HYPERPARATHYROIDISM:
The delicate balance of calcium physiology

Synopsis-- Anatomy and the Disease

The parathyroid glands are tiny powerhouses that can take a mammalian body to its knees. Producing parathyroid hormone (PTH), they are in key control of calcium metabolism by talking hormonally to bones, kidneys and the GI tract. The parathyroid glands can go haywire producing excessive PTH in neoplastic and hyperplastic states (and other neoplastic tissues jump on this specific bandwagon by acting like the parathyroid glands and producing parathyroid-like hormone in a classic paraneoplastic syndrome.) In either of the parathyroid gland disease states, the anatomy of these tiny glands changes on a small scale. A one-millimeter change from four to five can be the difference between normal and abnormal. Herein lies one of the treatment challenges.

When PTH is above normal, it is working harder than normal to keep calcium in the body. Hypercalcemia is the result. Many tissues do not like that, since calcium is a key ion in transmembrane cellular activity—nervous tissues, kidneys, heart, GI, skeletal muscle. Since calcium physiology is a feedback-loop process, an abrupt termination of the PTH source (i.e. excising a neoplastic parathyroid gland) results in changes that are rarely precise on a timeline or in scale. Large and small swings, slow and fast results are all possible; therein lies the second of our treatment challenges. Recent data remains variable in identifying reliable indicators that predict the post-treatment calcium behavior.

Hypercalcium (or its clinical signs) will be the first indicator of possible parathyroid disease. Elimination of paraneoplastic syndrome and kidney disease as primary etiologies is the first step toward a specific parathyroid etiology. Once there, quality ultrasound (equipment and interpretation) is the most useful diagnostic tool. At times, these results appear clear cut; other times, even with quality ultrasounds results, we remain head-scratching. Walking clients through these physiologic and diagnostic processes with some level of detail will help them understand the grey zones within which we often work. Generally, the outcomes are calm, cool and collected; the low instance of rebound hypocalcemia postop (10%) is noteworthy and highly discussable because it is life-threatening.

In the normal mammal, PTH is triggered in the parathyroid gland by low blood calcium levels; this PTH is released and moves through the system creating changes that bring calcium back up to appropriate levels.

1) PTH acts on bone cells to increase calcium in the blood;
2) PTH acts on precursors of vitamin D to make it an active substance.

Vitamin D is made in the skin (people) and/or eaten (major route in dogs) and then activated by PTH. Once active, it works in the intestine to absorb more calcium. When calcium is too high, it directly and vigorously closes down the production of PTH from normal parathyroid glands (but NOT tumor/abnormal parathyroid cells).

When PTH goes from high to suddenly low (i.e. surgical removal of the abnormal gland source will lower PTH w/in an hour), the body's calcium maintenance mechanism loses its primary regulator (usually only for a day/weeks while the chronically suppressed normal parathyroid cells regroup). Either we need to supply the activated vitamin D and calcium, or we need to wait for the body to start making normal levels of PTH again from normal glands. There are risks and benefits to each approach and only rough guidance from medical data.

Clinical hypocalcemia is life-threatening and needs urgent veterinary attention if signs develop. Catching signs early through attentive observation in the week after treatment will allow this to be treated effectively and simply with IV medications. Progression of signs can be recognized over several hours. Lack of appetite is an early sign and not to be ignored; minimizing postop medications that are known to disturb appetite will make

this trigger more recognizable. Restlessness (their "skin is crawling") and facial rubbing are very commonly reported. Later signs are vomiting and overt muscle fasciculations/twitching. Weakness and collapse are late signs and require immediate IV treatment. Cardiac arrest can follow.

Surgical Overview:

A ventral midline approach to the cranial-mid cervical region provides access to the parathyroid glands. Magnification and direct palpation are both instrumental in interpreting the parathyroid anatomy and pathology. Any one or multiple glands of four may be abnormal. Using ultrasound findings, visual appearance (color and "plumpness") and direct palpation (firmness) abnormal gland(s) is/are identified and removed with fine instruments and careful dissection and hemostasis.

The **indications & rationale** for surgical treatment are:

- Hypercalcemia attributable to parathyroid origin (paraneoplastic and renal disease ruled out)
- Persistent and elevating calcium over time
- Ultrasound identified parathyroid gland enlargement

Other options for treatment (besides surgery) are:

- Chronic diuresis and steroid administration geared toward serum calcium reduction
- Percutaneous ultrasound heat/chemical ablation of hyperplastic/neoplastic parathyroid glands

Supportive diagnostics and therapeutics with surgical treatment are:

- Serial postop serum calcium monitoring (daily x7d, then q1-3mo until stable.)
- Postop prophylactic oral calcium (25-50mg/kg q8-12hrs; as Calcium carbonate w/ 40% available calcium)
- Postop prophylactic vitamin D supplementation
    - Calcitriol = "activated" vitamin D (immediately available; higher side-effect risk)
        - 10-20 ng/kg q12 (*note: NANOgrams) x 4d, then 2.5-10 ng/kg q12, weaning 8-12wks.
    - Dihydrotachysterol = synthetic vitamin D (variable absorption; lower side-effect risk)
        - 0.01mg/kg q12 x 4d, then 0.01mg/kg q24, weaning 8-12wks.
- Clinical hypocalcemia treatment
    - 10% calcium gluconate 0.5-1.5ml/kg IV over 15min; monitor HR...if slows, reduce administration rate. Then 10ml 10% calcium gluconate in 250 LRS IV over 4hrs).
    - Start oral calcium and calcitriol (or dihydrotachsterol)

The **perioperative experience** for pet and owner includes:

- Oral medication administration and/or IV diuresis to normalize calcium preoperatively until stable level.
- Routine anesthesia, absent other comorbidities
- Absolute availability for intraoperative decision-making
- Mild postoperative surgical morbidity (3-5" incision ventral neck; light neck wrap x7d)
- Inpatient or outpatient serial blood calcium measurements daily for 7d
- Close monitoring for hypocalcemia signs and access to 24/7 veterinary care
    - Inappetence, ADR
    - Face rubbing
    - Muscle twitching (face, trunk, limbs)
    - Weakness/collapse
    - Vomiting
- Postoperative medications and/or serial blood calcium measurements x 2-3mo

Expectations for outcome are:

- Complete resolution of hypercalcemia
- Potential for recurrence of condition if new/different parathyroid gland becomes abnormal

Complications that may arise with this procedure are:

- Clinical hypocalcemia (serious/life-threatening, 10% risk of occurrence)
- Seroma (low, minor)
- Significant surgical nerve damage (very low)
- Dangerous surgical bleeding (very low)

Postoperative **outcomes may be poor** due to the above complications, and/or:

- No abnormal gland identified
- Gland(s) removed with no change in calcium homeostasis (likely other source)
- Laryngeal paralysis secondary to surgical nerve damage

What a surgeon needs prior to surgery:

- Skin near the surgery site CLEAR of infection (papules, pustules, crusts, collarettes, etc.) If urgent surgery, owner must be alerted to *increased risk* of incisional, deep and/or implant infections.
- Access to owner for urgent communications.
- Written ultrasound report.

General considerations and complications *for all surgery/anesthesia procedures are:*

- *Difficult and/or painful anesthetic recovery (variable; may require additional medications or re-hospitalization)*
- *Incisional infections (rare, minor; usually require oral antibiotics)*
- *Incisional dehiscence (rare, minor or major; may require surgical revision)*
- *Adverse anesthetic event (rare, major; may result in serious impairment or death)*

Proper owner expectations are important to a successful experience and patient outcomes. Please discuss this information with your clients while assisting them with decision-making for **Hyperparathyroid treatment**.

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