

Disorders of Calcium Metabolism

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LABORATORY EVALUATION

Usually measuring total calcium

Methods for determining ionized Ca are available

Degree of protein binding affected by pH

Ionized Ca decreases by 0.15 mg/dl for every 0.1 unit
increase in pH

DISTRIBUTION OF CALCIUM

Total calcium is divided into:

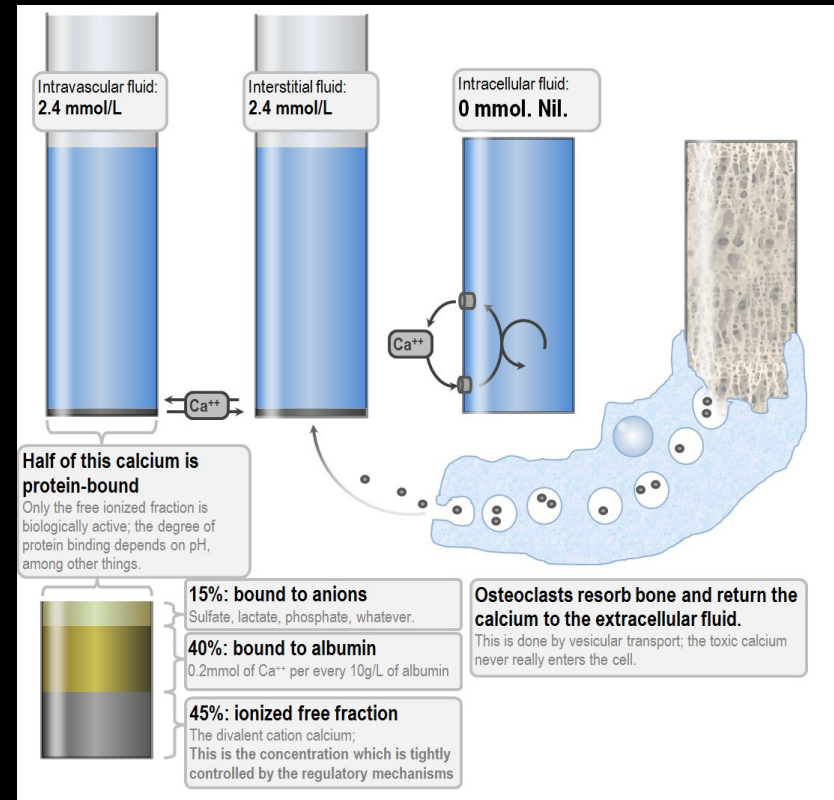
Protein bound (50%)

90% bound to albumin

Ultrafiltrable (50%)

Complexed Ca (15%)

Ionized Ca (45%)



CALCIUM REGULATION

Vitamin D

Liver converts D_3 to $25-D_3$

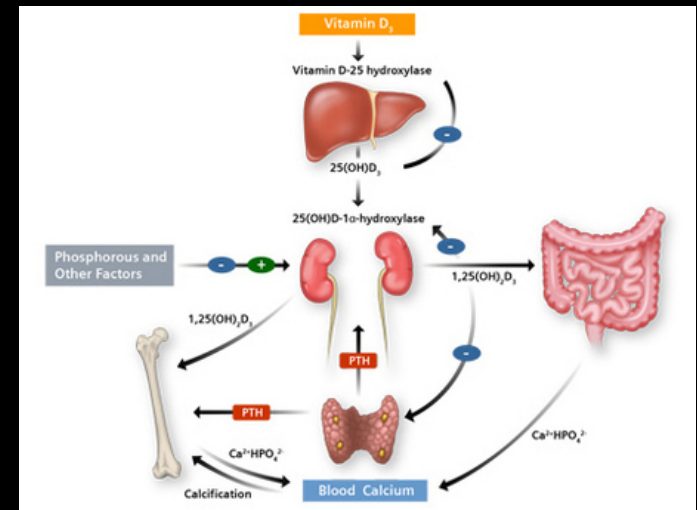
Kidney converts $25-D_3$ to $1,25-D_3$

Enhances GI absorption of Ca and PO_4

Mobilizes Ca and PO_4 release from bone

Enhances renal re-absorption of Ca and PO_4

Suppresses PTH release



CALCIUM REGULATION

Parathyroid hormone (PTH)

84 amino acid polypeptide

Biologic effects mediated through amino
terminus

PTH acts through adenyl cyclase increasing cAMP

Results in phosphaturia and hypocalciuria

CALCIUM REGULATION

PTH Related Peptide (PTH-rp)

Responsible for humoral hypercalcemia of malignancy
(HHM)

Lymphoma, anal sac carcinoma, others

Binds to the PTH receptor

Actions similar to PTH

Results in hypercalcemia; PTH levels low to
undetectable

DIAGNOSTIC APPROACH TO HYPOCALCEMIA

Clinical Signs

Weakness; lethargy

Ataxia; stiff gait

Focal trembling; twitching

Seizures

Generalized muscle
fasciculations

Polyuria, polydipsia

Cataracts

DIFFERENTIAL DIAGNOSIS OF HYPOCALCEMIA

Laboratory error

Puerperal tetany

Hypoalbuminemia

Hypomagnesemia

Chronic or acute renal failure

Malabsorption; enemas

Primary hypoparathyroidism

Pseudo-hypoparathyroidism

TREATMENT OF HYPOCALCEMIA INITIAL MANAGEMENT

Ca gluconate 10% solution
0.5 - 1.5 ml/kg IV slowly
Monitor EKG
Do not use CaCl

After initial control
Ca gluconate SQ every 6-8 hours
Dilute 50% with saline

TREATMENT OF HYPOCALCEMIA

Daily monitoring of Ca

Calcitriol

25 - 40 ng/kg PO q 24 hours

DIFFERENTIAL DIAGNOSIS OF HYPERCALCEMIA

Laboratory error

Malignancy

- Lymphoma

- Anal sac carcinoma

- Multiple myeloma

- Bone tumors

- Others (mammary, prostate, SCC)

DIFFERENTIAL DIAGNOSIS OF HYPERCALCEMIA

Primary hyperparathyroidism

Chronic renal failure

Hypoadrenocorticism

Young animals

Hypervitaminosis D

Granulomatous disease

- Blastomycosis

- Granulomatous skin disease

FELINE HYPERCALCEMIA

Neoplasia

SCC, LSA

Renal Failure

Primary Hyperparathyroidism

Diet

Acidifying diets

Role of fiber

Role of prednisone

Granulomatous disease

Cryptococcus

DIAGNOSTIC APPROACH TO HYPERCALCEMIA

Repeat Ca

Correction for albumin

Rule-out exposure to Vit D

Good physical examination

- Lymph node

- Anal sac

DIAGNOSTIC APPROACH TO HYPERCALCEMIA

CBC/SMA

Rule-outs

Ca x PO₄ product

With PTH or PTH-rp

Hypercalcemia with low or low normal PO₄

Urinalysis

Increased incidence of UTI

Specific gravity < 1.020

DIAGNOSTIC APPROACH TO HYPERCALCEMIA

Thoracic radiographs

If animal is symptomatic

Abdominal radiographs

Bone marrow

Abdominal US

If animal is asymptomatic

PTH, ionized Ca, PTH-rp

DIAGNOSTIC APPROACH TO HYPERCALCEMIA

PTH and Ionized Ca

PTH and iCa are elevated

Primary hyperparathyroidism

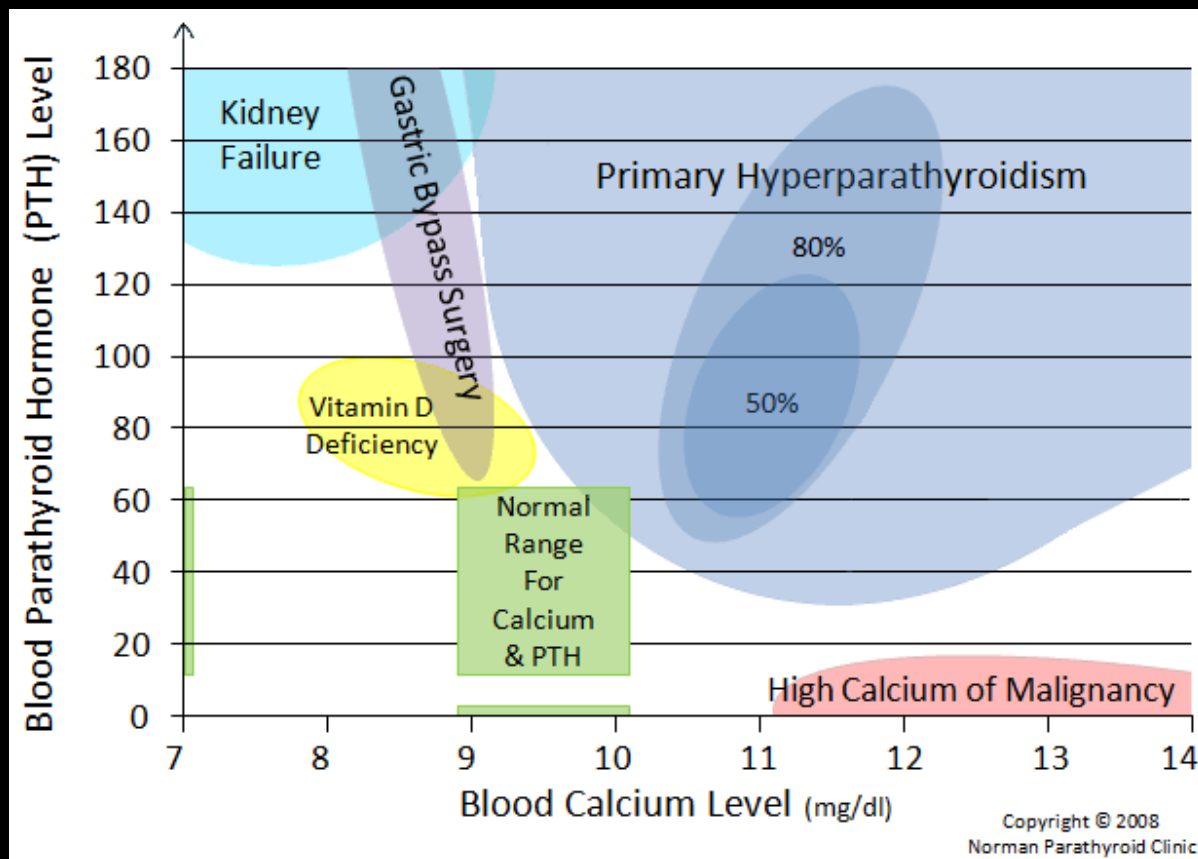
PTH elevated, iCa low

Renal secondary hyperparathyroidism

PTH low, iCa high

HHM

DIAGNOSTIC APPROACH TO HYPERCALCEMIA



TREATMENT OF HYPERCALCEMIA

Identify and treat the underlying disorder

Correct dehydration

- Saline diuresis

- Fluctuations in ionized Ca

- Lasix 2 - 4 mg/kg BID to TID

TREATMENT OF HYPERCALCEMIA

Glucocorticoids

- Cytotoxic

- Decrease GI Ca absorption

- Pros and cons

- 1 - 2 mg/kg/day

Salmon calcitonin

- 4 U/kg IV then 4 - 8 U/kg SC BID

TREATMENT OF HYPERCALCEMIA

When dietary modification and prednisolone are not successful, use of bisphosphonates should be considered. A number of cats have been successfully treated with 10 mg of alendronate (Fosamax) orally once weekly for up to one year. It's extremely important to give the drug on an empty stomach to increase GI absorption of the drug. Erosive esophagitis is a known side effect of oral bisphosphonates in humans, but has not been reported in cats. However, we recommend that the owner give 5–6 ml of water to their cat with a dosing syringe immediately after administration of alendronate; they then can apply a small amount of butter on the cat's lips to increase licking and salivation, which might further promote the transit of the pill to the stomach.

TREATMENT OF HYPERCALCEMIA

Pamidronate is the most commonly used parenteral drug.

The recommended dosage in dogs is 1.0–2.0 mg/kg administered intravenously mixed in 0.9 % saline over 2 hours. Adequate hydration is essential when treating with bisphosphonates since these drugs may cause nephrotoxicity, especially at higher doses.

The drug can be repeated in 3–4 weeks if needed.

PRIMARY HYPERPARATHYROIDISM

Etiology:

Adenomas >>> carcinomas
Hyperplasia (< 8%)

Pathogenesis:

Inappropriate secretion of parathyroid hormone (PTH) by autonomously functioning neoplastic or hyperplastic parathyroid "chief" cells.

Signalment:

>/= 7 yo (1), 11.2yrs (2)
Keeshonds over represented

Few reported cases in the cat.
Siamese overrepresented



CLINICAL SIGNS OF HYPERPARATHYROIDISM

PU/PD

Listlessness, Muscle weakness

Development of renal insufficiency is rare

Gastrointestinal Signs

LUTS attributed to urolithiasis or UTI (stranguria, pollakiuria, hematuria)

PE generally unremarkable

Seizures: one case report

In general, signs are mild to moderate.

DIAGNOSIS

Clinical Signs

CBC

Chemistry Panel

Calcium [hypercalcemia, elevated iCa]

Phosphorus [hypophosphatemia]

Chloride [mild hyperchloremia]

ALP [possibly mild elevation]

Urinalysis

Low USG

UTI

DIAGNOSIS- LOCALIZATION PROCEDURES

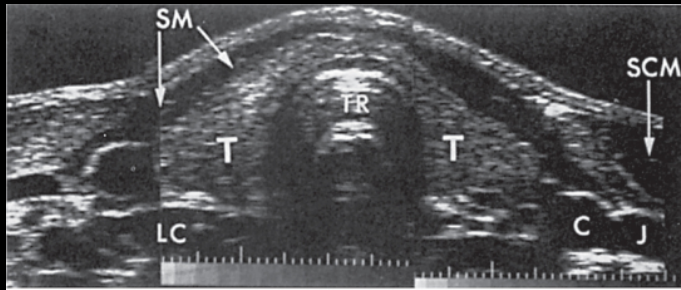
Approximately 10 % of parathyroid tissue is ectopic in location, and furthermore, approximately two thirds of "missed" adenomas are within the thyroid bed.

Historically CT, MRI, and US- these modalities are very insensitive for ectopic and mediastinal glands

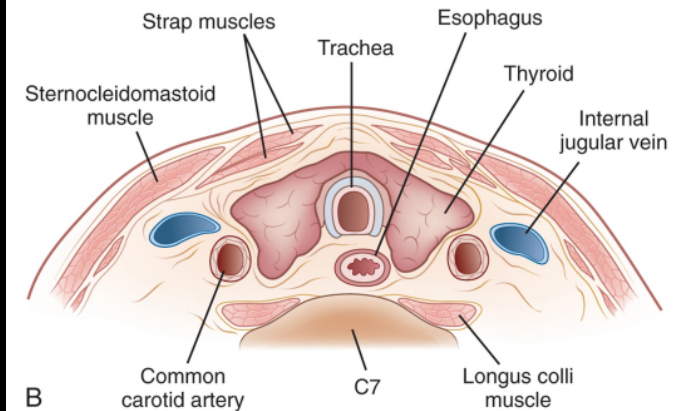
Angiography and venography with venous sampling for parathormone are cumbersome and invasive

Scintigraphy - Technetium-99m Sestamibi

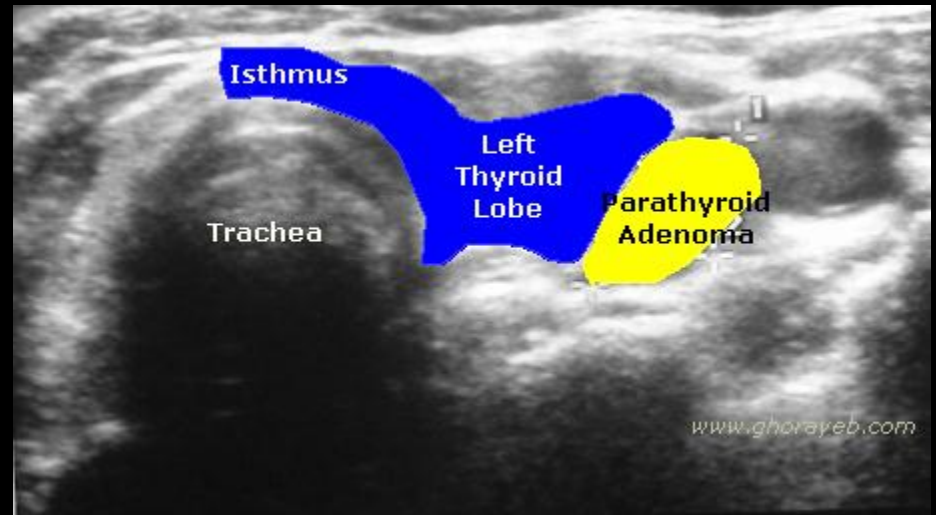
CERVICAL ULTRASOUND



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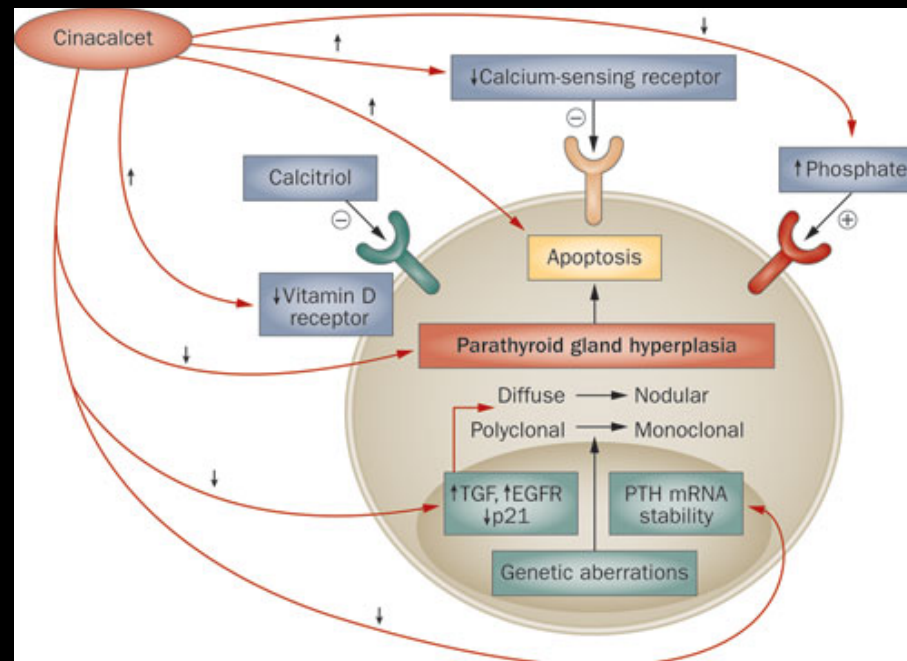
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Medical Options:

TREATMENT

To treat or not treat: Discuss the reasons why we treat and reasons why we might tell an owner we don't have to treat.

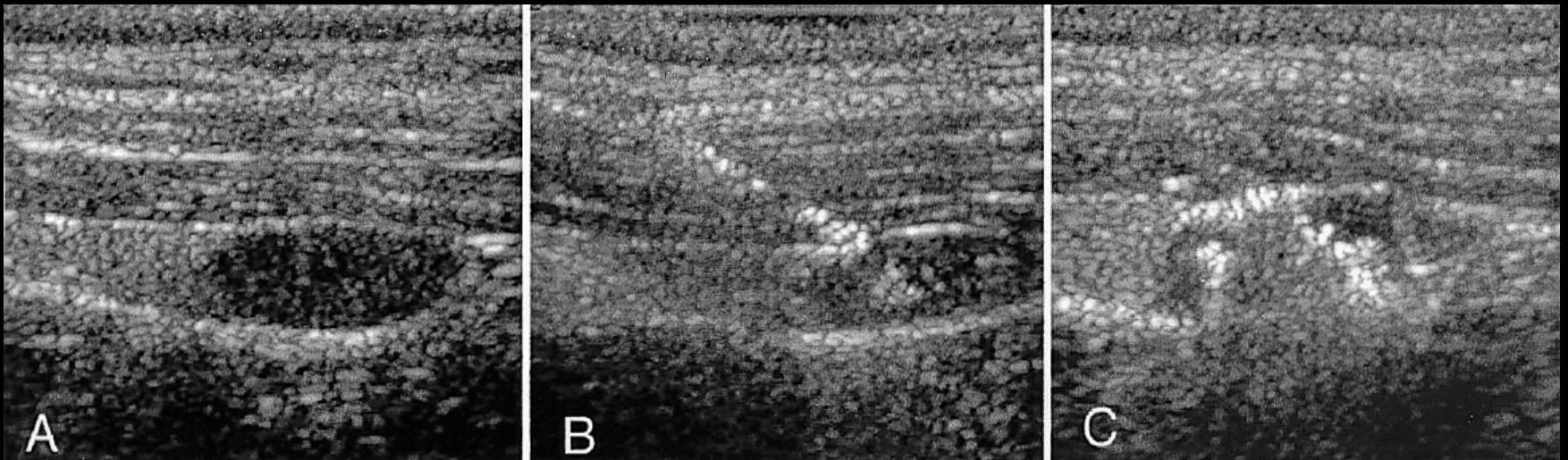


TREATMENT

Surgery -In experienced hands, surgical removal of an adenoma within the thyroid bed cures the hyperparathyroidism 90% to 95% of the time

Chemical or ethanol ablation

Heat Ablation



COMPLICATIONS OF TREATMENT

Hypocalcemia - Muscle fasciculations, tetany, and seizures, behavior and gait abnormalities

Trauma to recurrent laryngeal nerve

Hemorrhage

Recurrence

RETROSPECTIVE EVALUATION OF THREE TREATMENT METHODS FOR PRIMARY HYPERPARATHYROIDISM IN DOGS

The medical records of 110 dogs treated for primary hyperparathyroidism were reviewed. Dogs were treated via parathyroidectomy (n=47), percutaneous ultrasound-guided ethanol ablation (n=15), or percutaneous ultrasound-guided heat ablation (n=48). Forty-five of 48 (94%) parathyroidectomies resulted in control of hypercalcemia for a median of 561 days. Thirteen of 18 (72%) ethanol ablation procedures resulted in control of hypercalcemia for a median of 540 days. Forty-four of 49 (90%) heat-ablation treatments resulted in control of hypercalcemia for a median of 581 days.

SUMMARY

Think about primary hyperparathyroidism as a differential for hypercalcemia particularly in patients with...

Mild to mod clinical signs

High Ca, low Phos

Older dogs, Keeshonds

Diagnosis is based on clinical signs, laboratory data, and imaging of the parathyroid nodule

Treatment options include surgical parathyroidectomy and heat ablation

The most common complication post-procedure is hypocalcemia

RENAL SECONDARY HYPERPARATHYROIDISM

