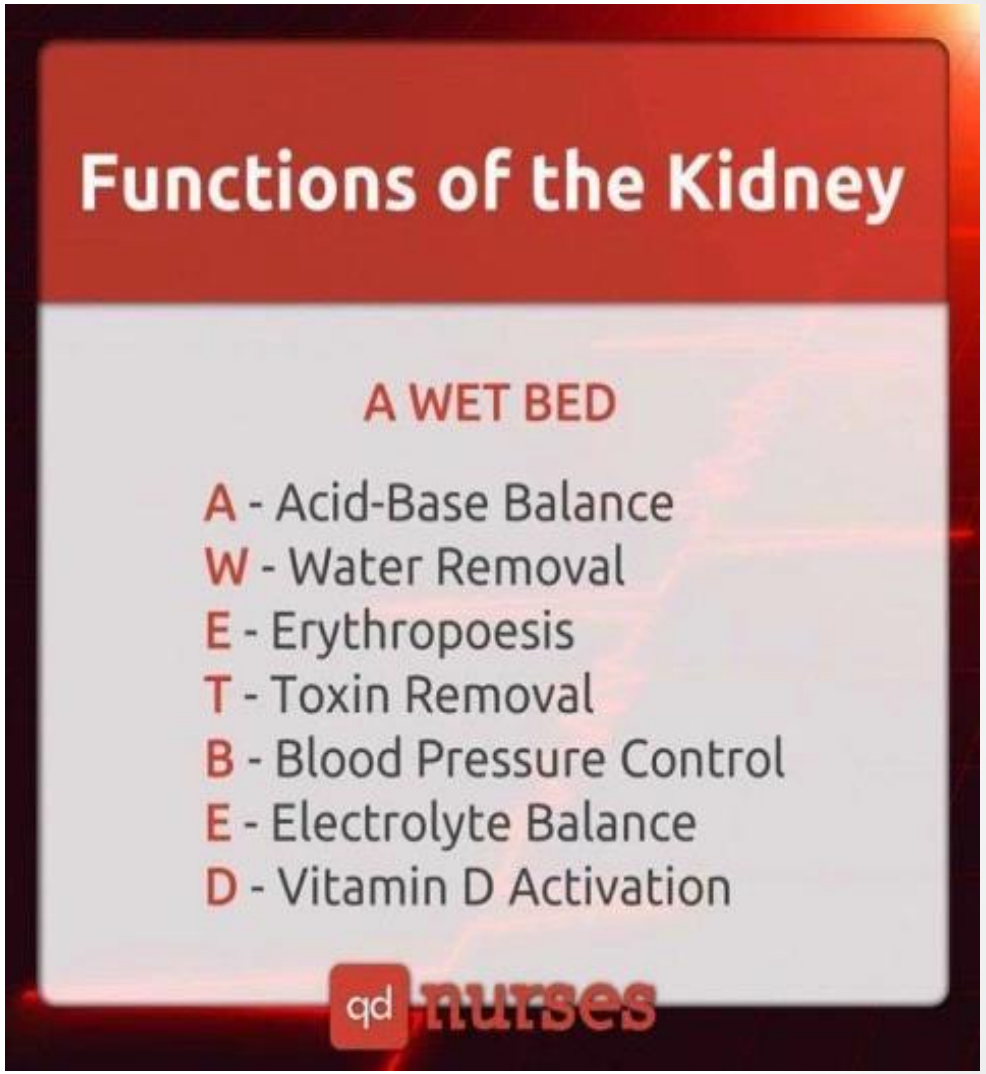
Urinary System Pathology

Kidney

- The essential requirements for normal renal function are:

  - adequate perfusion with blood (pressure >60 mm Hg),
  - adequate functional renal tissue, and
  - normal elimination of urine from the urinary tract



Renal failure

- It may be prerenal, renal or postrenal.

❖ PRERENAL FAILURE

The kidneys do not have enough blood.

❖ RENAL FAILURE

It is characterized by a disorder in the kidney parenchyma.

❖ POSTRENAL FAILURE

It occurs when urine excretion is prevented.

- In such cases, imbalance of acid-base and salt-water are formed, and residual products cannot be removed from the body.
- The most important indicator of renal insufficiency is the amount of urea that cannot be removed from the body.
- Urea itself does not have any detrimental effect, but other disorders in urinary function lead to uremia syndrome, with very important clinical signs.
- In renal disorders blood vessels, glomeruli, tubules and interstitium are affected.
- Although the kidneys constitute only about 0.5% of body weight, they receive 20-25% of cardiac output.

Renal disease, Renal failure, and Uremia

- **Renal disease**, which encompasses any deviation from normal renal structure or function, is usually subclinical.
- Severe renal disease may lead to **renal failure**, which is typically divided into **acute** and **chronic** forms.
- **Acute renal failure (ARF)** is characterized by rapid onset of oliguria or anuria and azotemia; it may result from acute glomerular or interstitial injury or from Acute Tubulus Necrosis (ATN), and is often reversible.
- **Chronic renal failure (CRF)** is the end result of many chronic renal diseases, is usually irreversible, and is characterized by prolonged duration of signs of uremia.

UREMIA

- **Uremia** literally means urine in the blood.
- It is a *clinical syndrome of renal failure*, caused by biochemical disturbances, and is often accompanied by extrarenal lesions.
- **Azotemia** is a biochemical abnormality characterized by *elevation of blood urea and creatinine*, but without obligatory clinical manifestations of renal disease.
- Azotemia may be of renal or of extrarenal origin.

UREMIA

In uremia;

- Disturbances in **electrolyte balance**
- **Acid-base imbalance**
- Failure to **excrete metabolic wastes**
- Disturbances **in endocrine function** can be seen.

❖ In uremia the kidney lesions are variable, but some common changes occur when the syndrome is chronic.

UREMIA

- As a result,
  - The kidney gets fibrotic and calcified;
  - Glomeruli become sclerotic, and
  - Hyperplastic and hypertrophic tubules may also be present.
  - Often this condition is identified as end-circuit kidney (nephrosclerosis).
- *The end result is a fibrosed, mineralized kidney with globally sclerotic glomeruli, and a mixture of atrophic and hypertrophic tubules*. Often, this can only be diagnosed as **"end-stage kidney."**

The term ENDSTAGE KIDNEY is used to describe renal disease which is chronic, advanced, generalized, progressive and irreversible. The term was adopted because of the inability to differentiate antecedent causes of "end stage kidneys".

At that point functional deficits are seen; the urine is not concentrated and wastes are not removed from the blood.

The animal is in RENAL FAILURE with chronic renal disease. Azotemia/or uremia occur because 3/4 of the nephrons have been lost.

UREMIA

- In uremia, extrarenal lesions are more common in dogs. These lesions are seen especially in chronic renal failure.
- Many animals dying with uremia are cachectic.
- This is probably caused by anorexia, vomition, and diarrhea as well as by body tissue catabolism to supply energy.
- Besides this general lack of condition, several distinctive lesions may develop in the gastrointestinal, cardiovascular, respiratory, and skeletal systems.

This is an example of mineralization secondary to renal failure and uremia.
The left atrium (as seen here) is a common sight of soft tissue mineralization in renal disease.

This is an example of **FIBRINOUS PERICARDITIS** with mineral deposition secondary to uremia in a dog with renal failure.

UREMIA

- ***Ulcerative, necrotic stomatitis*** occurs in dogs and cats, and there is usually a foul-smelling brown film coating the tongue and buccal mucosa.

UREMIA

- Like the gastrointestinal changes, oral lesions are more common in chronic than in acute uremia.
- The pathogenesis of the ulcers is not always clear, but some are associated with fibrinoid necrosis of arterioles, and some are related to bacterial production of ammonia from urea in the saliva.

UREMIA

- *Large areas of the gastric mucosa* are often swollen, suffused with red-black blood, and may be mineralized and partly ulcerated.
- Mucosal infarction occurs secondary to arteriolar necrosis.
- *Mineralization of the middle and deep zones of the gastric mucosa is common.*

UREMIA

- Intestinal lesions resemble those in the stomach, but they are less frequent, severe, and without mineralization.
- Gastrointestinal lesions probably account for much of the vomition, diarrhea, and melena of uremic dogs.
- In dogs with gastrointestinal lesions, intestinal invaginations are sometimes formed.

UREMIA

- Most animals dying in uremia develop *terminal pulmonary edema*. The mechanism is unknown.
- The edema is not always associated with significant pulmonary congestion; increased permeability of alveolar capillaries is the most likely pathogenesis.
- Pulmonary mineralization occurs in chronically uremic dogs.
- *At necropsy,* the lung is edematous and elastic, and the alveolar spaces contain fibrin in the fluid.
- *Microscopically,* leukocytes are present (but may be a response to accidental superimposed infection). Mineralization is extensive, with deposition particularly on reticulin of alveolar walls that are widened.
- The lesion is referred to as uremic lung or uremic pneumonitis; it is not common, and when it occurs, it may be multifocal.

UREMIA

- **This is an example of PLEURAL MINERALIZATION due to uremia.**
- **Note the surface of the intercostal muscles are covered by the mineralized pleura. This is called uremic frosting.**

This is an HxE stained section of lung from a dog in renal failure. Note the dark pink to purple foci (arrows) - these are foci of mineralization. The alveoli are also flooded with edema fluid; this also occurs with uremia and is also called uremic pneumonitis.

UREMIA

- Perhaps the most constant lesion in the dog is *mineralization beneath the parietal pleura* in the intercostal spaces.
- It is preceded by necrosis of the subpleural connective tissue with extension to intercostal muscle and overlying pleura. Once mineralization has occurred and the pleura repaired, the lesion appears as gray-yellow thickenings, horizontally wrinkled.

Necrosis and **mineralization** beneath the intercostal pleura between the ribs in a uremic dog.

Renal fibrosis (end stage kidney) -> chronic renal failure -> uremic tissue damage coupled with increased serum phosphorus and Ca levels -> pleural mineralization (dystrophic calcification)

UREMIA

- Uremic encephalopathy is an uncommon complication of uremia in domestic animals.
- It has been reported clinically in dogs.
- In a Holstein heifer with severe chronic interstitial nephritis showed uremic encephalopathy in the form of multifocal spongiform encephalopathy.

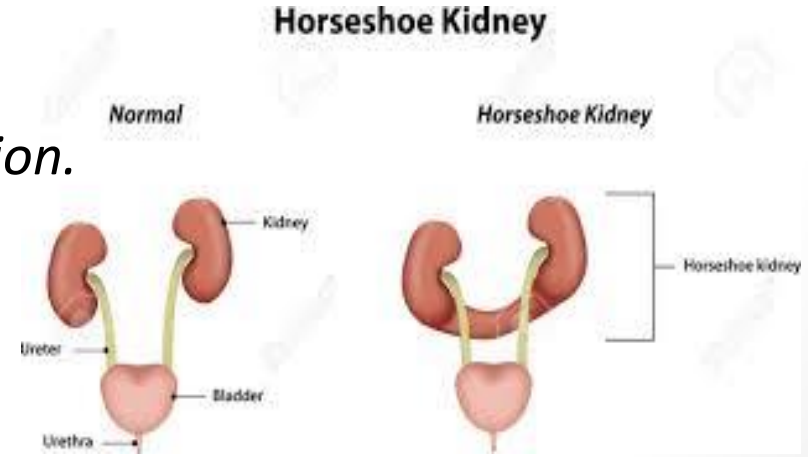
DEVELOPMENT ANOMALIES of KIDNEY

Abnormalities in the amount of renal tissue

- Agenesia ➔Lack of renal tissue may be complete *(agenesis)* or partial *(hypoplasia).*
- Hypoplasia
- Hypertrophy
- Ectopia: Malposition of the kidneys
- Horseshoe kidney:Fusion of the kidneys may occur in utero. Horseshoe kidney results from fusion of the cranial or caudal poles of the kidneys.
- Dysplasia: *is disorganized development*

of renal parenchyma due to anomalous differentiation.

- **Cyst**
- Hereditary kidney disease



KIDNEY (RENAL) CYSTS

- Cystic diseases of the kidney include various conditions characterized by one or more grossly visible cystic cavities in the renal parenchyma.
- *Cysts can occur in any part of the nephron, including the glomerular space, or in the collecting system.*

KIDNEY (RENAL) CYSTS

- Three **mechanisms,** which are not mutually exclusive, can lead to the formation of renal cysts:

1. Renal cysts may be caused by ***obstructive lesions;*** examples are the acquired retention cysts of chronic renal disease, some dysplastic cysts, and possibly those of glomerulocystic disease.
2. **A fundamental change**, of unknown origin, may occur in the *tubular basement membrane* and result in formation of saccular or fusiform dilations of the tubules.
3. **Disordered growth of tubular epithelial cells** may lead to *focal hyperplastic lesions and cyst formation.*

KIDNEY (RENAL) CYSTS

- Renal cysts **vary in size** from the barely visible to structures that exceed that of the organ itself.
- Cysts are often **more numerous in the cortex** than medulla.
- The cyst wall is **clear or opaque**, depending on the amount of surrounding connective tissue.
- The content is **watery**.
- Cysts are lined by **flattened or cuboidal epithelium**.

KIDNEY (RENAL) CYSTS

- Simple renal cysts
- Congenital form of Policystic Kidney Disease(PKD)
- Uremic medullary cystic disease
- Glomerulocystic disease
- Acquired cysts
- Perinephric pseudocysts

KIDNEY (RENAL) CYSTS

- **Simple renal cysts** occur in all species but are most common in pigs and calves. (The usual finding in pigs is one or a few unilocular cortical cysts, ~1-2 cm across, that bulge from the renal surface or are exposed when the kidney is sliced.)
- **Congenital form** of *Policystic Kidney Disease(PKD)*, of unknown inheritance, occurs in piglets, lambs, calves, goat kids, puppies, kittens, and foals. (This form of PKD in domestic animals is manifested by stillbirths or death in renal failure during the first few weeks of life. Grossly, the kidneys are large and pale, and contain numerous 1-5 mm cysts.)

CIRCULATORY DISTURBANCES and DISEASES of THE BLOOD VESSELS

- Renal hyperemia: *Active hyperemia or Passive hyperemia (congestion)*
- Renal hemorrhages
- Renal infarction *Infarcts of the kidney are common lesions of localized coagulative necrosis produced by embolic or thrombotic occlusion of the renal artery or of one of its branches.*
- Renal cortical necrosis and acute tubular necrosis
- Renal medullary necrosis
- **Hydronephrosis**

HYDRONEPHROSIS

- Hydronephrosis is dilation of the renal pelvis and calyces associated with progressive atrophy and cystic enlargement of the kidney.

HYDRONEPHROSIS

- The cause is *some form of urinary obstruction*, which may be complete or incomplete, existing at any level from the urethra to the renal pelvis.
- The obstruction may be caused by anomalous development of the lower urinary tract, or it may be acquired.

HYDRONEPHROSIS

- *Acquired causes* include:

✓Urinary calculi in any location;

✓Prostatic enlargement in the dog;

✓Cystitis (especially if it is hemorrhagic);

✓Compression of the ureters by surrounding inflammatory or neoplastic tissue;

✓Displacement of the bladder in perineal hernias;

✓Acquired urethral strictures.

HYDRONEPHROSIS

- Depending upon the site of obstruction,

✓Hydronephrosis may be unilateral or bilateral,

and

✓There may be some degree of hydroureter

and dilation of the bladder.

HYDRONEPHROSIS

- The degree of development of hydronephrosis depends on

✓whether or not it is bilateral,

✓the completeness of the obstruction,

✓other complications of obstruction.

- Bilateral obstruction, which includes obstruction localized to the bladder or urethra, results in early death from uremia.
- So, there is not enough time for hydronephrosis to occur.

HYDRONEPHROSIS

- Unilateral obstruction produces the greatest degree of hydronephrosis, especially if the obstruction is incomplete or intermittent, because glomerular filtration can continue.
- If an obstruction is removed within about 1 week, renal function returns.
- After about 3 weeks of complete obstruction, or several months of incomplete obstruction, irreversible renal damage occurs.

HYDRONEPHROSIS

- In unilateral hydronephrosis, the contralateral kidney can compensate if it is normal.
- Urinary stasis predisposes to infection; hence pyelonephritis might be superimposed on hydronephrosis.

GLOMERULAR DISEASE

- The term **glomerulitis** is used when inflammation is restricted to glomeruli, as may occur in acute septicemias.
- **Glomerulonephritis** has mostly immune origin and is the most common form of kidney disease in domestic animals.
- Result in *end-stage kidney disease* and *kidney failure*, especially in dogs and cats.

Table 4.1 Causes of immune-mediated glomerulonephritis in domestic animals

Viral	*African swine fever virus* *Aleutian mink disease virus* *Bovine viral diarrhea virus* *Canine adenovirus 1* (infectious canine hepatitis) *Classical swine fever virus* *Equine infectious anemia virus* *Feline immunodeficiency virus* *Feline infectious peritonitis virus* *Feline leukemia virus*
Bacterial	*Borrelia burgdorferi* Canine pyometra *Campylobacter fetus* Chronic pancreatitis Subacute valvular endocarditis
Protozoal	African trypanosomiasis Canine leishmaniasis Coccidiosis *Encephalitozoon cuniculi*
Helminths	*Dirofilaria immitis*
Neoplasms	Various
Autoimmune	Antiglomerular basement membrane disease Immune-mediated hemolytic anemia Polyarteritis Systemic lupus erythematosus
Hereditary	Canine familial renal disease Hypocomplementemia in Finnish Landrace lambs

GLOMERULAR DISEASE

- *Clinical presentations* can be nonspecific.
- Hematuria, proteinuria, oliguria, hyposthenuria, and azotemia can be seen in glomerular and the other kidney diseases.

GLOMERULAR DISEASE

- The following terms are currently used for the histologic description of **Glomerulonephritis** in domestic animals:
- **Membranous:** basement membrane thickening predominates
- **Proliferative (mesangioproliferative):** cellular proliferation predominates
- **Membranoproliferative (mesangiocapillary):** both changes are present
- **Glomerulosclerosis** (GS): combination of increased mesangial matrix and obliteration of capillary lumina; progressive hyalinization sometimes results in glomerular obsolescence, in which the glomerulus is a shrunken, eosinophilic, hypocellular mass.

GLOMERULAR DISEASE

❑ Histologic changes in glomerulonephritis

- Fibrin exudation into the urinary space leads to the proliferation of both visceral and parietal epithelial cells and often the infiltration of **macrophages and neutrophils**.
- These are the stages of a ***glomerular crescent***. Some of the cells produce collagen, and fibroblasts from the interstitium can also invade Bowman's capsule.

GLOMERULAR DISEASE

❑ Histologic changes in glomerulonephritis

- Glomerular capillary walls may be thickened in H&E stained sections (because of endothelial or epithelial swelling and/or thickening and/or remodeling of the GBM).
- Thickening deposits are caused by mostly **immune complexes**. (Thickening is particularly evident in *membranous GN*.)

GLOMERULAR DISEASE

❑Histologic changes in glomerulonephritis

- **Hyalinosis** is often seen concurrently with GS and is defined as the presence of glassy PAS-positive material in the capillary Wall.
- In GN (especially in chronic cases), there is widespread occurrence of **hyalinosis** in mesangium or homogenous, eosinophilic, PAS-positive, basement membrane-like material accumulation.
- **Hyaline material** is collected in the mesangium in diabetes mellitus and amyloidosis;
- In diabetes mellitus, diffuse or nodular hyaline depressions (Kimmelstiel-Wilson nodules) can be found in glomeruli.

GLOMERULAR DISEASE

❑Histologic changes in glomerulonephritis

- **Thickening of Bowman's capsule** may occur with various combinations:

✓Hyperplasia of parietal epithelial cells in crescents,

✓Infiltrations of monocytes,

✓Thickening of the basement membrane,

✓Periglomerular fibrosis.

- These changes are mainly observed in glomerulus ischemia due to vascular occlusion.
- **Glomerular cystic atrophy** may occur subsequent to tubulointerstitial scarring, which constricts tubules, inhibits or stops tubular fluid flow, and dilates Bowman's capsules. If glomerulocystic atrophy is diffuse and severe, small cysts can be seen grossly in the cortex and is called glomerulocystic disease.

GLOMERULAR DISEASE

❑ Pathogenesis of generalized glomerulonephritis:

Glomerulonephritis may result from

- the deposition in glomeruli of circulating Immune Complexes,
- formation *in situ* of antibodies against the GBM,

or

- from activation of the alternative pathway of complement.

GLOMERULAR DISEASE

❑ Pathogenesis of generalized glomerulonephritis:

- Accordingly, two glomerulonephritis can be mentioned pathogenetically:

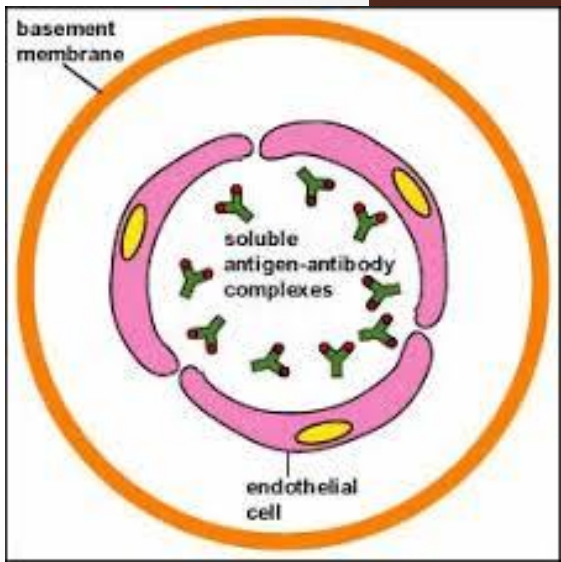
1. **Immune Complex glomerulonephritis**
2. **Anti-GBM** (Glomerular Basemant Membrane) **glomerulonephritis**

GLOMERULAR DISEASE

1. Immune Complex Glomerulonephritis:

- Circulating antigen-antibody complexes localize in glomeruli and are visible by IF or TEM within, or on either side of, the GBM (seen in *granular pattern*).
- Causative antigens may be exogenous (e.g., bacterial or viral proteins) or endogenous (e.g., nucleic acid in systemic lupus erythematosus in humans).
- Immune complex deposition leads to acute or chronic, membranous or proliferative lesions. In the structure of the immune complexes

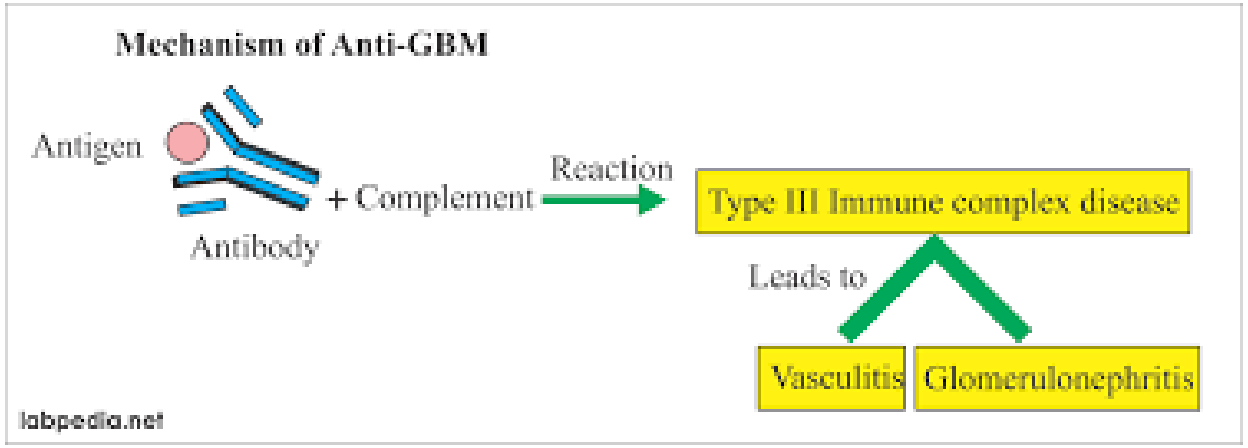
(the antigen and the antibody), there is also complement.



GLOMERULAR DISEASE

2. Anti-GBM (Glomerular Basement Membrane) **glomerulonephritis:** antibodies are formed against intrinsic GBM antigens resulting in a *linear pattern of immunofluorescence* reflecting the uniform distribution of immunoglobulins and complement along the GBM.

- In domestic animals, anti-GBM disease is very rare.



GLOMERULAR DISEASE

- **Morphology of glomerulonephritis**
  - **Acute glomerulonephritis**
  - **Subacute glomerulonephritis**
  - **Chronic glomerulonephritis**

GLOMERULAR DISEASE

➢ Acute glomerulonephritis:

- **Acute glomerulonephritis** may not significantly alter the gross appearance of the kidney,
- May be slightly or markedly enlarged, pale, soft, and edematous.
- Petechiae may be visible if bleeding has occurred from the inflamed glomeruli.

GLOMERULAR DISEASE

Histology of Acute glomerulonephritis:

- Initially hyperemic glomeruli transforms into ischemic form in a short time.
- Neutrophils and/or monocytes marginate in the capillaries and, together with the swollen proliferating endothelial and mesangial cells, give a distinct impression of hypercellularity.
- Occasionally, fibrin thrombi form in the capillaries, or there is fibrinoid necrosis of the tuft. This form of GN with the formation of fibrin thrombi is the usual picture seen in swine with petechiae.

GLOMERULAR DISEASE

➢ Subacute glomerulonephritis:

- In **subacute glomerulonephritis,** the kidney is often enlarged and pale tan with a smooth surface and nonadherent capsule.
- There may be a large number of petechial hemorrhages associated with recurrent acute attacks in the cortex.
- The capsule is tense, and the cut surface bulges. The pale tan cortex is well demarcated from a normal-colored medulla.

GLOMERULAR DISEASE

❑Histology of Subacute glomerulonephritis:

- There is often mesangial hypercellularity or glomerular crescent.
- Fatty degeneration can be seen in tubular epithelial cells.
- Hyaline droplets or necrosis are also found.
- The lumen of the tubules may contain protein, leukocyte and necrotic epithelial cells.

GLOMERULAR DISEASE

➢ **Chronic glomerulonephritis:**

- The kidney is shrunken and contracted with generalized fine granularity of the capsular surface. The capsule may be adherent.
- On cut surface, the cortex is often uniformly narrowed, and the corticomedullary markings are obscured.
- Small cysts, which are obstructed tubules, are often present.
- When contraction is severe, it is grossly indistinguishable from diffuse chronic interstitial nephritis.

Causes of Chronic Glomerulonephritis

- Strep Throat
- Bacterial or viral infections
- Diseases of the immune system such as lupus, immune lung disorder, Good pasture's syndrome, etc.
- Polyarteritis
- Diabetic kidney disease
- Focal segmental glomerulosclerosis (causes scarring of the glomeruli)

GLOMERULAR DISEASE

❑Histology of Chronic glomerulonephritis:

- In the **chronic** phase, scarring of glomeruli occurs.
- There may be a reduction in the apparent number of glomeruli as obsolescent glomeruli blend with surrounding scar tissue.
- The interstitial reaction initiated during the acute phase progresses with fibrosis and lymphocytic infiltration.
- Large numbers of tubules undergo atrophy and are replaced by scar tissue.
- Tubules that remain connected to functioning glomeruli may become dilated.

GLOMERULAR DISEASE

❖**In Period of Renal failure related with chronic GN:**

- An increased volume of urine of low specific gravity can occur.
- Albuminuria can vary and casts may be absent.
- Death is caused by uremia.
- Once the GFR has decreased to 30-50% of normal, progression to end-stage renal failure tends to be unavoidable.

DISEASES OF TUBULES

- *The tubules and interstitium are intimately associated, and damage to one affects the other.*
- *Diseases that involve both compartments are discussed* later under Tubulointerstitial diseases.

DISEASES OF TUBULES

- Acute tubular necrosis/nephrosis
- Aminoglycosides
- Tetracyclines
- Sulfonamides
- Amphotericin
- Ethylene glycol
- Oxalate
- Mycotoxins
- Amaranthus
- Oak poisoning

Acute tubular necrosis/nephrosis

- Acute tubular necrosis, or nephrosis, is a reversible condition in which tubular degeneration is the primary process, and it is an important cause of acute renal failure.
- **"Nephrosis"** is an imprecise term applied to **noninflammatory renal disease**, particularly tubular degeneration; acute tubular necrosis is a more accurate descriptor of the changes to be discussed here.
- Affected animals are oliguric or anuric and die within a few days unless given appropriate therapy.
- The principal causes of acute tubular necrosis are ischemia and nephrotoxins.

Acute tubular necrosis/nephrosis

- Another major cause of acute renal failure is postrenal, namely complete urinary outflow obstruction.
- The renal tubules, and particularly the proximal straight tubule and the medullary thick ascending limb, are metabolically very active and are hence the renal components that are most susceptible to ischemia or nephrotoxins.
- Ischemic or tubulorrhectic acute tubular necrosis follows a period of hypotension (shock) that causes marked renal ischemia.
- *Prolonged renal ischemia causes renal cortical necrosis.*

Acute tubular necrosis/nephrosis

1. *Ischemic acute tubular necrosis*
2. *Nephrotoxic tubular necrosis*

Acute tubular necrosis/nephrosis

1- Ischemic acute tubular necrosis *is characterized histologically by focal necrosis along nephrons, particularly of the proximal tubules, and distal tubules to some extent, plus disruption of tubular basement membranes (tubulorrhexis) and occlusion of lumina by casts.*

- Eosinophilic hyaline and granular casts commonly occur in the distal tubules and collecting ducts.

Acute tubular necrosis/nephrosis

2- Nephrotoxic tubular necrosis: Numerous toxic substances can cause acute tubular necrosis in domestic animals.

- Some of these agents are no longer important as nephrotoxins; for example, organomercurials were commonly used as fungicides on seed grains.
- Kidney tubules (especially proximal tubules) are highly sensitive to various toxic agents.
- The enzyme systems of the cells are exposed to various agents
- (eg heavy metals bound to sulfhydryl groups) or inactivated by various agents.

Table 4.2 Agents that are nephrotoxic in domestic animals

Exogenous	Animal venoms Antimicrobials Aminoglycosides (neomycin, kanamycin, gentamicin, streptomycin, tobramycin, amikacin) Amphotericin B Cephalosporins Polymixins Sulfonamides (sulfapyridine, sulfathiazole, sulfadiazine) Tetracyclines Antineoplastic agents (cisplatin, doxorubicin, methotrexate) Cantharidin (blister beetle) Chlorinated hydrocarbons *Clostridium perfringens* type D, epsilon toxin (pulpy kidney) Contrast media Ethylene glycol Menadione (vitamin K_3) Metals (arsenic, bismuth, cadmium, lead, mercury, thallium) Methoxyflurane Monensin Mycotoxins – citrinin, ochratoxin A Paraquat Plants *Amaranthus retroflexus* (pigweed) *Isotropis* *Lantana camara* Oxalates – various plants *Quercus* spp. (oak) – tannins *Terminalia oblongata* (yellow-wood) Sodium fluoride (superphosphate fertilizer)
Endogenous	Bile Hemoglobin Myoglobin

Acute tubular necrosis/nephrosis

2- Nephrotoxic tubular necrosis:

Nephrotoxic ATN is characterized histologically by the common necrosis of the proximal tubules, but the tubulus basal membranes remain intact.

✓**These two features** serve to distinguish **toxic ATN from ischemic ATN**; **in ischemic necrosis ATN is sometimes localized and the basement membranes are affected.**

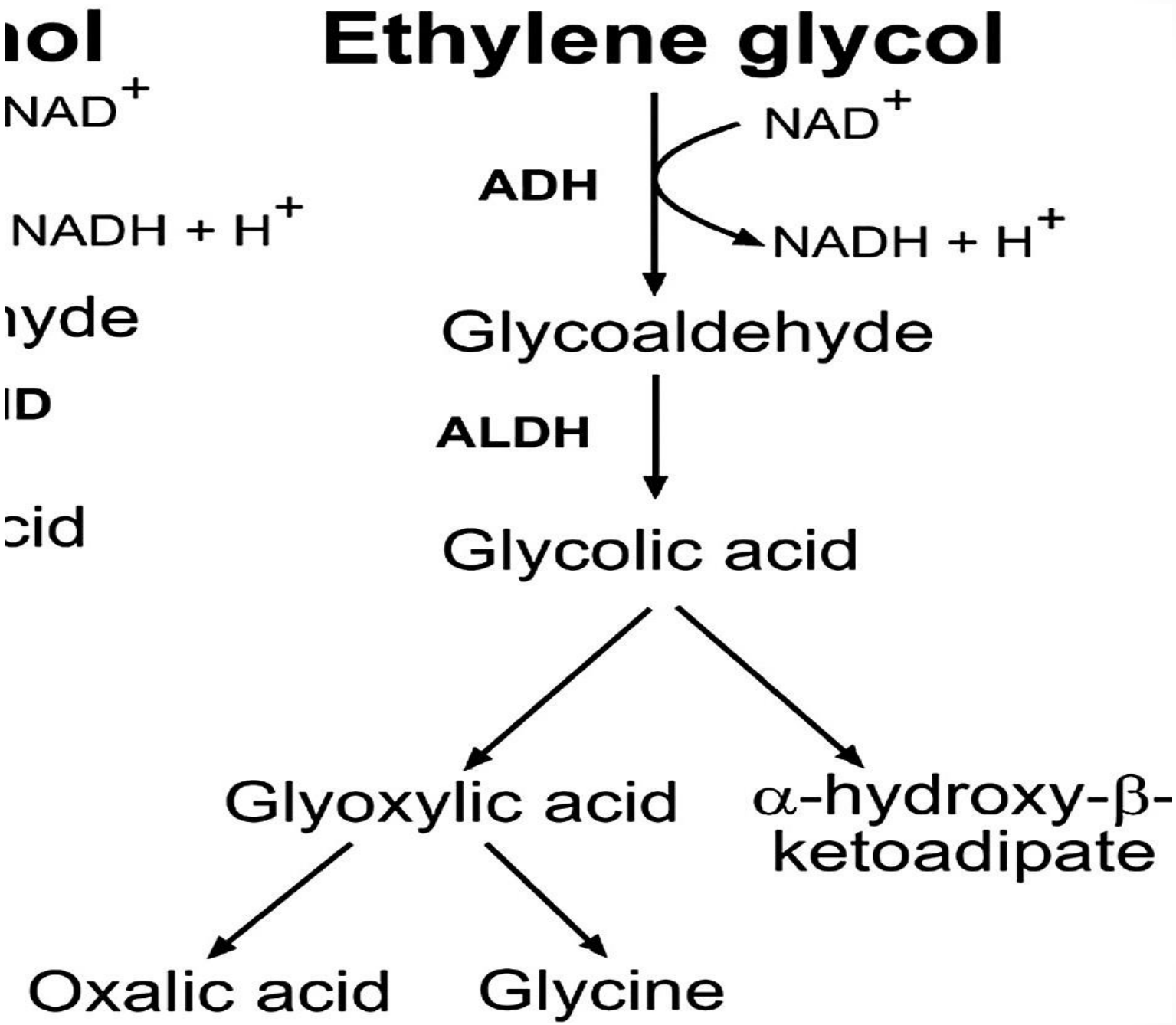
- The integrity of the tubular basement membranes is essential for epithelial regeneration; therefore, ischemic destruction in the kidney is worse in terms of prognosis than toxic degradation.

ETHYLENE GLYCOL

- *Dogs and cats are commonly poisoned by ingestion of ethylene glycol.*
- *The seasonal incidence of this poisoning coincides with* the changing of engine antifreeze solutions in the spring and autumn.
- Ethylene glycol, which is present in a 95% concentration in antifreeze solutions, has a sweet taste and is usually ingested voluntarily, especially by young dogs.
- Cats are more susceptible, but less commonly affected, than dogs; the minimum lethal dose is 1.5 mL/kg for cats and 6.6 mL/kg for dogs.
- Cattle are also occasionally poisoned.

ETHYLENE GLYCOL

- Ethylene glycol, which itself is of low toxicity, is rapidly absorbed from the gastrointestinal tract.
- Most is excreted unchanged in the urine.
- A small percentage is oxidized by alcohol dehydrogenase in the liver to glycoaldehyde, which is in turn oxidized to glycolic acid, glyoxylate, and finally oxalate.
- Glycolic acid (glycolate) is the primary nephrotoxic metabolites.
- Other end products of metabolism are lactic acid, hippuric acid, and carbondioxide.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Glycoaldehyde
ALDH
Glycolic acid
Glyoxylic acid
α-hydroxy-β-ketoadipate
Oxalic acid
Glycine

ETHYLENE GLYCOL

- Depression, ataxia, and osmotic diuresis develop within a few hours after ingestion of ethylene glycol.
- Although oxalate crystals are deposited around cerebral vessels and in perivascular spaces, nervous signs are the result of the effect of aldehydes and possibly to the severe metabolic acidosis that develops as a result of accumulation of lactic acid, glycolate, and glyoxylate.
- Over the next 12 hours, pulmonary edema, tachypnea, and tachycardia occur.
- If the animal survives for 1-3 days after ingestion, Acute Renal Failure (ARF) develops, primarily as the result of nephrotoxicity.

ETHYLENE GLYCOL

- Severe renal edema impairs intrarenal blood flow and contributes to injury.
- Calcium oxalate crystals may be found in tubular lumens, in tubular cells, and in the interstitium; they are light yellow, arranged in sheaves, rosettes, or prisms, and are birefringent with polarized light.
- Tubular lesions, which are most severe in proximal tubules, range from hydropic degeneration to necrosis to regeneration.

ETHYLENE GLYCOL

- In animals surviving the acute toxic insult, calcium oxalate crystals are thought to be of importance in causing renal failure.
- Large numbers of crystals in tubules are virtually pathognomonic of ethylene glycol poisoning.
- Some crystals are seen with

chronic tubular obstruction.