Disease of the Urinary System

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Functions of the urinary system

1. Excretion – removal of waste material from the blood plasma and the disposal of this waste in the urine.

2. Elimination – removal of waste from other organ systems.

- From digestive system – undigested food, water, salt, ions drugs.
- From respiratory system – CO2, H^+, water, toxins.
- From skin – water, NaCl , nitrogenous wastes (urea , uric acid, ammonia, creatinine).

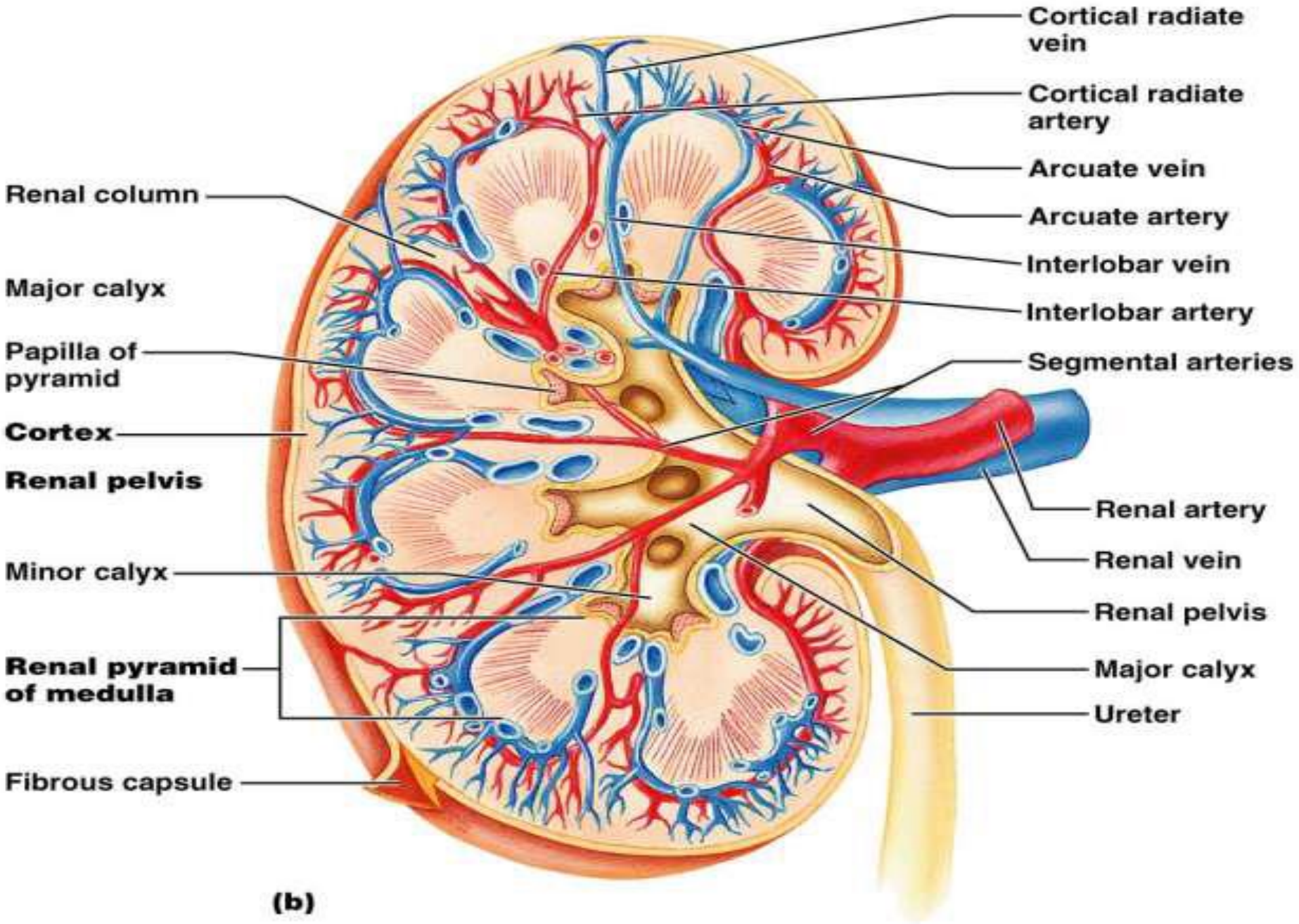
3. Water balance - kidney tubules regulate water reassertion and urine concentration.

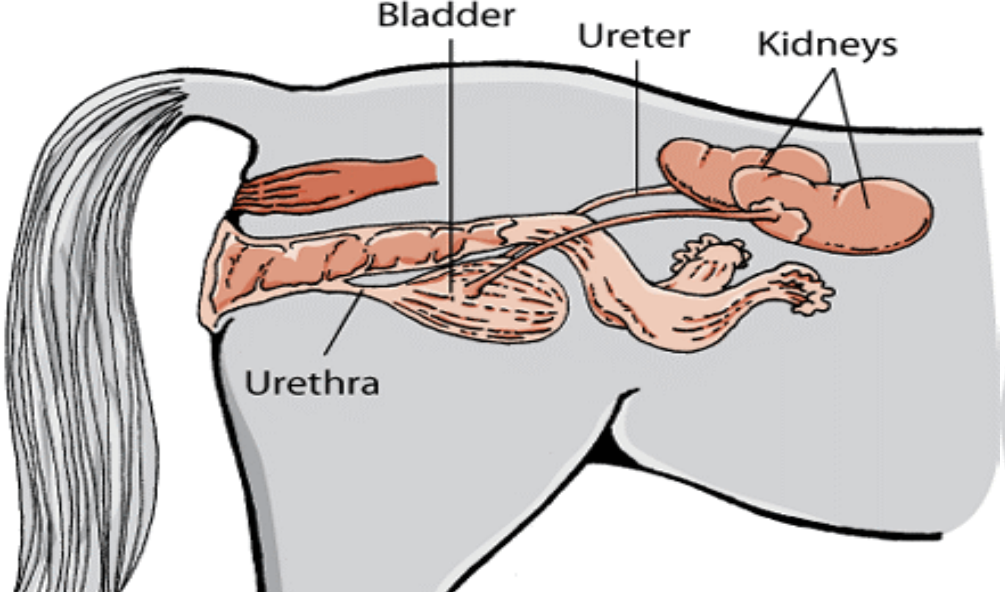
4. Regulation of pH - volume, and composition of body fluids.

5. Production of erythropoietin: for hematopoieses, and **Renin** for blood pressure regulation.

Anatomy of the urinary System

- **Kidneys** – a pair of bean, lobulated, heart – shaped organs located retroperitoneally , responsible for blood filtering and urine formation.
- **Renal capsule** – a layer of fibrous connective tissue covering the kidneys.
- **Renal cortex** – outer region of the kidneys where most enthrones is located.
- **Renal medulla** – inner region of the kidneys where some enthrones is located, also where urine is collected to be excreted outward.
- **Renal calyx** – duct – like sections of renal medulla for collecting urine from nephrons and direct urine into renal pelvis.
- **Renal pyramid** – connective tissues in the renal medulla binding various structures together.
- **Renal pelvis** – central urine collecting area of renal medulla.
- **Hilum** – concave notch of kidneys where renal artery, renal vein, ureter, nerves, and lymphatic vessels converge.
- **Ureter** – a tubule that transport urine (mainly by peristalsis) from the kidney to the urinary bladder.
- **Urinary bladder** – a spherical storage organ that contains urine.
- **Urethra** – a tubule that excretes urine out of the urinary bladder to the outside, through the urethral orifice.

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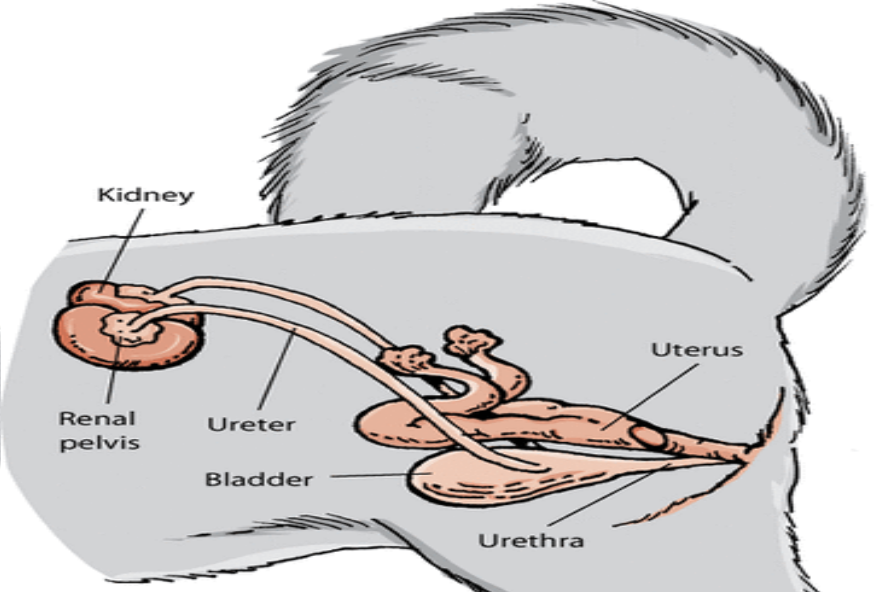
Kidney
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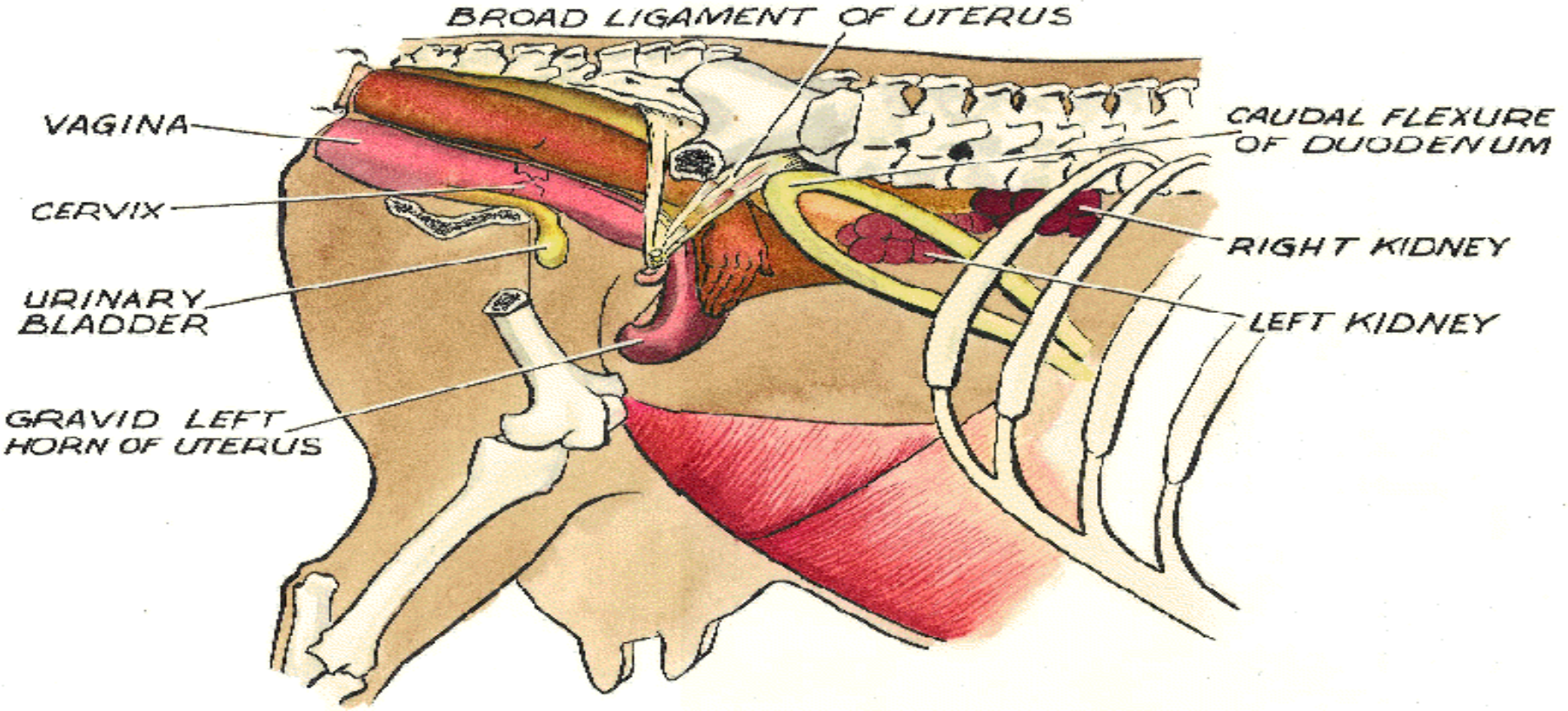
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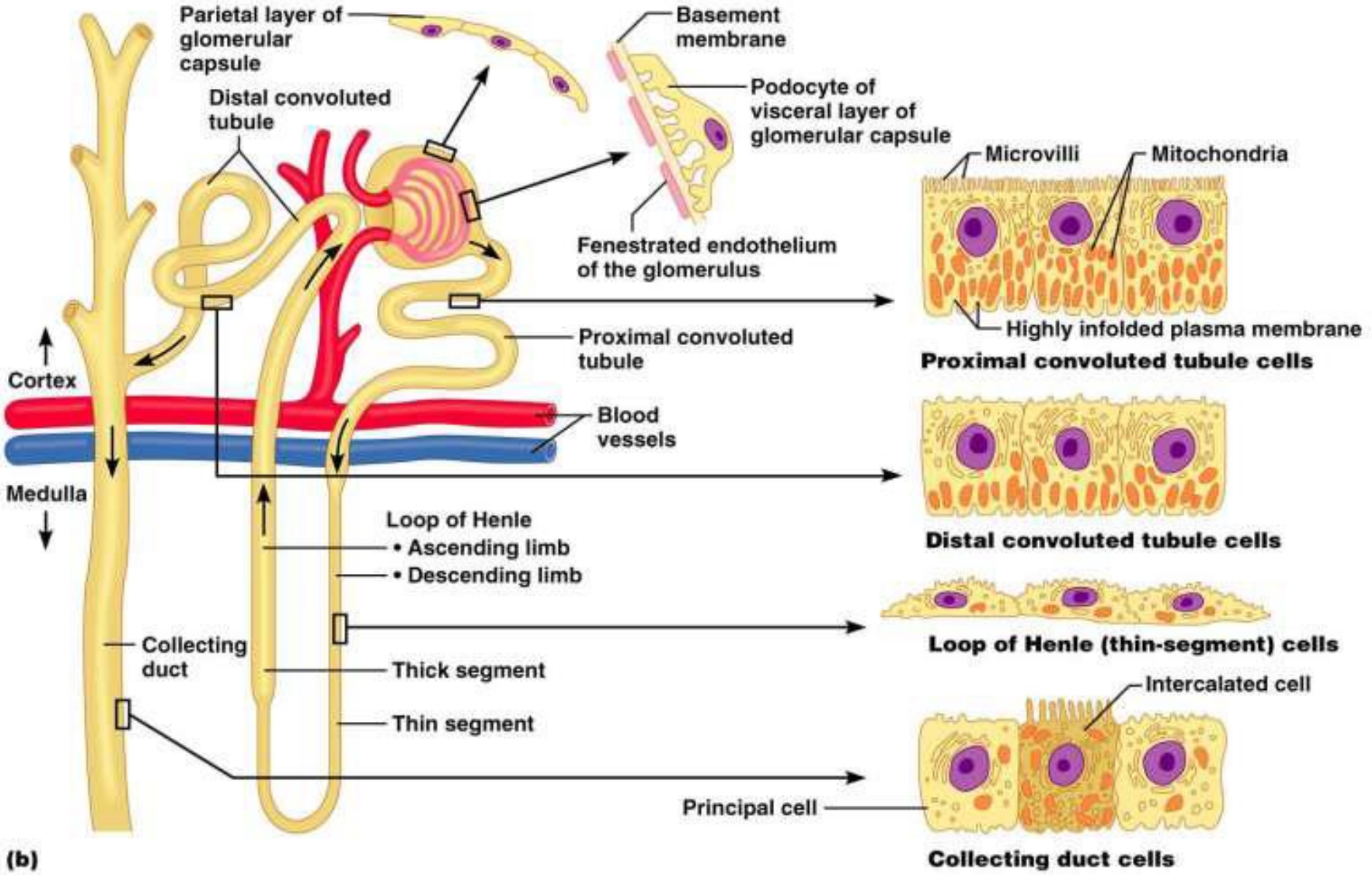
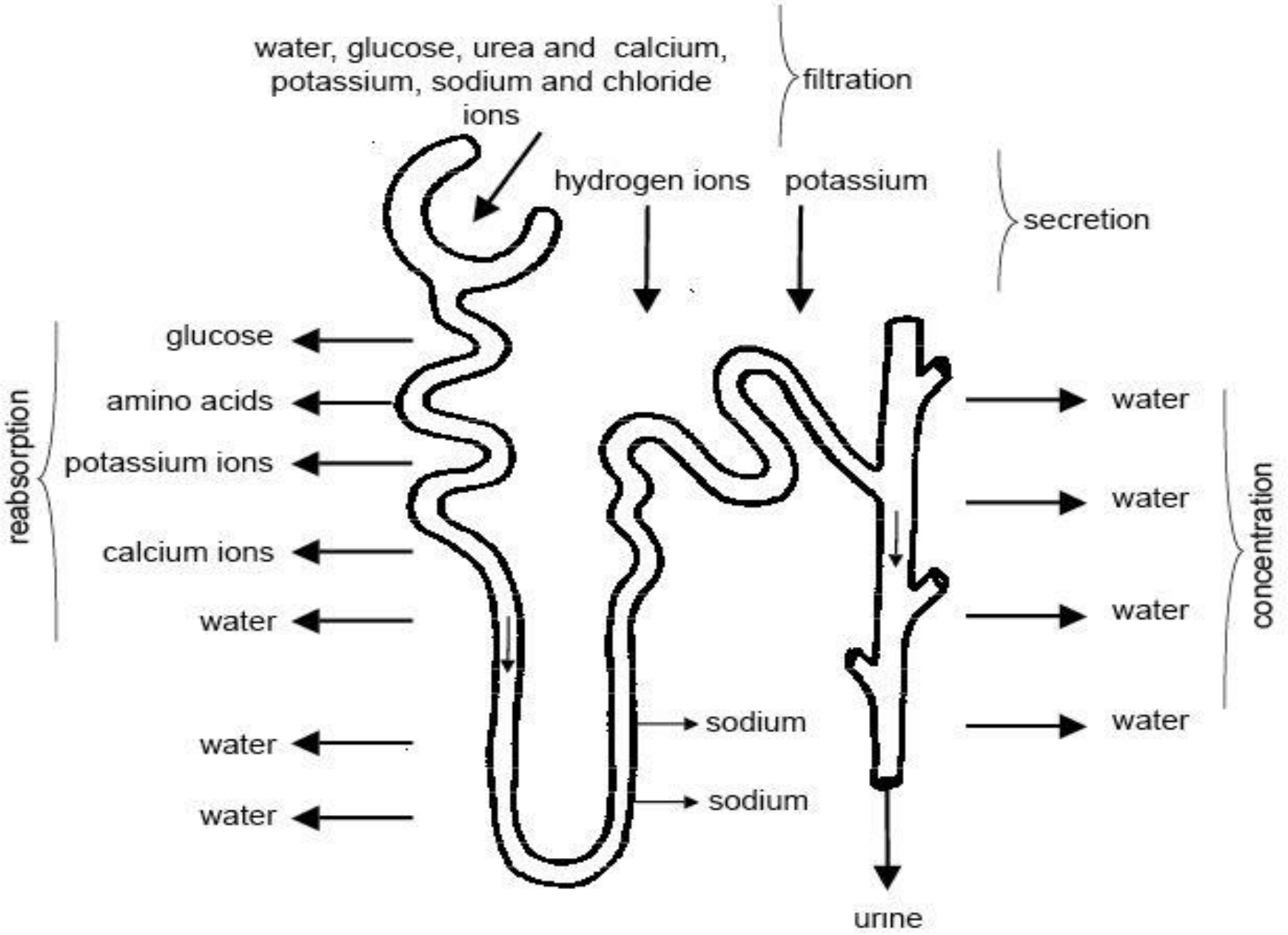
The Nephron




water, glucose, urea and calcium, potassium, sodium and chloride ions
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The Principal of Renal Insufficiency

• The principal mechanism that regulates water reabsorption by the renal tubules is **antidiuretic hormone (ADH).**

Tissue dehydration + ↑ serum osmolality → **ADH** (p. pituitary gland)

Renal tubules —ADH→ serum osmolality to normal → concentrated urine

•Diseases of the kidneys, and in some instances of the ureters, bladder, and urethra, reduce the efficiency of the kidney's functions, resulting in: disturbances in protein, acid-base, solute and water homeostasis and in the excretion of metabolic end-products.

•**A partial loss** of function is described as **renal insufficiency**

•When the kidneys can no longer regulate body fluid and solute composition, **renal failure** occurs

Renal insufficiency and renal failure

Insufficiency can occur from abnormalities in:

1. **The rate of renal blood flow** (vasomotor) such as shock, dehydration, and hemorrhage ⟹ marked reduction in glomerular filtration (**not true causes of renal insufficiency**) However, prolonged circulatory disruption can cause renal ischemia and ultimately renal insufficiency

2. **The glomerular filtration rate**
3. **The efficiency of tubular reabsorption**.

- Clinically differentiate glomerular disease from tubular disease. This is because the clinical and clinicopathological signs of renal dysfunction depend on the anatomical location of the lesion and the imbalance in function between glomeruli and tubules.
- Renal dysfunction tends to be a dynamic process so the degree of dysfunction varies with time.
- If renal dysfunction is so severe that the animal's continued existence is not possible it is said to be in a state of renal failure and the clinical syndrome of uremia will be present.

Causes of renal insufficiency and uremia

The causes of renal insufficiency, and therefore of renal failure and uremia, can be divided into: (a) pre renal, (b) renal, and (c) postrenal groups.

(a): Prerenal causes include congestive heart failure and acute circulatory failure, either cardiac or peripheral.

Decrease renal blood flow ⟹ acute renal ischemia (more in Proximal tubules)

- However, those parts of the tubules within the medulla are particularly susceptible to **hypoxic damage** because of the low oxygen tension in this tissue, the dependency of blood flow on glomerular blood flow and the high metabolic rate of this tissue.

- Renal medullary necrosis is a direct consequence of these factors.

- In ruminants, severe bloat can interfere with cardiac output and lead to renal ischemia.

Causes of renal insufficiency and uremia

(b) Renal causes include

1. Glomerulonephritis
2. Interstitial nephritis
3. Pyelonephritis
4. Embolic nephritis
5. Amyloidosis.
6. Acute renal failure due to administration of a variety of toxins
7. The disease can also occur secondary to sepsis and hemorrhagic shock
8. Experimental uremia by surgical removal of both kidneys

(c) Postrenal uremia may also occur, specifically in:

1. Complete obstruction of the urinary tract by vesical or urethral calculus
2. more rarely by bilateral urethral obstruction
3. Internal rupture of any part of the urinary tract, such as the bladder, ureters, or urethra, will also cause postrenal uremia.

Pathogenesis of renal insufficiency and renal failure

- Initially, as renal tissue loses function, there are few abnormalities because the remaining tissue increases its performance (**renal functional adaptation**); a **loss of 75%** of renal tissue causes a fall in **GFR to only 50%** of normal.

- Decreased renal function interferes with the kidneys' ability to maintain fluid and electrolyte homeostasis.

- The ability to concentrate urine declines early and is followed by decreases in ability to excrete phosphate, acid, and potassium.

- When renal failure is advanced (**GFR ≤ 10 mL/min/1.73 m^2**), the ability to dilute urine is lost; thus, urine osmolality is usually fixed close to that of plasma (**300 to 320 mOsm/kg**), and urinary volume does not respond readily to variations in water intake.

Pathogenesis of renal insufficiency and renal failure

Creatinine and urea

- Plasma concentrations of creatinine and urea (which are highly dependent on glomerular filtration) begin a hyperbolic rise as GFR diminishes. These changes are minimal early on.
- When the GFR falls below 10 mL/min/1.73 m^2 (normal = 100 mL/min/1.73 m^2), their levels increase rapidly and are usually associated with systemic manifestations (uremia).
- Urea and creatinine are not major contributors to the uremic symptoms; they are markers for many other substances that cause the symptoms.

Sodium and water

- Despite a diminishing GFR, sodium and water balance is well maintained by increased fractional excretion of sodium and a normal response to thirst.

- Thus, the plasma sodium concentration is typically normal, and hypervolemia is infrequent unless dietary intake of sodium or water is very restricted or excessive.

- Heart failure can occur due to sodium and water overload, particularly in patients with decreased cardiac reserve.

Pathogenesis of renal insufficiency and renal failure

Potassium

- Potassium adaptation usually maintains plasma levels at normal until renal failure is advanced.
- Potassium-sparing diuretics, ACE inhibitors, beta-blockers, NSAIDs, cyclosporine, tacrolimus, trimethoprim/sulfamethoxazole, pentamidine, or angiotensin II receptor blockers may raise plasma potassium levels in patients with less advanced renal failure.

Calcium and phosphate

- Abnormalities of calcium, phosphate, parathyroid hormone (PTH), and vitamin D metabolism and **renal osteodystrophy** can occur.
- Decreased renal production of calcitriol contributes to **hypocalcemia.**
- Decreased renal excretion of phosphate results in **hyperphosphatemia**.
- Secondary **hyperparathyroidism** is common and can develop in renal failure before abnormalities in calcium or phosphate concentrations occur.
- For this reason, monitoring PTH in patients with moderate CKD, even before hyperphosphatemia occurs, has been recommended.

Pathogenesis of renal insufficiency and renal failure

pH and bicarbonate

- Moderate acidosis (**plasma bicarbonate content 15 to 20 mmol/L**) is characteristic.
- Acidosis causes muscle wasting due to protein catabolism, bone loss due to bone buffering of acid, and progression of kidney disease.

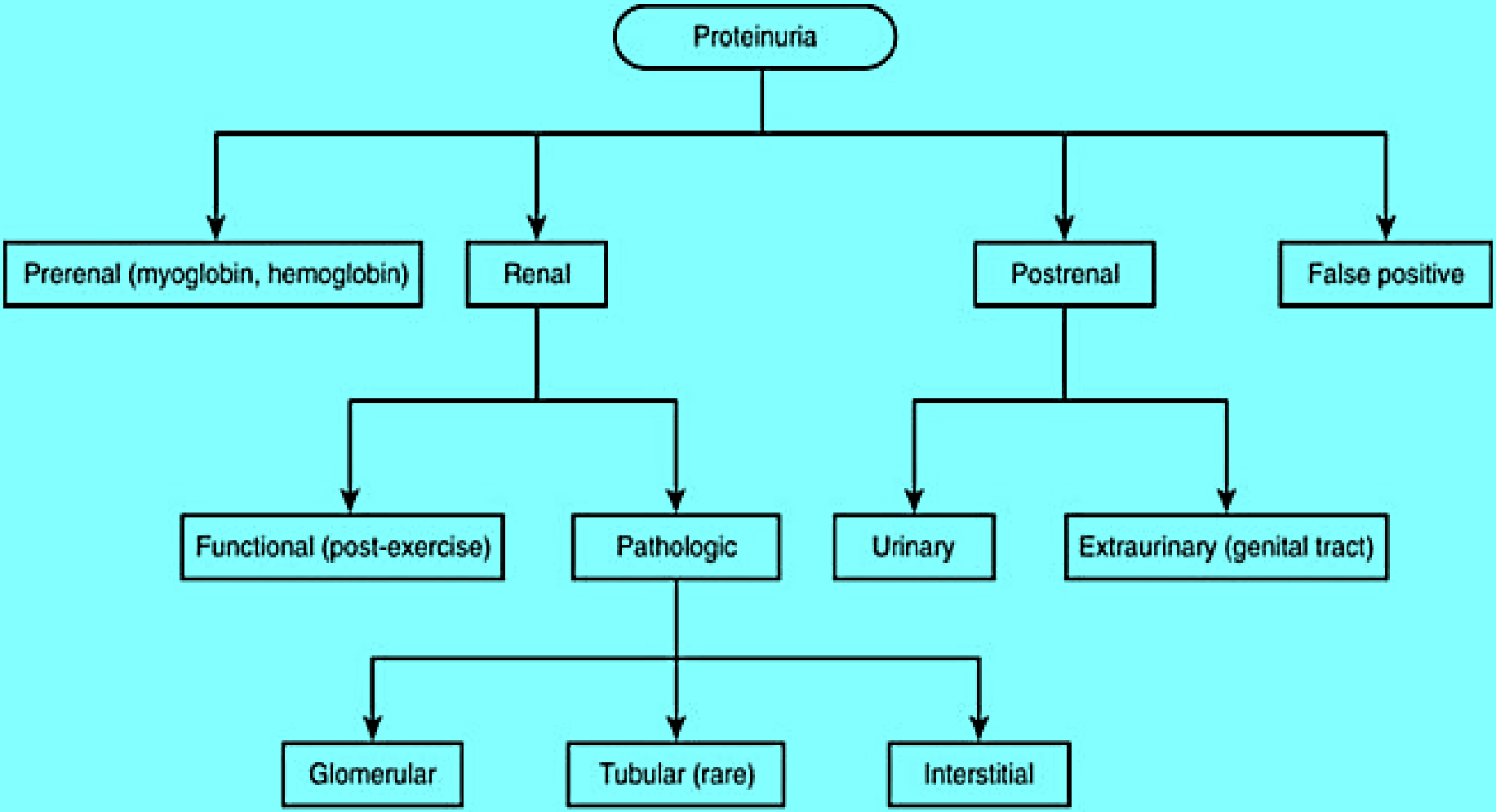
Anemia

- Anemia is characteristic of moderate to advanced CKD (≥ stage 3).
- The anemia of CKD is normochromic-normocytic, with an Hct of **20 to 30%** (35 to 40% in patients with polycystic kidney disease).
- It is usually caused by **deficient erythropoietin** production due to a reduction of functional renal mass.
- Other causes include deficiencies of **iron, folate, and vitamin B_{12}**.

Clinical features of urinary tract disease

Abnormal constituents of urine

1. Proteinuria



Abnormal constituents of urine

2. Casts and cells

Casts are present as an indication of inflammatory or degenerative changes in the kidney, where they form by agglomeration of desquamated cells and Tamm-Horsfall protein.

3. Hematuria

The problems causing hematuria can range from relatively minor disorders to more severe disease processes that may result in life-threatening hemorrhage.

Causes:

- Urolithiasis
- Urinary tract infection
- Neoplasia
- **Exercise**-associated hematuria
- Proximal urethral **tears** in stock-type horses
- Idiopathic renal hematuria
- Idiopathic cystitis.

5. Hemoglobinuria

- **False** hemoglobinuria: hematuria lysed and release hemoglobin + cellular debris.
- **True** hemoglobinuria causes a deep red to brown coloration of urine and gives a positive reaction to biochemical tests for hemoglobin without erythrocyte debris

Causes: intravascular hemolysis due to Hemolytic anemia

Abnormal constituents of urine

5. Myoglobinuria

The presence of myoglobin (myo hemoglobin) in the urine is evidence of **severe muscle damage**. The only notable occurrence in animals is **azoturia of horses**.

The myoglobin molecule (molecular weight 16 500) is much **smaller** than hemoglobin (molecular weight 64 000) and passes the glomerulus much more readily.

6. Pyuria and Bacteriuria

Leukocytes or pus in urine indicates inflammatory exudation at some point in the urinary tract, usually the renal **pelvis or bladder**.

- Pyuria may occur as grossly visible **clots or shreds**, but is often detectable only by **microscopic** examination of urine sediment.
- Individual cells and leukocytic casts may be present.
- Pyuria is usually accompanied by the presence of **bacteria in urine**.

Abnormal constituents of urine

7. Glucosuria

Glucosuria in combination with ketonuria occurs only in diabetes mellitus, an extremely rare disease in ruminants

- Glucosuria might occur in association with enterotoxemia due to ***Clostridium perfringens*** type **D** and can occur after parenteral treatment with **dextrose solutions, adrenocorticotropic hormones or glucocorticoid** analogs.
- Horses with **tumor** of the pars intermedia of the pituitary gland often have glucosuria.
- Glucosuria occurs also in **acute tubular nephrosis** as a result of failure of tubular resorption.

8. Ketonuria

Ketonuria is a more common finding in ruminants, occurring in **starvation, acetonemia** of cattle and **pregnancy toxemia** of ewes and does. A small amount of ketonuria is normally present in dairy cows in early lactation.

Variations in daily urine flow

An increase or decrease in urine flow is often described in animals

1. Polyuria

Polyuria occurs when there is an increase in the volume of urine produced

- extrarenal causes as when horses habitually **drink excessive quantities of water**
- in **central diabetes insipidus**, when there is inappropriate secretion of antidiuretic hormone (ADH) from the pituitary
- Polyuria occurs in horses with **tumors** of the pars intermedia of the **pituitary gland**.
- administration of **diuretic drugs** including corticosteroids.

- **Kidney disease** results in polyuria when the resorptive capacity of the remaining tubules is exceeded
- Polyuria can also occur when the **osmotic gradient** in the renal medulla is not adequate to produce concentrated urine.
- **Nephrogenic diabetes insipidus** causes polyuria because the tubules fail to respond to ADH

Variations in daily urine flow

2. Oliguria and anuria

Reduction in the daily output (oliguria) and complete absence of urine (anuria) occur under the same conditions and vary only in degree

- In **dehydrated animals**, urine flow naturally decreases in an effort to conserve water as plasma osmolality pressure increases
- **CHF** and **peripheral Circulatory failure** may cause such a reduction in renal blood flow that oliguria follows
- Complete anuria occurs most commonly in **urethral obstruction**, although it can also result from acute tubular nephrosis
- Oliguria occurs in the terminal stages of all forms of **nephritis**
- Anuria and polyuria lead to retention of solutes and disturbances of **acid-base balance** that contribute to the pathogenesis of **uremia**

3. Pollakiuria This is an abnormally frequent passage of urine

is commonly associated with disease of the **lower urinary tract** such as **cystitis**, the **presence of calculi in the bladder**, **urethritis** and **partial obstruction of the urethra**.

4. Dribbling

is a steady, **intermittent passage** of small volumes of urine reflecting inadequate or lack of sphincter control.

Occurs in large animals with incomplete obstructive **urolithiasis** and from **persistent urachus**

Painful and diffcult urination

Dysuria or painful/difficult urination

- Occurs in **cystitis, vesical calculus**, and **urethritis**
- Manifested by the **frequent passage** of small amounts of urine.
- **Grunting** may occur with painful urination and the animal may remain in the typical posture after urination is completed
- Differentiating pain caused by urinary disease from pain due to other causes depends largely upon the presence of other signs indicating **urinary tract involvement**.

Stranguria

- is slow and painful urination associated with disease of the **lower urinary tract** including cystitis, vesical calculus, urethral obstruction, and urethritis.
- The animal strains to pass each drop of urine.
- **Groaning and straining** may precede and accompany urination when there is urethral obstruction.
- In urethritis, **groaning and straining** occur immediately after urination has ceased and gradually disappear and do not recur until urination has been repeated.
- **Urine scalding** of the perineum or urinary burn is caused by frequent wetting of the skin with urine.
- It may be the result of urinary incontinence or the animal's inability to assume normal posture when urinating.

Acute and chronic renal failure

Uremia

Uremia is the systemic state that occurs in the terminal stages of **renal insufficiency**.

Anuria or oliguria may occur with uremia. Oliguria is more common unless there is complete obstruction of the urinary tract

Chronic renal disease is usually manifested by **polyuria**, but oliguria appears in the terminal stages when clinical uremia develops.

Clinical sigs:

1. The uremic animal is **depressed** and **anorexic** with **muscular weakness** and **tremor**.
2. In chronic uremia, the **body condition is poor**, as a result of continued loss of protein in the urine, dehydration and anorexia.
3. The **respiration** is usually **increased** in rate and depth but is not dyspneic; in the terminal stages it may become periodic in character.
4. The **heart rate** is markedly **increased** because of terminal dehydration and myocardial asthenia but the temperature remains normal except in infectious processes and some cases of acute tubular nephrosis.
5. An **ammoniacal or uriniferous** smell on the breath is often described but is usually undetectable.
6. **Uremic encephalopathy** occurs in a small proportion of cattle and horses with chronic renal failure.
7. The animal becomes **recumbent and comatose** in the terminal stages.
8. The **temperature falls** to below normal and death occurs quietly, the whole course of the disease having been one of gradual intoxication.

Principles of treatment of urinary tract disease

Fluid and electrolytes

Treatment of acute renal failure: removing the primary cause and restoring normal fluid balance by correcting of:

- Dehydration, acid-base disorders and electrolyte abnormalities.

Ruminants with chronic renal failure typically have mild to marked

1. Hyponatremia and Hypochloremia ↓ **Na, Cl**
2. serum **Ca** and **K** may be decreased because of inappetence ↓
3. serum **Mg** and **Ph** may be normal or ↑ because urine provides a route of excretion.
4. the acid-base status is characterized by **metabolic acidosis** in severely affected cases to **metabolic alkalosis** in mildly affected cases.

Ruminants with acute renal failure have similar clinicopathological changes
serum **phosphorus** is usually markedly **elevated** because many cases are initiated by decreased renal blood flow.

Horses with acute or chronic renal failure have similar electrolyte changes with the marked difference being the presence of:

- **hypercalcemia** and **hypophosphatemia** in some horses.
- The hypercalcemia is marked and is thought to result directly in hypophosphatemia in horses with renal failure.

Principles of treatment of urinary tract disease

Fluids and electrolytes abnormalities:

- ✓ Balanced electrolyte solutions or normal saline supplemented with **potassium** and **calcium** (depending on the severity of dehydration).
- ✓ As the fluid deficit is corrected, the patient should be **observed for urination**.
- ✓ If anuria or oliguria is present, the rate of fluid administration should be monitored to **prevent overhydration**.
- ✓ If the patient has anuria or oliguria after the fluid volume deficit is corrected, a **diuretic** should be administered to help restore urine flow.
- ✓ **Furosemide** (1-2 mg/kg BW every 2 h) or **mannitol** (0.25-2.0 g/kg BW in a 20% solution) may be used, but furosemide is preferred because of its much lower cost and ease of administration.
- ✓ Diuretics should not be used until dehydration has been corrected.
- ✓ **B vitamins** should be administered because their rate of loss in the urine is high in case of renal failure.

Principles of treatment of urinary tract disease

- ✓ Animals **nonresponsive** to fluid loading and diuretics could be administered low-dose **dopamine** as a continuous intravenous infusion (2-5 µg/kg BW/min) with dopamine being diluted in 0.9% NaCl, 5% dextrose or lactated Ringer's solution.

- ✓ Dopamine **increase renal blood flow** and therefore **glomerular filtration rate** in animals with renal failure

- ✓ low-dose dopamine infusion **does not alter creatinine clearance** (an index of glomerular filtration rate) in healthy adult horses and has not been shown to be of benefit in treating renal failure in humans.

- ✓ At low doses (<5 µg/kg BW /min) dopamine acts primarily as an **inotropic** agent (increase contraction of muscles) and at higher doses primarily as a **vasopressor**.

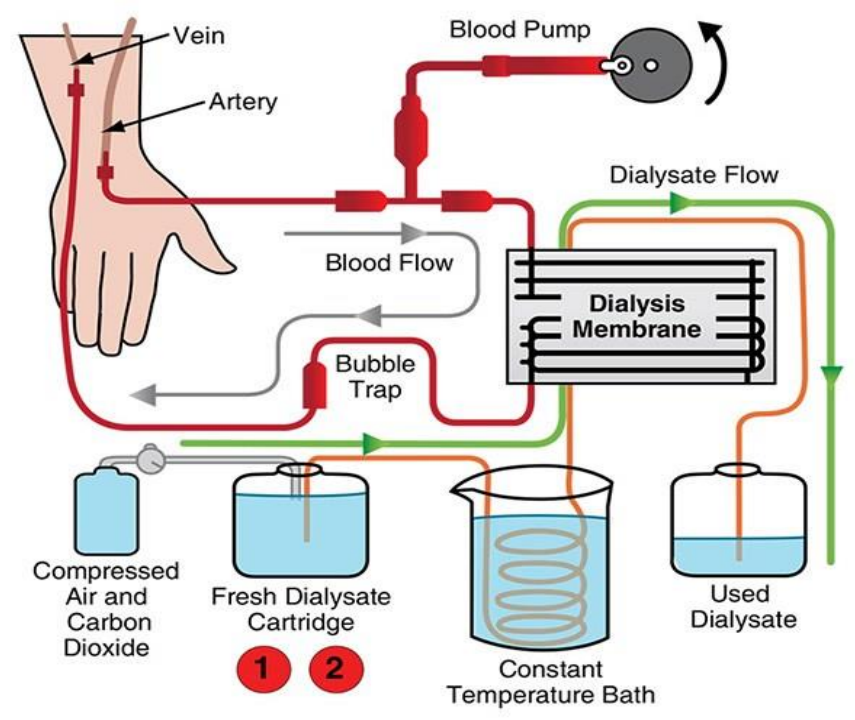
- ✓ Animals that remain **anuric** after intravenous fluid administration of furosemide/mannitol and dopamine have a grave prognosis and can only be managed with **peritoneal dialysis** or **hemodialysis**.

Principles of treatment of urinary tract disease

Hemodialysis

It used successfully to treat a foal with oxytetracycline nephrotoxicosis. Hemodialysis was performed under **isoflurane** anesthesia after surgical placement of a Teflon/Silastic arteriovenous shunt in the median artery and vein using a dialysis delivery system, **a hollow- fiber artificial kidney,** and **acetate-base dialysate**. Anticoagulation during dialysis was accomplished with a loading dose of heparin (100 U/kg BW) and then hourly boluses of 20 U/kg BW to prolong the activated clotting time.

Three dialysis treatments, lasting 4-6 hours, were administered over a 4-day period, resulting in a marked reduction in azotemia.



Principles of treatment of urinary tract disease

- The treatment of chronic renal failure will depend on **the stage of disease** and the **value of the animal**.
- In chronic failure, therapy is aimed at **prolonging life**.
- In food-producing animals, emergency slaughter is not recommended because the carcass is usually **unsuitable for human consumption**.
- Animals in chronic failure **should have free access to water and salt**, unless **edema** is present.
- **Stresses** such as sudden environmental and dietary changes should be **avoided**.
- The **ration** should be high in energy-giving food and properly balanced for protein.
- Acute renal failure may occur in patients in chronic failure and can be treated like other cases of acute renal failure.

Principles of treatment of urinary tract disease

Antimicrobial agents

Selection of antimicrobial agents for the treatment of urinary tract infections should be based on **quantitative urine culture** of a catheterized urine sample.

A clinically relevant bacterial concentration indicative of **cystitis** or **pyelonephritis** is **1000 or 40 000 cfu/mL** of urine from a catheterized or midstream free- catch sample, respectively.

The ideal antimicrobial for treatment of urinary tract infections should meet several criteria. It should:

- Be active against the causal bacteria
- Be excreted and concentrated in the kidney and urine
- Be active at the pH of urine
- Have low toxicity, particularly nephrotoxicity
- Be easily administered
- Be low in cost
- Have no harmful interactions with other concurrently administered drugs.

Principles of treatment of urinary tract disease

- **Appropriate first-line antimicrobials include:**
- penicillin, ampicillin, amoxicillin, ceftiofur, and cefquinome in **ruminants** and trimethoprim-sulfa and ceftiofur in **horses**.

- Antimicrobial therapy for **lower urinary tract** infections should continue for at least **7** days; for **upper urinary tract** infections **2-4 weeks** of treatment is often necessary.

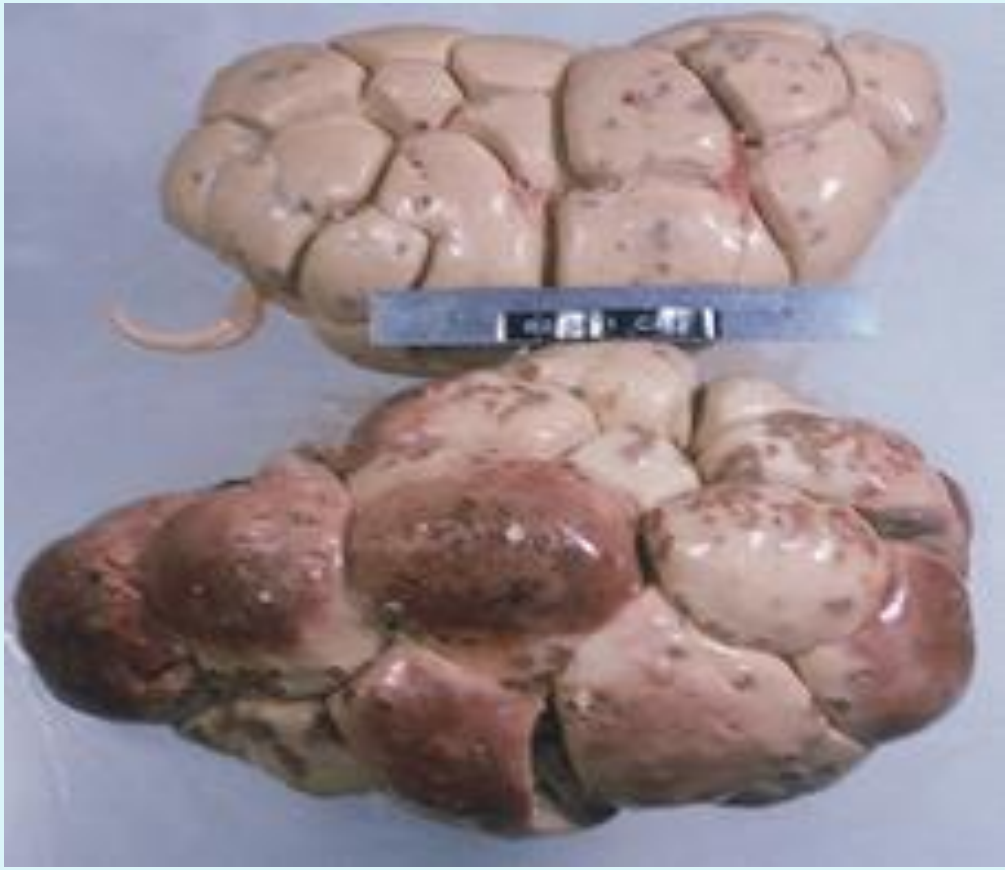
- Success of therapy can be evaluated by repeating the urine culture 7-10 days after the last treatment.

- **Manipulation of urine pH** should be considered as part of the treatment of bacterial urinary tract infections.
- In general, ***Escherichia coli*** attach best to urinary epithelial cells at **pH 6.0**, whereas ***Corynebacterium renale*** attaches best in **alkaline** urine.
- In other words, when treating an *E. coli* pyelonephritis or cystitis, the diet should be altered to ensure an alkaline urine pH.
- Likewise, urine pH should be acidic when treating urinary tract infections due to *C. renale*.

Disease of Kidney

Embolic Nephritis

This condition occurs in septicemic calves and cows or occasionally in endocarditis patients with left-sided valvular disease.



Clinical signs:

- Fever
- Septicemia
- Specific organ dysfunction, such as (mastitis, joint infections)

Clinical Pathology:

Urine test (strips): **++** blood, **++** protein

Microscopic Examination of the urine

- Increase numbers of WBCs
- Increase numbers of RBCs
- Bacteria in some cases.

Therapy must be directed against the **primary disease**

Renal Ischemia

Renal ischemia-reperfusion injury (IRI) frequently follows a sudden temporary impairment of blood flow and reoxygenation of tissue after a period of hypoxia or ischemia

Causes:

- Decreased renal perfusion → reduced glomerular filtration (dehydrated patients)
- Renal failure when both **sepsis** and **dehydration** are concurrent
- Severe **ruminal distention**
- Cattle with **severe dehydration** resulting from **gastrointestinal obstruction** or diarrhea frequently develop renal infarcts

Urine Constituents:

- RBCs, WBCs, and protein in the urine
- Serum chemistry indicates **azotemia** in dehydrated patients
- Further laboratory tests that help distinguish between prerenal and true renal azotemia should be utilized including **fractional excretion** of electrolytes, particularly **sodium**
- **Prerenal azotemia** is properly diagnosed only when a dehydrated, azotemic cow possesses the ability to **concentrate urine**

- As in other species, renal prostaglandin levels are **cytoprotective** to the kidney during reduced perfusion

- Therefore **prostaglandin inhibitors** such as NSAIDs should be used in **reduced dosages or not** at all in severely dehydrated cattle, lest further ischemic damage with increased **infarction or papillary necrosis** occurs

- If **sepsis** is present, the **benefits** of the NSAID would likely **exceed** negative effects on the kidneys, such as might be the case in individuals with severe gram-negative mastitis or severe metritis.

Treatment:

❖ **Remove the primary causes** and the patient rehydrated with IV fluids to improve renal perfusion, urine production, and to correct existing prerenal azotemia

❖ **Nephrotoxic drugs** such as aminoglycosides, oxytetracycline, and NSAIDs should be avoided if possible

❖ **If nephrotoxic drugs** must be used:

1. Repeated **serum creatinine** values
2. **Serial urinalyses**
3. **Fractional excretion** ratios should be considered to monitor **renal function**.

Toxic Nephrosis

Damage to the renal tubules (tubular degeneration, inflammation, and in some instances interstitial nephritis**) caused** by **toxins**, **certain drugs**, and **physiologic events** linked to hemoconcentration, endotoxemia, and ischemic changes

- ❑ Usually both kidneys are affected equally

Etiology:

- Antibiotics such as **aminoglycosides**, **tetracycline**, and **sulfa** drugs.
- **Neomycin**, **gentamicin**, **amikacin**, **streptomycin** and other aminoglycosides can cause renal tubular damage in cattle and other species.
- **Vehicles** used in certain injectable forms of tetracycline, may contribute to renal tubular nephrosis.
- **Propylene glycol** and **some other vehicles** are used in many oxytetracycline hydrochloride preparations, may cause **hemodynamically mediated reduced renal perfusion**.
- **Sulfa preparations** possess the ability to damage kidney tubules and **precipitate** in the renal tubules.

Most antibiotic nephrotoxicity occurs as a result of :

1. **Overdosage**
2. Proper dosage administered to calves or cattle that are **dehydrated**, hypovolemic, and have reduced renal perfusion, thereby increasing the potential for renal damage

- Drugs such as **phenylbutazone** and **flunixin meglumine** inhibit renal prostaglandins synthesize, loss of this protective effect, then the kidneys are more susceptible to **ischemic damage**

- Once again, the use of NSAIDs in **dehydrated/hypotension** patients increases the risk of nephrotoxicity.

- The risk of toxicity can be further exacerbated by **hypoalbuminemia** such as occurs with **acute gastrointestinal diseases** because more of the NSAID being administered will be non–protein bound and therefore pharmacologically active drug.

- Therefore **reduction of the dosage** or **total avoidance** of these drugs, unless concomitant fluid therapy restores renal perfusion, should be practiced when devising therapy for a dehydrated patient.

- Other nephrotoxins include the **heavy metals** (i.e., lead, mercury, and arsenic) and plant toxicities, such as **oxalates**, **oak**, and **pigweed**.

Clinical Signs:

Cattle affected with toxic nephrosis usually have **nonspecific signs**, including:

- Depression
- Anorexia that varies from mild to absolute
- Dehydration
- Potentially recumbency.

Cattle with drug-related nephropathies usually have **more blatant lesions** in other body systems, such as:

- Septic mastitis
- Septic metritis
- Abomasal disorders
- Diarrhea
- Polyuria may be present in some
- Pneumonia, therefore the primary diseases may **mask** the existence of nephrosis

- Rectal palpation may suggest enlargement of the **left kidney**.

- In nephrosis due to heavy metals, **neurologic signs** (lead, arsenic) or **gastrointestinal signs** (lead, arsenic, and mercury) may be present and raises suspicion of intoxication.
- In many such plant toxicities (no history of Antibiotics, NSAID and infectio), diagnosis must be assisted by clinical pathology and necropsy.

Clinical Pathology and Diagnosis Guide of Nephrotoxicity

- **Renal failure** will be documented by a urine specific gravity in the isosthenuric range (,**1.022**) despite obvious dehydration

- RBCs, WBCs, granular casts, and proteinuria usually are confirmed by urinalysis in acute nephrosis

- Azotemia is present and characterized by elevations of serum urea nitrogen and creatinine

- Specific causes may be suggested by the history (i.e., previous use of aminoglycosides, NSAIDs) or simply suspected (severe dehydration in a patient with salmonellosis)

- Serum chemistry reveal **Hypochloremia**, which may be more severe than that seen with intestinal obstruction, hypokalemia, hyponatremia, hypocalcemia, hyperphosphatemia, and hypermagnesemia.

- Renal biopsy is the most definitive means of diagnosis and can be accomplished by percutaneous biopsy of the left kidney

- Ultrasound study of the kidney may be a helpful ancillary procedure if available.

Treatment:

Therapy must attempt to **reestablish renal function** and to **correct primary disorders**

- ✓ N**ephrotoxic drugs** should be **avoided** in the therapy
- ✓ Primary therapeutic goal is the **fluid therapy** for adequate renal perfusion, tailored to the individual patient
- ✓ Because **hypochloremia**, **hypokalemia**, and **hyponatremia** usually are present, physiologic NaCl with supplemented KCl added at 20 to 40 mEq/L is frequently used
- ✓ **Unless the patient is anuric**, large volumes of **IV fluids** are required to treat **dehydration** and **establish diuresis**
- ✓ **If** an adult patient is **anuric** or **oliguric** following an initial 20 to 40 L of IV fluids, 250 to 500 mg of **furosemide** may be administered IV one or more times at 15- to 30-minute intervals in an effort to initiate diuresis
- ✓ Failure to produce urine in the face of high volume fluid therapy alongside diuretic administration should be taken as a **negative prognostic sign**
- ✓ **Repeated bladder evaluation** by rectal palpation or ultrasonography to confirm urine production and accumulation may be a **useful monitoring technique**

- ✓ A 500-kg cow that is **azotemic, isosthenuric,** and **10% dehydrated** requires **50 L** of fluids simply to counteract dehydration. Therefore, require a total of 80 to 100 L during the first 24 hours of therapy to establish adequate diuresis.

- ✓ IV or S/C **calcium borogluconate** should be utilized in **hypocalcemic** patients.

- ✓ A low percentage of **dextrose** may be added to the basic fluids by adding 1 L of 50% dextrose to each 20 L of saline/KCl if desired.

- ✓ **Acidotic**, **hyperkalemic** patients should receive IV saline, dextrose (half-strength saline mixed equally with 2.5% dextrose), and supplemental $NaHCO_3$

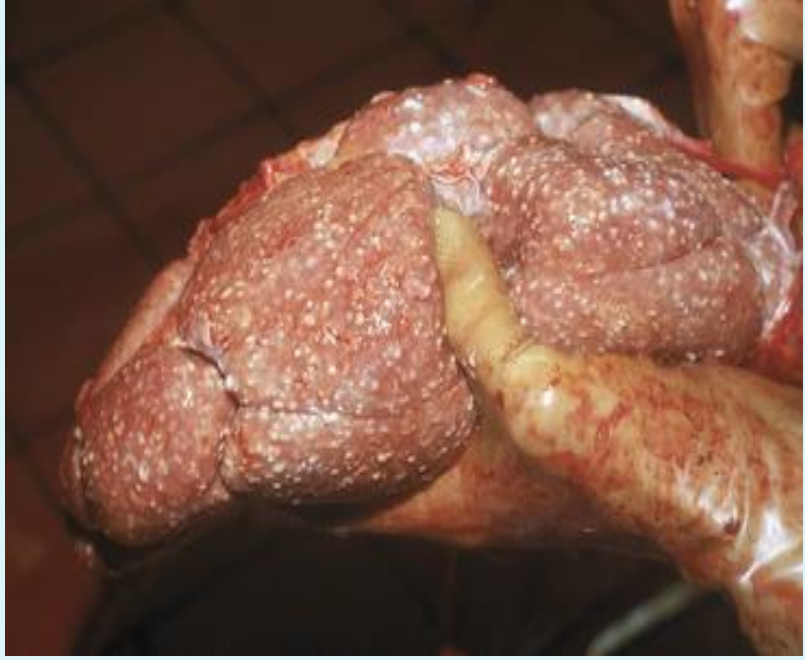
- ✓ **Salmonellosis** patients (either calves or cows) with secondary tubular nephrosis may be **acidotic** and require bicarbonate therapy

- ✓ **Oliguric** or **anuric** patients also may require **20 L** of **10% dextrose** solution in addition to **furosemide** to stimulate osmotic diuresis

- ✓ **Anuria** that is unresponsive to fluid diuresis and furosemide therapy may also necessitate **dopamine** (3 to 5 µg/kg/min) and/or dobutamine (2 to 5 µg/kg/min) in 5% dextrose **if all other therapy fails**

- ✓ Other potential treatments include **mannitol**, **norepinephrine**, **vasopressin (ADH)**, and **aminophylline**.
- ✓ Serum **urea nitrogen** and **creatinine** initially should be monitored each day.
- ✓ The **length of treatment** varies from a **few days** to **2 weeks** in most cases. The **prognosis** is guarded until normal renal function is reestablished
- ✓ The more prolonged the azotemia, the more likely the patient is to develop chronic renal failure
- ✓ **Response to therapy** and the results of renal biopsies, once available, afford the best means of prognosis.
- ✓ **If a potential nephrotoxic drug** must be used to treat a primary condition, reduced dosages and monitoring of blood levels are essential to continued usage.

Pyelonephritis



Infectious nephritis caused by bacterial infection of the kidney is usually an ascending infection from the lower urinary tract of dairy cattle.

Etiology:

- In cattle, bacterial pyelonephritis has been attributed to ascending infection of the urinary tract by ***Escherichia coli*** or ***Corynebacterium renale***.
- At least **three *C. renale* serotypes** exist as normal flora of the caudal portion of the reproductive tract of female cattle and the sheath of male cattle.
- Unlike most gram-positive organisms, *C. renale* possesses **pili** that promote attachment to and colonization of the urinary tract mucosa.

Conditions that provide **physical** or **chemical damage** to the mucosa in the lower portion of the urinary tract such as **dystocia, bladder paralysis, or catheterization** may predispose the cow to pyelonephritis as a result of *C. renale* **ascending** infection from the urinary bladder to the ureters and kidneys.

Clinical Signs:

1. Acute primary pyelonephritis causes fever (39.72 to 40.83° C), anorexia, and a precipitous decrease in milk production.

2. Some cows with acute pyelonephritis have colic manifested by kicking at the abdomen, restlessness, and treading.

3. Signs of colic usually are associated with renal or ureteral inflammation and pain, but urinary obstruction caused by blood clots blocking urine outflow from a kidney (ureter) or bladder (urethral) also may contribute to colic.

4. Further excitation, such as swishing of the tail, may be observed in cow has cystitis as a precursor lesion of pyelonephritis.

5. Stranguria, polyuria, an arched stance, gross hematuria, blood clots, fibrin, or pyuria also are observed in some patients with *C. renale* infection.

6. Acute pyelonephritis should be considered as a differential for acute colic in postparturient cattle.

7. Consequently left kidney and ureter palpation per rectum should be mandatory components of the physical examination of any sick cow with signs of colic.

8. Chronic pyelonephritis is associated with weight loss, poor hair coat, anorexia, poor production, diarrhea, polyuria, anemia, stranguria and gross urine abnormalities.

9. Lordosis (spinal cord bending) and stretching out may be apparent in some cows with chronic pyelonephritis because of renal pain.

10. Latent or subclinical pyelonephritis may exist in cattle with multiple medical problems, especially during the first few months of lactation.

11. Cattle with concurrent abomasal displacement, metritis, mastitis, or cattle that had dystocia may develop pyelonephritis that is “masked” by more obvious signs in other systems.

12. Only through screening urine and subsequent urinalysis will the condition be confirmed.

13. Specific physical signs of pyelonephritis in these instances are minimal unless, on rectal palpation, the left kidney is large, painful, and has indistinct lobulations, thereby increasing the possibility of pyelonephritis.

Diagnosis

- Diagnosis of pyelonephritis is made by combining the clinical signs, rectal palpation findings, vaginal palpation findings, and urinalysis.

- Fever usually is present in acute pyelonephritis but may be absent in chronic pyelonephritis.

- Urinalysis abnormalities such as RBCs, WBCs, protein, and bacteria may be present in both cystitis and pyelonephritis.

- However, cystitis does not usually lead to systemic illness, and the ureters would not be enlarged as determined by palpation per vagina or per rectum.

- Vaginal palpation remains an essential aid to diagnosis because it allows detection of unilateral or bilateral ureteral enlargement.

- Rectal palpation may reveal enlargement of the left kidney in unilateral left kidney infection, not helpful to diagnosis in right kidney infections unless the infection is very chronic with massive enlargement of the right kidney.

- Normal lobations of the kidney may be lost; the kidney may feel “mushy”; and there may be a pronounced arterial pulsation.

- Ultrasonography is another helpful ancillary aid to diagnosis and may reveal valuable prognostic information.

- Hypoalbuminemia is present in most pyelonephritis patients and is more severe in chronic pyelonephritis.

- Proteinuria appears to be very significant in pyelonephritis and occurs in most cases.

- Serum globulin values may be higher (.5.0 g/dl) if infection has been chronic.

- Generally a period of 10 to 14 days of renal infection is necessary to elevate globulin values, and adult cattle tend to have higher globulin levels than calves with chronic infection.

- Urine culture is the most important laboratory aid because it allows identification of the causative organisms and more importantly the sensitivity of the causative organism to antibiotics.

- Previous treatment with antibiotics by the owner may interfere with in vitro growth.

Treatment:

1. Early diagnosis and sustained treatment are needed for a successful recovery.

2. Urine sample should be taken for culture and antimicrobial susceptibility testing.

3. The treatment of choice for pyelonephritis due to *Corynebacterium* spp is penicillin (22,000 IU/kg, IM, bid) or trimethoprim-sulfadoxine (16 mg combined/kg, IM, bid) for ≥3 wk.

4. The dosage, frequency, and length of administration for both of these drugs is extra-label, and adequate precautions must be taken to prevent antibiotic residues from entering the human food supply.

5. *E coli* infections require a broad-spectrum antimicrobial, Ceftiofur (1.1–2.2 mg/kg/day, IM or SC) or gentamicin (2.2 mg/kg, IM, bid) for ≥3 wk have been used successfully in some cases.

6. Manipulation of urine pH may be of value because *E coli* grow best in acidic urine (pH <7), whereas *Corynebacterium* spp grow best in alkaline urine (pH >7).

7. Even though the organisms are ubiquitous in the environment, affected animals should be isolated from the herd to restrict buildup of organisms.

Thank You