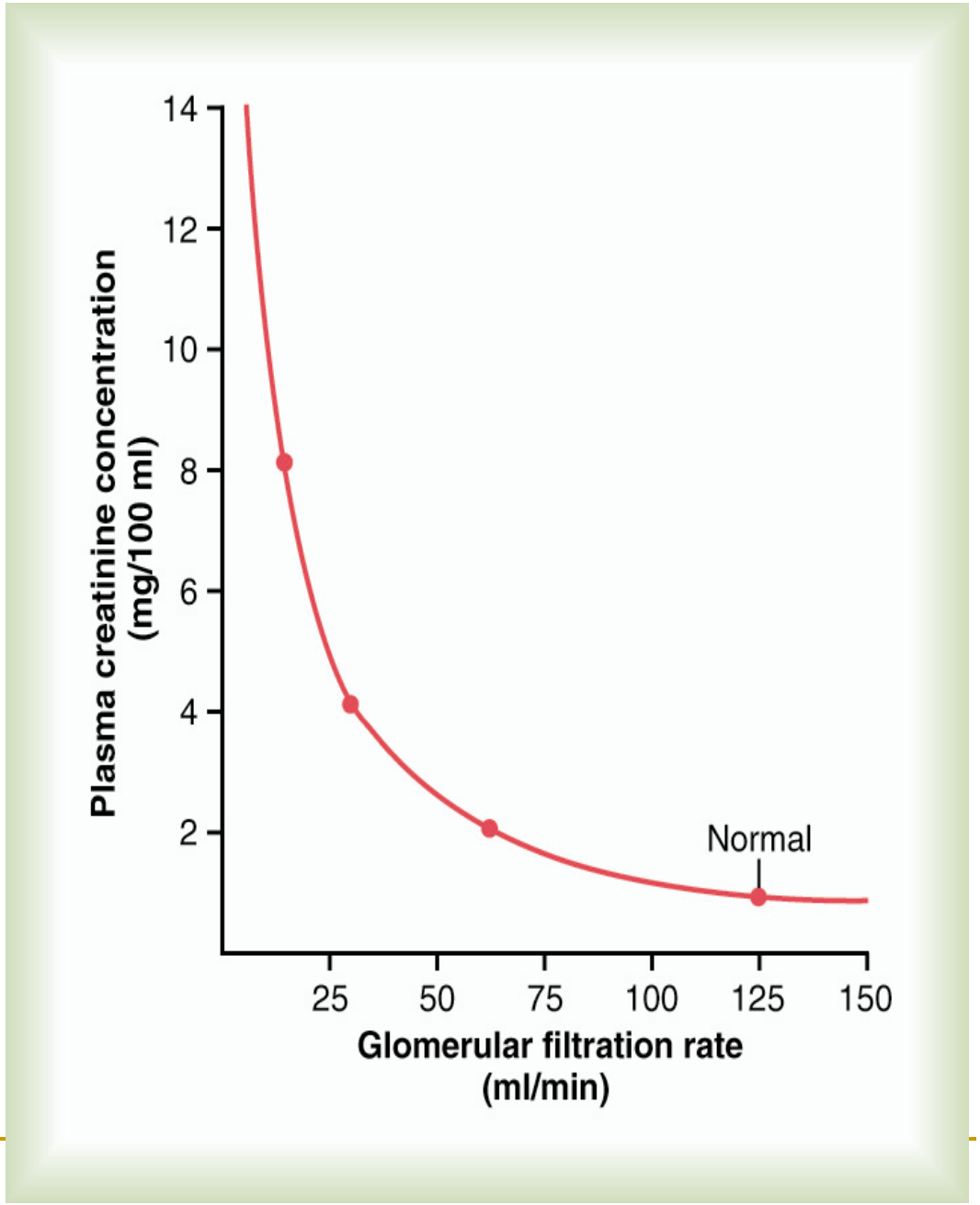
Chronic Renal Failure and Plasma Concentrations of Solutes



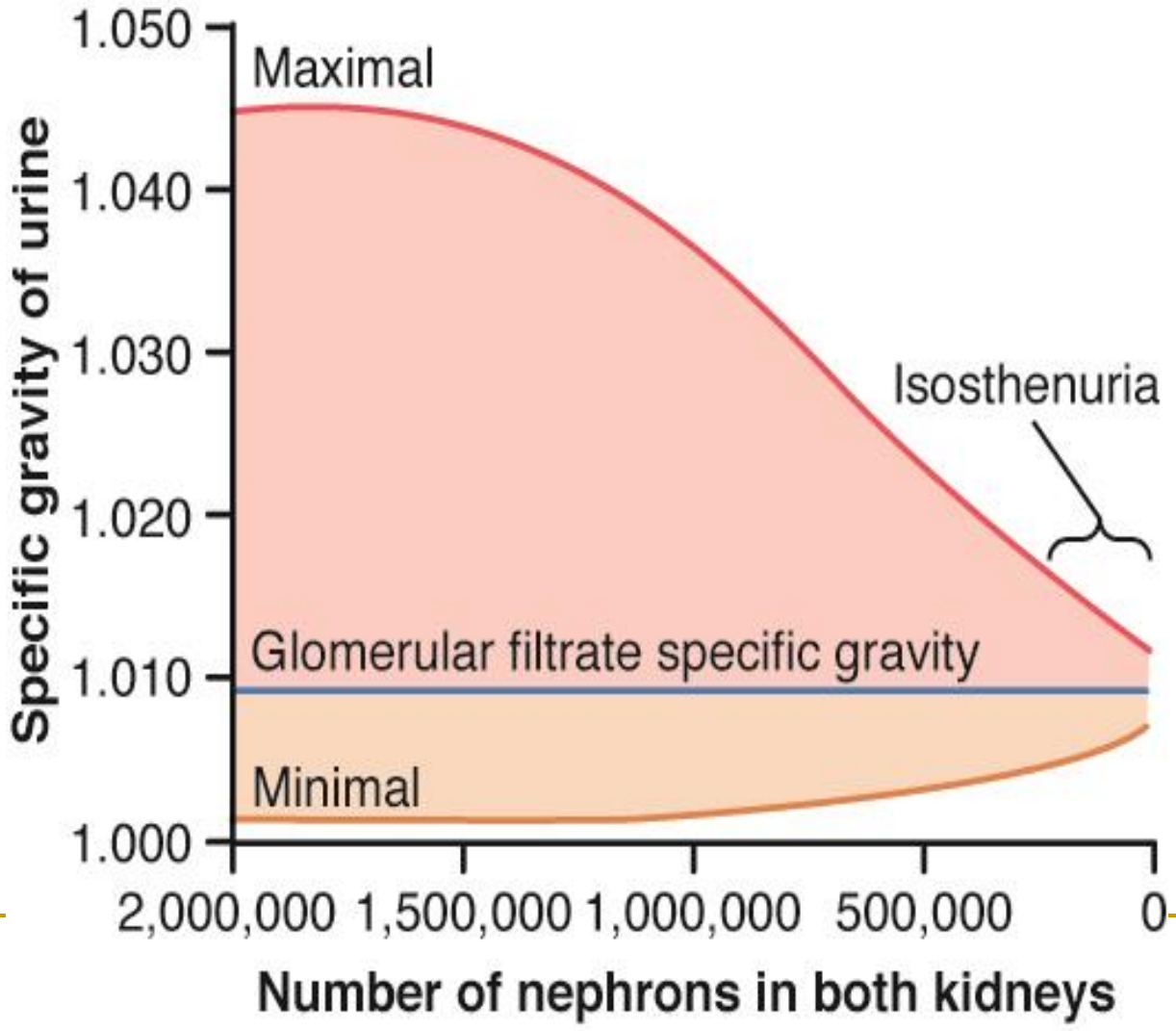
Effect of reducing GFR by 50 % on serum creatinine concentration and on creatinine excretion rate



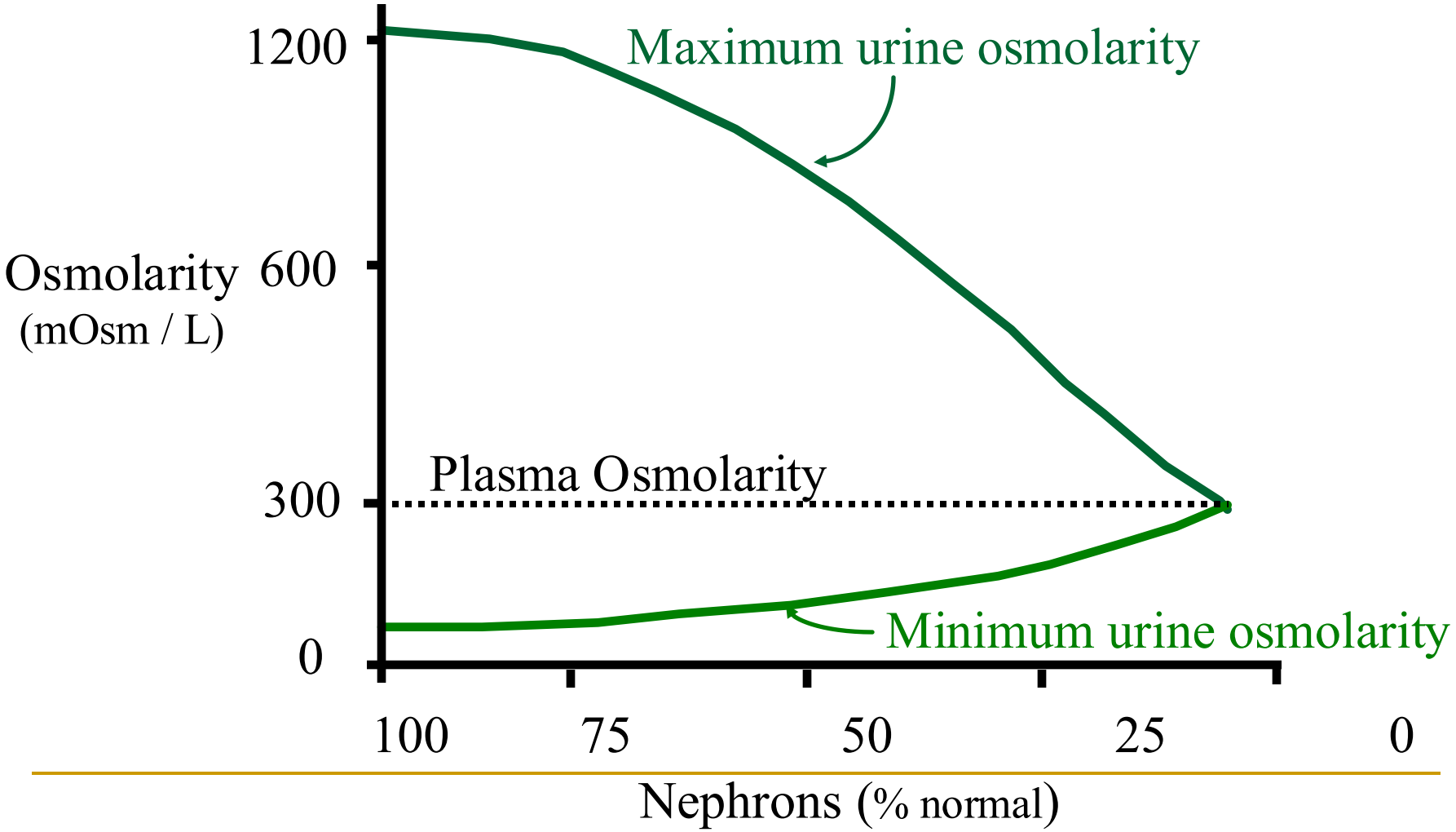
Plasma creatinine Can be used to estimate changes in GFR



Development of isothenuria with loss of functional nephrons



Development of Isosthenuria With Nephron Loss in Chronic Renal Failure (inability to concentrate or dilute the urine))



Renal failure:

Is of 2 types:

- **Acute: from days to weeks.**
- **chronic: months → years.**

Most common causes of chronic renal failure are:

1. hypertension 2. diabetics 3. infectious

Acute kidney injury (AKI), previously called acute renal failure (ARF), is an abrupt loss of kidney function that develops within 48 hours

CAUSES:

1. Prerenal 2. intrarenal 3. postrenal

- **Prerenal: intact tubules, as in vomiting diarrhea, bleeding, renal artery, stenosis, hypotension, glomerulus abnormality.**
- **Intrarenal: as in:**

Drugs: antibiotics, Mercury: Other Nephrotoxic agents.

- **Postrenal: obstruction.**
- **90% of causes are of the first two types (pre-and-intrarenal).**
- **the use of urea / creatinine ratio can be helpful to differentiate these three types:**

BUN:Cr

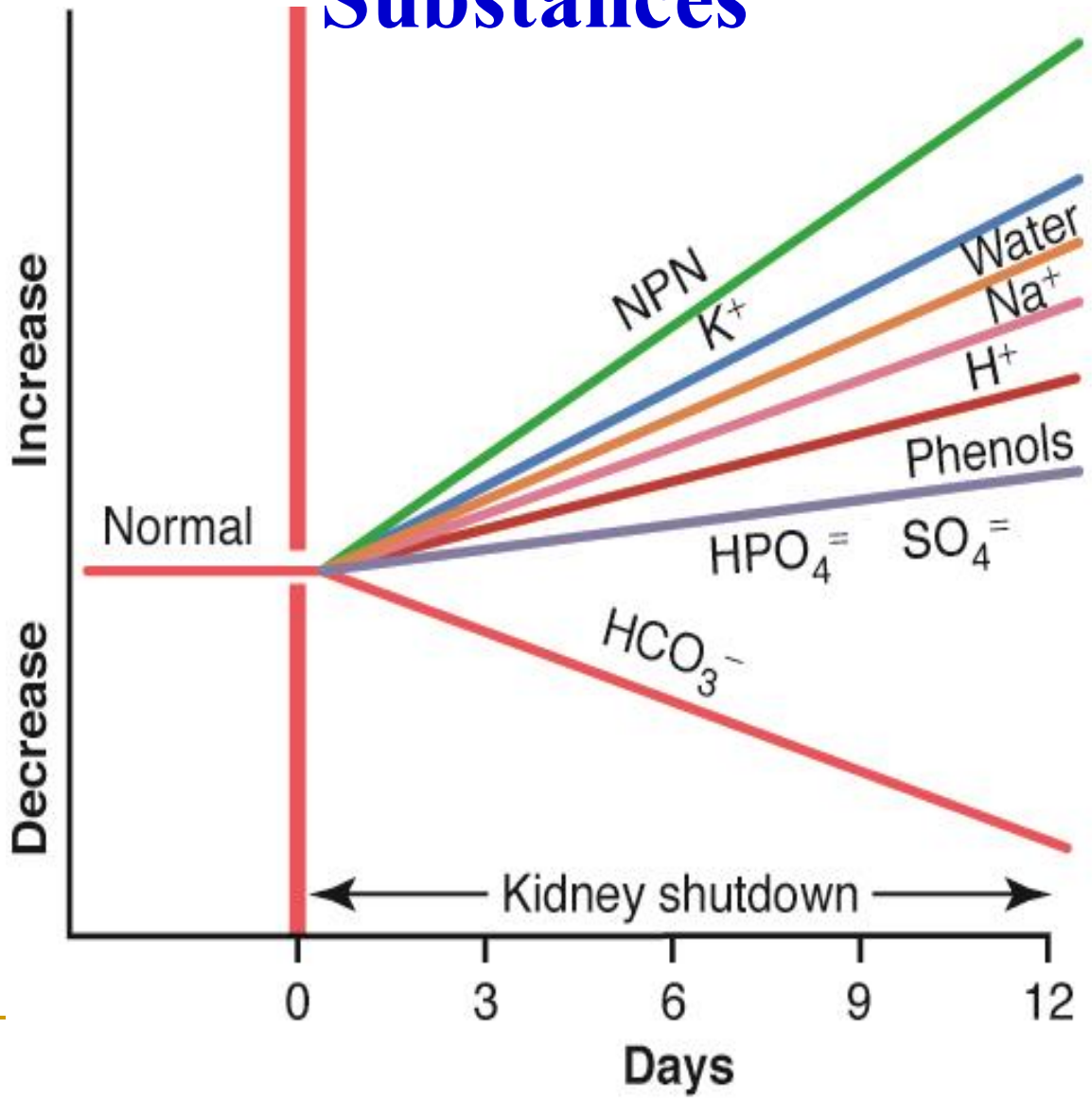
BUN:Cr	Urea:Cr	Location	Mechanism
>20:1	>100:1	Prerenal (before the kidney)	BUN reabsorption is increased. BUN is disproportionately elevated relative to creatinine in serum. Dehydration is suspected.
10-20:1	40-100:1	Normal or Postrenal (after the kidney)	Normal range. Can also be postrenal disease. BUN reabsorption is within normal limits.
<10:1	<40:1	Intrarenal (within kidney)	Renal damage causes reduced reabsorption of BUN, therefore lowering the BUN:Cr ratio.

Fractional sodium excretion

$$FE_{Na} = 100 \times \frac{\text{sodium}_{\text{urinary}} \times \text{creatinine}_{\text{plasma}}}{\text{sodium}_{\text{plasma}} \times \text{creatinine}_{\text{urinary}}}$$

Value	Category	Description
below 1%	prerenal disease	the physiologic response to a decrease in renal perfusion is an increase in sodium reabsorption to control hyponatremia, often caused by volume depletion or decrease in effective circulating volume (e.g. low output heart failure).
above 2% to 3%	acute tubular necrosis or other kidney damage	either excess sodium is lost due to tubular damage, or the damaged glomeruli result in hypervolemia resulting in the normal response of sodium wasting.
intermediate	either disorder	In renal tract obstruction, values may be either higher or lower than 1%.[The value is lower in early disease, but with renal damage from the obstruction, the value becomes higher.

Effect of kidney Failure on Extracellular Substances



In ARF:

85% will recover: good prognosis.

15% will go to chronic RF.

Problems with ARF:

1. **daily increase in creatinine and urea.**

   Plasma Urea will increase (In complete renal shutdown it rises by about 5 mmol/L per day).

   Creatinine will increase by 1 mg daily.

2- **Hyperkalemia**

3- **Acidosis: (increase H+)**

4- **Extracellular volume expansion → Malignant hypertension, pulmonary edema (can be fatal)**

***Treatment*:**

- **Treat underlying cause**
- **Restrict Na+, Cl-, H2O intake.**
- **Peritoneal dialysis, hemodialysis for at least (2-3) weeks till recovery.**

***How to know patient is recovering*??**

By the decrease of urea, creatinine back to normal.

Follow-up

Less protein intake→ less urea production
Therefore, we must maintain the patient with chronic RF in low protein diet and instead of going to end-stage RF in 3 years, it will take him 10 years.
So, urea increases load on the kidney, though it is passively transported.

Dialysis

- **Dialysis is primarily used to provide an artificial replacement for lost kidney function. It aims to restore the composition of the body's fluid environment toward normal**
- 1) **Hemodialysis**: relatively a new practiced procedure, in this type the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a semipermeable membrane. The cleansed blood is then returned via the circuit back to the body; **all in all it is a complicated procedure done for(4-6) hours, 3 times per week and needs an A-V shunt**

Dialysis Therapy

Some key aspects of hemodialysis are:

- blood is typically transferred from an arm artery
- after dialysis, blood is typically returned to an arm vein
- to prevent clotting, blood is typically heparinized
- dialysis sessions occur about three times a week
- each dialysis session can last four to eight hours!
- long term dialysis can lead to thrombosis (fixed blood clots), infection and death of tissue around a shunt (the blood access site in the arm).

Dialysis

- 2) **Peritoneal dialysis: In this procedure a sterile solution containing minerals (even potassium at LOW concentrations) and glucose is run through a tube into the peritoneal cavity, the abdominal body cavity around the intestine, where the peritoneal membrane acts as a semipermeable membrane. The dialysate is left there for a period of time to absorb waste products, and then it is drained out through the tube and discarded…*this procedure needs a long time (may reach 24 hours).***

Table 31-7

Comparison of Dialyzing Fluid with Normal and Uremic Plasma			
	Normal Plasma	Dialyzing Fluid	Uremic Plasma
Electrolytes (mEq/l)			
Na^+	142	133	142
K^+	5	1	7
Ca^{++}	3	3	2
Mg^{++}	1.5	1.5	1.5
Cl^-	107	105	107
HCO_3^-	24	36	14
Lactate			
HPO4-			
Urate			
Sulfate			
Nonelectrolytes			
Glucose	100	125	100
Urea	26	0	200

Treatment of kidney failure with dialysis