Regulation of Calcium – Phosphorus Balance in the Body

- **Diet** – a healthy diet should approximate the normal 2:1 ratio of Ca:P found in bone. Too little Ca and too much P can lead to disease.
- **Hormones** involved in Ca-P balance
  - Vitamin D; 1,25 dihydroxycholecalciferol
  - Parathormone
  - Calcitonin
Stimuli for hormone secretion

- **Vitamin D**
  - ↑ calcium
  - ↑ PTH

- **Parathormone (PTH)**
  - ↓ calcium
  - ↑ phosphorus

- **Calcitonin**
  - ↑ calcium

Above: Ultrastructure of thyroid C cell

Calcification and mineralization are terms used interchangeably to describe the process by which certain tissues (bone and teeth) are converted to hard tissues. This is a normal event.

Pathological calcification is a lesion in which calcium salts (typically calcium phosphate) are deposited abnormally in soft tissues.
Pathologic calcification - two forms

- **Dystrophic** – occurs in degenerating and necrotic (dead) tissue
  - Elevations in serum calcium or deranged calcium metabolism are not required
- **Metastatic** –
  - Associated with elevations in serum calcium

These distinctions overlap with some disorders

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Dystrophic Calcification

- Can occur with any type of necrosis but not as common with liquefaction
- Common tissues affected
  - Heart, skeletal muscle
  - Caseating granulomas (tuberculosis) anywhere
- Dead and dying cells cannot regulate calcium content – accumulation commonly occurs initially in mitochondria
- Significance – calcification, per se, has little unless there is mechanical interference

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Nutritional Myopathy – Vit E / selenium deficiency
Calf w/ Vit E-Selenium Deficiency

Calcification of necrotic cardiac myocytes – Minoxidil toxicity in a pig

note the line of demarcation with viable cells

Lamb – periventricular leukomalacia
Dystrophic Calcification – the skin

- **Calcinosis circumscripta** – fairly common in large dog breeds. Rarely reported in humans and uncommon in other animals
- **Sites** – commonly occurs over boney prominences or at sites of previous trauma
- **Lesions**...
Calcinosis cutis

- **Occurrence** - Most commonly seen in dogs with hyperadrenocorticism (Cushing’s disease)
- **Mechanism** - How cortisol excess leads to mineralization is unknown but it is regarded as either a form of dystrophic mineralization or idiopathic
- **Lesions** are most commonly microscopic and these will be covered first.

Mineral is primarily deposited in collagen bundles inciting a variable inflammatory reaction.

Other sites of mineralization are hair follicles.

In chronic, severe cases, mineralization is dramatic and extrudes through the skin to the surface.
Metastatic Calcification

• Associated with elevated serum calcium and/or deranged calcium metabolism.
  – **Hyperparathyroidism** – too much parathormone
    • Primary
    • Secondary
      – Nutritional
      – Renal
    • Neoplastic
  – **Hypervitaminosis D**
  – **Destruction of bone**

Primary Hyperparathyroidism

• Increased secretion of PTH leads to hypercalcemia and hypophosphatemia
  – Hereditary hyperplasia – German shepherd puppies
  – Secretory parathyroid neoplasms

Secondary Hyperparathyroidism – **Nutritional**

• Too much phosphorus in the diet
  – Seen in herbivores
  – Due to feeding grain-based rations that are high in phosphorus and low in calcium
  – High phosphorus stimulates PTH
  – Ca resorption from bone → Hypercalcemia
• Too little calcium in the diet
  – Does not usually result in metastatic mineralization. WHY?
Secondary Hyperparathyroidism
Chronic Renal Failure - Uremia

• Mechanisms
  – Hyperphosphatemia – failing kidney is no longer able to excrete P
  – Low vitamin D – failing kidney cannot convert vit D to more active form
  – Hypocalcemia
  – Stimulation of PTH
  – Resorption of Ca from bone
  – Hypercalcemia widespread mineralization of soft tissues

Severe mineralization further compromises renal function!

Uremic mineralization of the costal pleura
Mineralization in the kidney commonly involves Bowman's capsule and tubular basement membranes.

Mineralization in the lung can involve alveolar septae and connective tissue supporting bronchi and bronchioles.

Uremic mineralization of stomach – commonly affects the middle 1/3 of mucosa

Von Kossa stain for calcification
Osteopenia
Another consequence of excessive parathormone production

Paraneoplastic Syndromes
Hyperparathyroidism
• Some cancers produce biologically active hormone-like substances
• Occurs when the cells originating the cancer do not normally produce hormonal substances
• In animals, production of active PTH-like substances occurs most commonly with:
  – Lymphoma – a cancer of the lymphoid system
  – Anal sac apocrine adenocarcinoma in dogs

Anal sacs are paired and lie on either side of the anus.
Apocrine (sweat) glands are associated with the sacs.
EM – anal sac adenocarcinoma

Metastatic Calcification
Vitamin D poisoning

- Overzealous supplementation – rabbits very susceptible
- Poisonous plants containing vitamin D-like compounds
  - *Cestrum diurnum*
  - *Solanum malacoxylon*
Ectopic Bone

- Ectopia = displacement or malposition
- Ectopic bone – bone in a tissue where it is not normally found
- Two types of ectopic bone:
  - Heterotopic
  - Osseous metaplasia

Heterotopic Bone

- Heterotopia – typically normal tissue found in an abnormal location
- Thought to originate from embryonic rests of cells that occur during development

Lungs – Dogs and Cattle

*Usually of no clinical significance*
Dural ossification – ossifying pachymeningitis
Sometimes blamed for back pain and paresis

Osseous metaplasia

- Transformation of a cell or tissue from one type to another type
- Osseous metaplasia commonly develops from connective tissues at sites of:
  - Chronic inflammation
  - Florid reparative processes
  - Certain types of neoplasms

Neoplasms and osseous metaplasia

- **Connective tissue neoplasms – sarcomas**
  - Example: fibrosarcoma; ossifying fibroma
- **Epithelial neoplasms**
  - Mixed tumors: mammary, salivary, thyroid, apocrine (sweat) glands
  - Others - pilomatrixicoma
  - **Significance: the osseous component can become neoplastic also**
Sample Question #1

Define and explain the differences between dystrophic and metastatic calcification.
Sample Question #2

Briefly explain the pathogenesis of pathological calcification in vitamin D poisoning. Is this a form of metastatic or dystrophic calcification.