PATHOLOGY OF ORAL CAVITY AND OESOPHAGUS

ORAL CAVITY

Portals of Entry into Alimentary System:

Include ingestion, coughed up by lungs and swallowed, systemic blood-borne infections and parasite migration.

What are the defence mechanisms of the oral cavity?

- Structure
  - The stratified squamous epithelium is resistant to trauma and some irritants
  - The epithelium has very high turnover- they get renewed once every week and that is how oral ulcers are healed very rapidly
  - The taste buds reject potentially toxic materials based on taste or tactile sense.
- Resident flora
  - Natural flora is a protective mechanism to avoid overgrowth of other pathogens. They inhibit the overgrowth of deleterious agents by occupying attachment sites
- Innate immunity
  - Saliva contains secreted immunoglobulin like IgA, that provide specific immunity to many infectious agents
  - There are a lot of phagocytic cells clustered in the submucosa, they can be rapidly mobilized to initiate an inflammatory response
- Saliva
  - Saliva is a good lubricant in the oral cavity, it flushes out deleterious agents
  - It contains several antimicrobial agents including lysozymes, lactoferrin and lactoperoxidase

What are the basic reactions of the GI tract?

1. Altered physiology
   - When mucosa is injured, there is an increase in the secretion of saliva.
   - Sometimes the motility is increased to pass the toxic substances more quickly from the GI tract, resulting in vomiting or diarrhoea
2. Cellular degeneration and necrosis
   - Injury to the cells may be caused by infectious agents, inflammatory mediators or hypoxia leads to degeneration of the cells and subsequent cell death (necrosis).
3. Inflammation
   - Inflammation follows from cell death or due to an infection
4. Cell proliferation and neoplasia
   - In some cases, cells proliferate uncontrollably and lead to cancer. Oral cancers are quite common in domestic animals

Colour changes of oral mucosa:

Examination of the oral mucosa is a part of the routine clinical examination of all animals

- salmon pink, smooth and glistening - normal.
- black = normal melanin deposition is variable in distribution in many species and is progressive with age.
- yellow = jaundice/icterus (e.g. liver/biliary diseases, haemolytic diseases)
- white = anaemia (decreased number of erythrocytes)
- blue =cyanosis (e.g. decreased venous drainage, heart disease)
- red = inflammation, haemorrhage/congestion

- brown = methaemoglobinaemia, porphyruria (e.g. altered erythrocyte oxygen carrying dynamics)

Food:
The presence of food within the oral cavity is abnormal (except in ruminants).
Presence of food can indicate brain disease, oral/pharyngeal/oesophageal disease, gastric disease etc.

Developmental anomalies

Facial Clefts
Due to failure of fusion during embryogenesis. Have been reported in all domestic species. They are usually idiopathic, but some are genetic and heritable, and others are secondary to toxic agents. Include cleft palate (palatoschisis) and cleft lip/hare lip (cheiloschisis).

Palatoschisis is due to failure of closure of the lateral palatine processes of the maxillary bones.
Important sequelae to the animal are starvation due to the inability to create a negative pressure in the mouth and resultant failure to suckle and aspiration pneumonia (no effective separation between nasal and oral cavity).

Mandibular/maxillary anomalies

- Brachygnathia - inferior = short mandible "parrot mouth". Occurs in cattle, sheep, horses and dogs. Genetic cause in some breeds of cattle, sheep and long-nosed dogs.
- Brachygnathia – superior = short maxilla. Heritable in dog, swine and cattle breeds. Progressive with age
- Agnathia = absence of mandible. Most common in lambs, usually associated with other facial abnormalities

Dental disease

- Abnormalities in the number of teeth
- Abnormalities in the position of teeth
- Enamel hypoplasia
  Enamel is fully formed when the tooth erupts. Some infections like BVDV virus (Bovine Viral diarrhoea) in cattle (in utero infection) and canine distemper virus in dogs leads to necrosis and disorganisation of the enamel organ. Segmental enamel hypoplasia results from lack of enamel formation during the period of virus infection.
- Odontodystrophies (Odonto = teeth, dystrophy = abnormalities in development)
  - Calcium and phosphorus deficiency
  - Fluorosis, lead and silver poisoning

Excessive fluoride in the diet can lead to fluoride incorporation into the enamel and dentine. This result is soft chalky discoloured enamel, usually yellow, dark brown or black

- Plaque and calculus (tartar)
- Tooth abscess

Dental diseases are briefly mentioned here and will be taught elsewhere.

Inflammation

Terminology**:**

- **Stomatitis** = diffuse inflammation of the oral cavity

Localized inflammation of the oral cavity is described as follows:

- **Cheilitis** = inflammation of the lips
- **Pharyngitis** = inflammation of the pharynx
- **Glossitis** = inflammation of the tongue
- **Tonsillitis** = inflammation of the tonsils
- **Gingivitis** = inflammation of the gingiva

Clinical signs of oral cavity inflammation:

- anorexia
- hypersalivation (**ptyalism)**
- bad breath **(halitosis)**
- reddening, swelling, exudates affecting the oral tissues (indicating inflammation)
- ulcers, erosions, masses

Classification of inflammation based on macroscopic appearance

- Vesicular stomatitis
  - Foot and mouth disease
  - Vesicular stomatitis
  - Swine vesicular disease
  - Vesicular exanthema
  - Autoimmune disease
  - Photo irritation
- Erosive and ulcerative stomatitis
  - Viral
  - Metabolic
  - Other causes
- Papular stomatitis
  - Bovine popular stomatitis
  - Orf
- Idiopathic stomatitis
  - Oral eosinophilic granuloma
  - Feline lymphoplasmacytic gingivitis
- Deep stomatitis
  - Necrotising stomatitis
  - Granulomatous stomatitis

- **Papule**: raised flat topped lesion
- **Vesicle**: A thin walled, raised, fluid-filled lesion
- **Erosions:** partial loss of epithelium, forming a shallow indentation
- **Ulcers**: full thickness loss of epithelium forming a deep indentation.
- **Necrosis**: cell death
- **Granuloma**: collection of macrophages often surrounding a necrotic centre

Causes of oral cavity inflammation:

The oral cavity contains a finely balanced array of bacterial organisms. Stress, systemic illness, nutritional or hormonal imbalances may tip the balance and allow overgrowth or invasion of pathogenic bacteria. Catarrhal stomatitis is a common, non-specific condition which often develops in systemic disease states. e.g. Overgrowth of commensal organisms. Resolves when the normal oral function is restored.

Causes of stomatitis

- Infectious agents – virus, bacteria, migrating parasites, fungal organisms (overgrowth of commensal candida species leading to thrush)
- Trauma due to sharp feed, overgrown teeth, improper use of drenching or balling guns (in ruminants)
- Chemical injury – accidental ingestion
- Autoimmunee disease

Vesicular stomatitis

- Foot and mouth disease
- Vesicular stomatitis
- Swine vesicular disease
- Vesicular exanthema
- Autoimmune disease
- Photo irritation

Vesicles are small, clear, fluid-filled lesions common on the lips, tongue and oral mucosa. The vesicles are very short-lived as they quickly rupture to leave a raw, erosive surface.
Causes are most commonly viral, auto-immune disease and photo irritation.

Viral

Viruses are cytolytic (cause lysis of cells) and the resultant release of viruses from cells infect the neighbouring cells. The lesions enlarge centripetally forming vesicles. Bullae result from vesicle coalescence. The epithelium covering large bullae easily ruptures, subsequently ulcers are created. Important causes of oral vesicles are viral, and most are exotic to Australia. Examples include:

- **Foot and mouth disease (FMD) (exotic)**

Family: Picornavirus Genus: Aphthovirus

The most economically important of the vesicular diseases. It affects ruminants and pigs. An acute, febrile disease which produces vesiculo-erosive lesions affecting the muzzle, oral mucosa, tongue, mammary epithelium, and the coronary band of the hooves.

- **Vesicular stomatitis (exotic)**

Family: Rhabdovirus Genus: Vesiculovirus

Infects horses, cattle, pigs, humans, lab animals, wildlife. Animals are bright and alert.
Generally, only one foot is affected; primarily get extensive tongue ulceration that heals rapidly. Americas.

- **Swine vesicular disease (exotic)**

Family: Picornavirus Genus: Enterovirus

Only in pigs. Clinically indistinguishable from FMD. Produces a vesiculo-erosive disease mainly affecting the feet, but can cause stomatitis, myocarditis and meningitis. Swill feeding uncooked pig meat.

- **Vesicular exanthema (exotic)**

Family: Calicivirus

Pigs only. Historically important as it produced an identical clinical disease to FMD.

Disease	***Cause***	***Ruminants***	***Pigs***	***Horses***
FMD	Picornavirus	+	+	-
Vesicular stomatitis	Rhabdovirus	+	+	+
Vesicular exanthema	Calicivirus	-	+	-
Swine vesicular disease	Enterovirus	-	+	-

Another Calicivirus of importance is **Feline Calicivirus**
This is an **endemic disease in Australia**. Generally, produces a respiratory disease in cats, but the condition may be complicated by oral ulcers that start out as vesicles.

- **Autoimmune diseases**

A number of autoimmune disease cause vesicle in companion animals. Desmosomes are adherence junctions between epithelial cells. In some animals, the body produces antibodies against desmosomal proteins leading to lysis of cell to cell junctions. This leads to vesicle formation in the epithelial layer with freely floating epithelial cells (acantholysis). Pemphigus refers to a group of autoimmune disease characterised clinically by vesicles, which later progress to bullae, pustules, erosions and ulcers. Histologically, these diseases are characterised by loss of adhesion between cells (acantholysis).

- **Photo irritation**

Ingestion of plants containing photodynamic agents leads to accumulation of photoreactive substance under the skin. On exposure to sunlight, these agents become activated and cause vesicle formation. Compared to FMD, the animals do not exhibit fever and there are no foot lesions. However, it can occur as a herd outbreak, as most of the animals are fed similar food.

*Also, with vesicular stomatitis, erosion and ulceration can occur; in those however ulceration/erosion is preceded by vesicle formation and rupture.

Erosive and ulcerative stomatitis

Ulcers are typically red and depressed. They are painful and often lead to excess salivation and/or decreased food intake.

- Viral causes
  - Bovine viral diarrhoea
  - Rinderpest
  - Malignant catarrhal fever

Blue tongue

- Metabolic
  - Uraemia
  - Vitamin C deficiency
- Other causes
  - Photosensitization
  - Upper alimentary ulcerative syndrome
  - NSAID treatment

- **Bovine viral diarrhoea virus (BVDV) - mucosal disease**

Family: Flavivirus Genus:Pestivirus
BVDV is **endemic in Australia**
Different forms of infection depending on the virus genotype (cytopathic and non-cytopathic), time of the infection, and pregnancy status of the animal.

There is initial transplacental (in utero) infection of the early fetus with the non-cytopathic virus results in the birth of a calf that has a lifelong persistent viraemia (persistent infection). These calves (and only these calves) may later develop mucosal disease as a result of superinfection with a "homologous" cytopathic BVDV. In the field, mucosal disease usually affects animals of six to 18 months of age. In these animals, characteristic lesions include sharply demarcated erosions and ulcers in the tongue, gingiva, palate, oesophagus, rumen, abomasum and coronary band of the hooves.

- **Rinderpest (exotic) – ruminants and pigs**

Lesions are similar to BVDV. It is caused by a morbillivirus. Acute necrosis of all lymph nodes and epithelial lining of alimentary tract including ulcers of the oral cavity and nasal planum

- **Malignant catarrhal fever**

Caused by a herpes virus, clinical signs overlaps with BVDV, but a distinctly different syndrome. Seen in cattle farmed with sheep. Pathogenesis is slightly different to BVDV, it mainly causes arteritis, thrombosis, reduced blood flow, ischaemia (reduced blood flow), infarction and ulceration.

<u>Other viral diseases that cause similar lesions include:</u>

- Border disease (sheep)
- Peste des Petits Ruminants (exotic) – small ruminants
- Bluetongue – sheep/cattle
- Bovine rhinotracheitis (IBR) - cattle
- Feline viral rhinotracheitis – cats

<u>Metabolic causes</u>

- **Uraemia**

This is an example of systemic disease with secondary involvement of the tongue. There is extensive ulceration of the mucosal epithelium of the tongue associated with increased concentrations of serum blood urea nitrogen (BUN) and creatine forms which cause vasculitis (inflammation of blood vessels) and thrombosis (occlusion of the vessel) with consequent necrosis of the epithelium. It occurs typically at the margins of the tongue.

- **Vitamin C deficiency**

Ulcerative stomatitis in primates and guinea pigs can result from vitamin C deficiency

Other causes

- **Photosensitization**. This most commonly affects the skin, but tongue may be affected as well if exposed to sunlight (covered in skin pathology next year)
- **Upper alimentary ulcerative syndrome** Recently identified syndrome of weight loss, diarrhoea and mortality in weaned dairy claves. Characteristic lesions are alimentary tract ulceration and enteritis. Etiology is unknown
- **NSAID toxicity** – common cause of oral ulceration in horses

Papular stomatitis

Due to Parapox viral infections and include **Orf** (contagious ecthyma) of sheep and goats, and **bovine papular stomatitis**. These initially produce papillomatous lesions (wart-like) which become ulcerative, and then form proliferative scabs prior to healing.

Idiopathic stomatitis

- **Eosinophilic stomatitis (Oral eosinophilic granuloma, rodent ulcer)**

Oral granulomas or ulcers ("rodent ulcers") occur frequently in cats. They are also termed oral eosinophilic granulomas. Although the aetiology of this condition is unknown, the histologic appearance of lesions suggests an immune-mediated mechanism.

Lip lesions are commonly visible near the philtrum and may extend through the adjacent haired skin. Oral lesions may occur anywhere in the mouth including gingiva, hard and soft palate, oral and nasal pharynx, tongue.

It also occurs in dogs (rarely), more frequently in the lateral margins of the tongue. Histologically eosinophilic granulomas are characterized by eosinophils, giant cell and mast cell infiltrate and multifocal areas of collagenolysis (collagen is acellular, it cannot undergo necrosis).

- **Feline lympho-plasmacytic stomatitis.**

This is an idiopathic condition of cats named on the basis of the histological appearance of the lesion. It is a chronic condition characterized by red, inflamed gums, fetid breath, and inappetence. The oral mucosa is hyperplastic and ulcerated. Associations have been hypothesized between this condition and the presence of bacteria or calicivirus associated with Feline Leukaemia Virus (FeLV) and Feline Immunodeficiency Virus (FIV).

Deep stomatitis

Deep stomatitis involve layers beneath the epidermis (connective tissue, muscle and bone). These can be due to viruses, bacteria, chemical or thermal injury. Conditions in domestic animals often become necrotic and include:

- **Calf diphtheria (Oral necrobacillosis)**

Occurs in cattle, sheep and pigs and is characterized by a necrotising stomatitis. In calves, referred to as **calf diphtheria** where it causes an acute, necrotizing ulcerative inflammation of the buccal and pharyngeal mucosa. Oral necrobacillosis is often caused by *Fusobacterium necrophorum*. Necrotizing stomatitis is the end stage of all other forms of stomatitis when they are complicated by infection with *Fusobacterium necrophorum.* Noma is a rapidly spreading gangrenous stomatitis and is

associated with tissue invasion of normal microflora, particularly fusobacteria and spirochetes.

- **Actinobacillosis - wooden tongue**

Occurs in cattle (also pigs and sheep), due to infection with *Actinobacillus lignieresii* which often gains entry through traumatic injuries of the mucosa. It is a granulomatous inflammation (macrophages are the main cell infiltrate) and it affects lymphatics.

- ***Actinomycosis*– lumpy jaw**

Occurs in cattle and many species due mainly to *Actinomyces bovis*. The bacterium infects soft tissues of the oral cavity (connective tissue and muscle) and typically spread to bone, causing osteomyelitis (inflammation of bone). Inflammation is typically pyogranulomatous (macrophages and neutrophils)

Both *Actinomyces* and *Actinobacillus* live in the mouth and invade tissue through breaks in the lining of the mouth cavity. Low-quality dry stalky feed, grass seeds, coarse hay and scrub can cause mouth abrasions which allow entry of infection. These factors are commonly associated with dry times and drought. Breaks in the gums that occur as teeth erupt in young animals can also predispose to lumpy jaw. Ironically, increased incidence has also been reported after flooding.

- **Foreign body granulomas**

Implanted foreign material e.g. plant awns can stimulate a focal chronic granulomatous response (macrophage rich) anywhere in the oral cavity, with or without secondary bacterial infection.

PROLIFERATIVE CONDITIONS

In dogs, 70% of tumours of the alimentary system are in the oral cavity.

HYPERPLASTIC DISEASES

- **Fibrous hyperplasia (Gingival hyperplasia)**

Benign overgrowth of gingival mucosa, which can be mild to severe where it buries the adjacent teeth. Common in brachycephalic dogs such as Boxer dogs. Grossly it is indistinguishable from other tumors in particular from epulides.

- **Epulides**

Epulis = generic and clinical term for tumour-like masses on the gingiva. Can be hyperplastic or neoplastic (benign).
There are different types of epulides, the most common are the **fibromatous** and the **acanthomatous**. The fibromatous (characterized by submucosal proliferation of fibrous tissue) arises from the peri-odontal ligament and has a benign behaviour. The acanthomatous is characterized by proliferation of epithelium and has a malignant/infiltrative behaviour (invades bone and can be destructive). More recent classification of these tumours has placed them together as variants of **peri-odontal fibroma**.

- **Oral papillomatosis (warts)**

This condition is due to a papillomavirus and occurs primarily in puppies, and less so in foals, calves and rabbits. The lesions are transmissible and occur in young animals less than 1 year. Lesions are papilliform or cauliflower-like, white and friable and occur throughout the oral cavity. Lesions usually regress spontaneously, and immunity is long lasting.

NEOPLASTIC DISEASES

In the oral cavity, neoplasms are usually malignant. Types include:

- **Squamous cell carcinoma**

Most common in older cats, also common in dogs. In cats, tumour is generally located on the

ventrolateral surface of the tongue. In dogs, they are frequently located on the tonsils, and less commonly, the gingivae.
Squamous cell carcinomas arise from the squamous epithelium (lining) of the oral cavity

- **Melanoma**

This is the most common oral tumour in dogs, over 90% are malignant, and most are considered to have metastasized by the time of diagnosis to regional lymph nodes and lung. Characterized by rapid growth, with necrosis and ulceration common.

Melanomas arise from resident melanocytes of the mucosa; some tumors have pigment (melanin); a large proportion of oral melanomas doesn't have pigment (amelanotic melanoma). Amelanotic forms are extremely malignant.

- **Fibrosarcoma**

Frequently seen in dogs <5 years of age. Occurs mainly in gums of the upper molars and adjacent soft palate, and the anterior half of the lower mandible. They frequently invade bone, grow rapidly and frequently recur after surgical removal. About 35% metastasize to regional lymph nodes and lungs early in disease course. Tumours are grey to red, large and firm, irregularly shaped and usually ulcerated.
It arises from the fibroblasts/connective tissue of the oral mucosa.

Tonsils

- Tonsils are lymphoid structures covered by stratified squamous epithelium
- Inflammation of tonsils = tonsillitis, caused by viral and bacterial infections
- Foreign bodies may lodge in tonsils leading to inflammation
- Two types of neoplasm 1) Squamous Cell Carcinoma – originating from the stratified squamous epithelium. It is a locally invasive malignant neoplasm. 2) Lymphoma – originating from the lymphoid structures.

Salivary glands

- There are major and minor salivary glands, minor glands are distributed throughout the oral cavity
- Ptyalism – range of reasons could lead to increased salivation
    - stomatitis
    - CNS disease causing salivation, e.g. Rabies
    - Poisoning with organophosphates, caused by stimulation of muscarinic receptors
- Salivary cyst – soft fluctuating mass- pure mucus obtained in fine needle aspiration – also known as salivary mucocele, accumulation of salivary secretions in cavities present in the soft tissues of the mouth or neck. Most commonly arise from sublingual salivary gland, but other locations are sporadically described
- Sialadenitis – etiology is unknown – necrotising inflammation, could lead to septic shock.
- Adenocarcinoma do occur occasionally – often arise from minor salivary glands, difficult to identify

OESOPHAGUS

The oesophagus is lined by non-keratinised stratified squamous epithelium in carnivores, and is keratinised in pigs, horses and ruminants. It is unique in that it lacks a serosa, therefore perforations due to foreign bodies will not seal themselves off, nor will sutures seal an incision.

Clinical signs suggestive of oeosophageal diseases include ptyalism, regurgitation, vomiting, dysphagia, inadequate growth rate in young animals, weight loss and aspiration pneumonia.

- **Megaoesophagus**

Can be congenital or acquired, and occurs in dogs, cats and horses. Results from segmental or diffuse dysfunction of eosophageal musculature, producing a dilated, flaccid oesophagus. Uncoordinated or insufficient peristaltic movements mainly affect the mid and cervical oesophagus. Ingesta accumulate in the lumen and are regurgitated. The oesophagus is generally uniformly dilated, which results in a ventral displacement of the heart on radiography.

Congenital conditions are generally idiopathic. A specific cause is a **persistent right fourth aortic arch**. This results in eosophageal dilation cranial to the heart, whereas all other mega eosophageal conditions produce dilation cranial to the stomach. Occurs in dogs, occasionally in cats, rarely in other species.

Acquired megaoesophagus may be idiopathic and/or attributable to neurological (innervation, denervation) disorders, (e.g. autonomic neuropathy), partial physical obstructions to stenosis, secondary to inflammatory diseases of eosophageal musculature. Specific disease conditions include myasthenia gravis, hypothyroidism (due to general muscle atrophy), lead poisoning (due to neurological damage), snakebite, neck trauma or brain stem disease.

- **Oesophagitis**

Oesophagitis can be erosive or ulcerative and may be associated with ulcerative intraoral disease (diseases extending from the mouth), gastric reflux (reflux oesophagitis) or exposure to irritant chemicals (paraquat, oak toxicosis).

The most serious sequelae to chronic oesophagitis is **stenosis** (narrowing of the lumen) due to scarring. Superficial epithelial damage heals uneventful, but deep lesions produce scar tissue, which upon contraction leads to stenosis.

- **Obstruction, perforation and stenosis**

Choke = oeosophageal obstruction due to impaction or is secondary to stenosis or motility disorders. Impaction of the oesophagus occurs when large, or inadequately chewed food material, such as potatoes, corn cobs, apples, bones, masses of grain, lodge in the oesophageal lumen.

Commonly occurs where the diameter of the oesophagus is the smallest: larynx; thoracic inlet; heart base; anterior to diaphragm. Obstruction leads to mucosal damage (due to pressure necrosis) which then leads to perforation and/or stenosis. Stenosis may also be due to external constriction by vascular ring anomalies such as persistence of the right aortic arch.

From a mechanistic perspective, obstructions of tubular organs such as the oesophagus can be considered to be of intramural, mural or extramural origin.

Oesophageal perforation can occur with obstructive lesions or can occur with ingestion of sharp foreign bodies (e.g. bones in carnivores).

Muscular hypertrophy of the distal oesophagus Idiopathic, reported in horses and pigs. Usually of no clinical significance, even though the hypertrophy can look impressive! (see prac images)

Parakeratosis and squamous metaplasia of oesophageal submucosal glands. A degenerative change that occurs with chronic vitamin A deficiency or zinc deficiency, mostly seen in birds.

- **Parasitic infections**

Generally incidental findings at post-mortem, rarely cause disease or functional abnormalities.

Incidental parasites include:

- ***Sarcocystis* spp** = protozoa that parasitise striated and cardiac musculature of various herbivores such as sheep. Affected muscles include the oesophagus where ovoid, 1 cm long, white nodules project from the musculature.
- ***Gongylonema* spp** affects ruminants, pigs, horses. They reside under the mucosa and can be seen as thin red serpentine structures.
- ***Trichomonas spp*** commonly affect the oral cavity, oesophagus and crop of birds leading to formation of inflammation and formation of caseous plaques on the mucosal surfaces.

Pathogenic parasites include:

- ***Spirocerca lupi*** is a parasite that uncommonly causes lesions in dogs and canids. It causes a florid inflammatory reaction that is granulomatous and fibrosing. The lesion frequently evolves and transform into neoplasia (fibrosarcoma). Intraluminal nodules may protrude into the eosophageal lumen and can result in a dysphagia or obstruction.

- **Neoplastic disease**

Oesophageal neoplasms are rare but include squamous cell carcinomas (arising from the epithelial lining of the mucosa) and smooth muscle tumours (leiomyomas, leiomyosarcomas).