

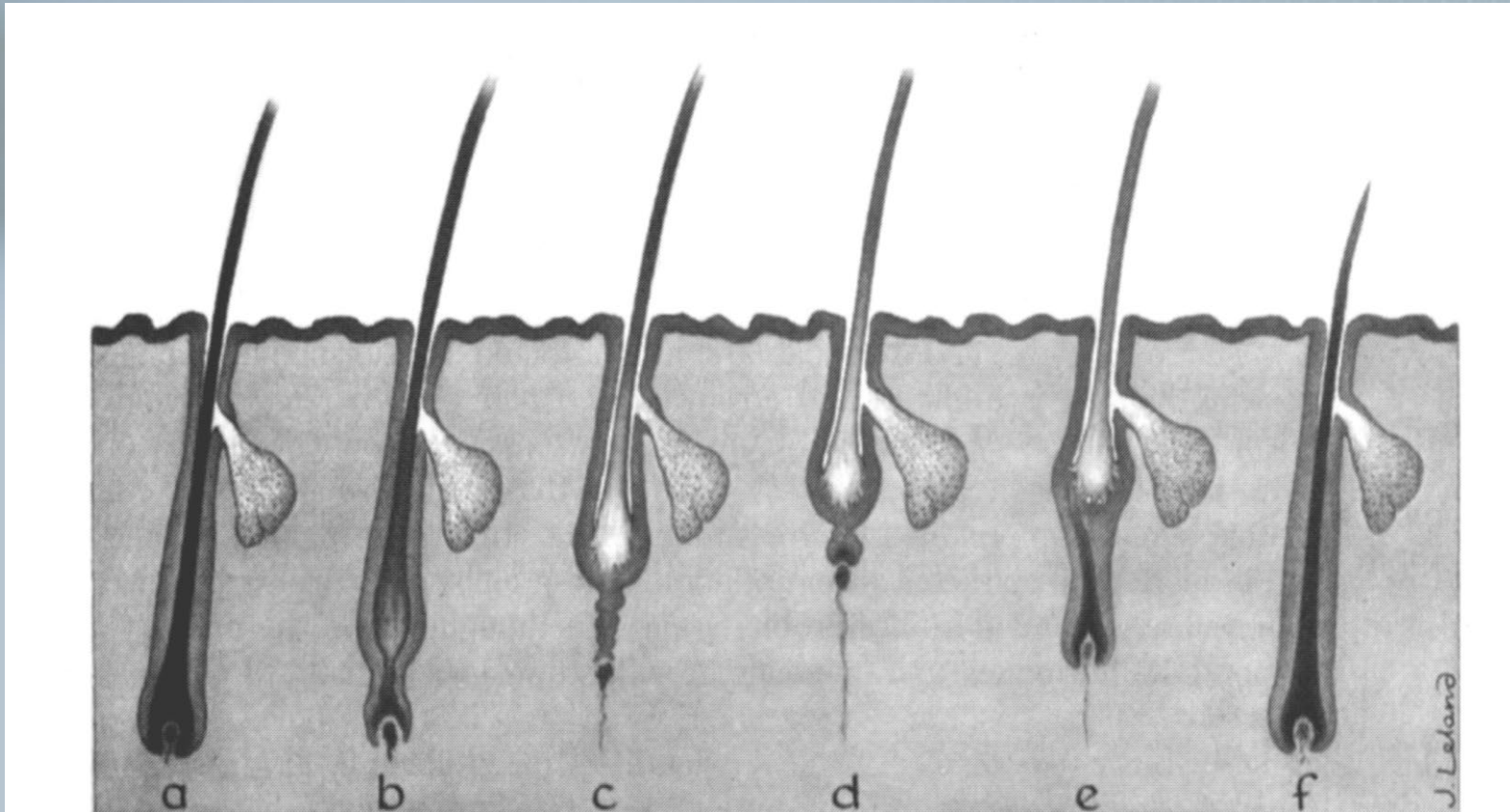


«Endocrine» alopecia

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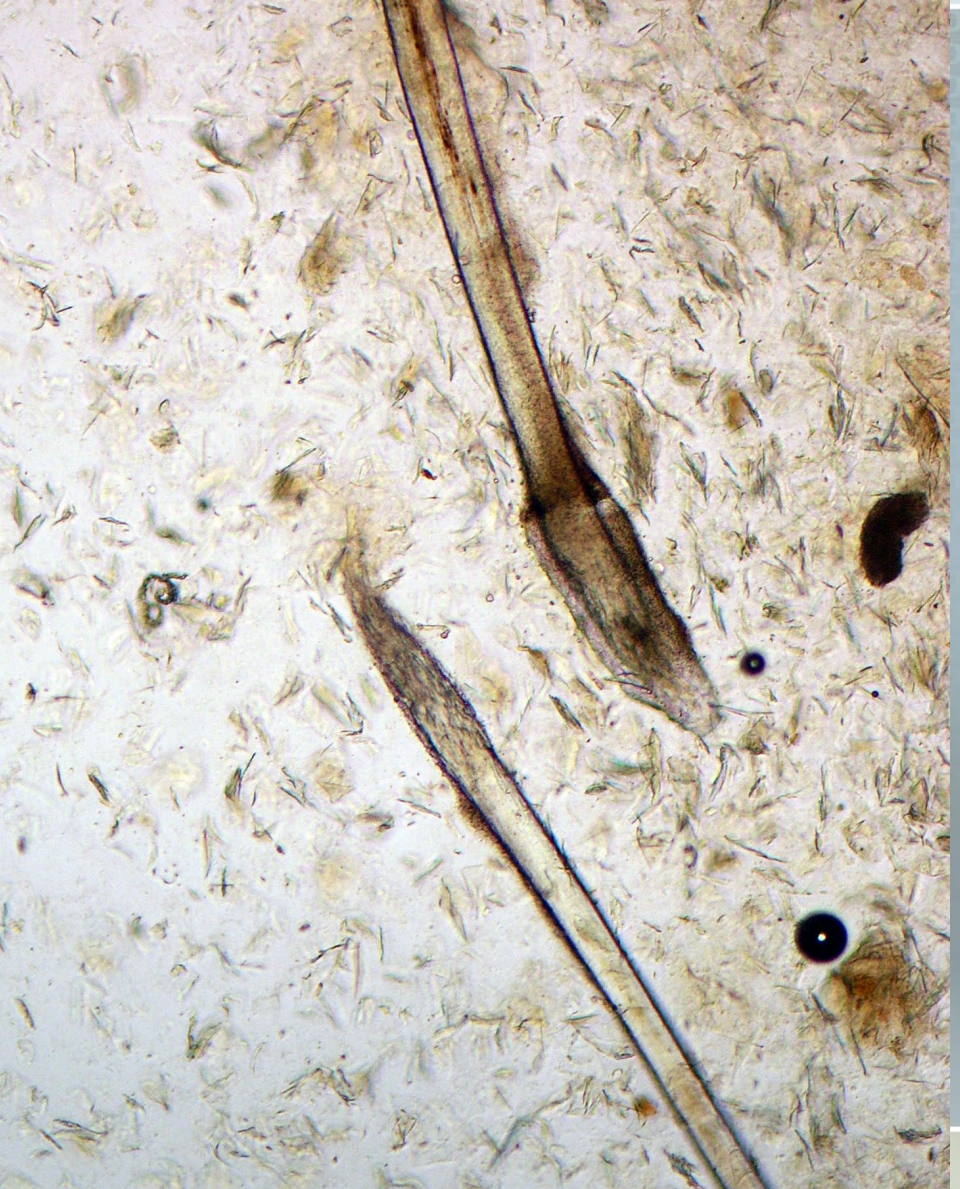
How do hairs grow?

■ Anagen – Catagen – Telogen



Scott Miller Griffin, Small animal dermatology

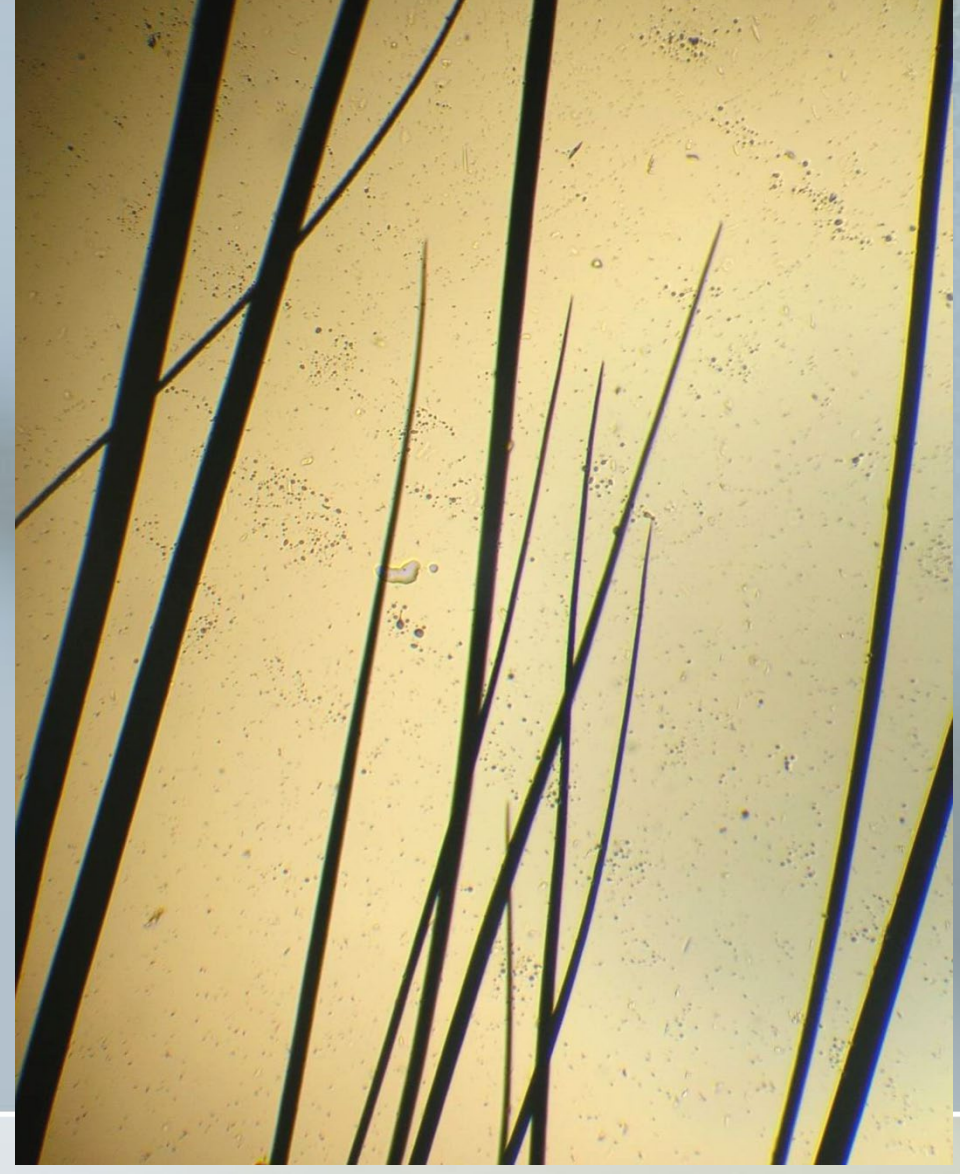
Trichoscopy



Alopecia

- Self-induced
 - Pruritus (parasites, allergies...)
- Spontaneous
 - Focal or multifocal
 - Demodicosis
 - Dermatophytosis
 - Pyoderma
 - Diffuse
 - Endocrinopathy
 - Telogen / Anagen defluxion
 - Follicular dysplasia...

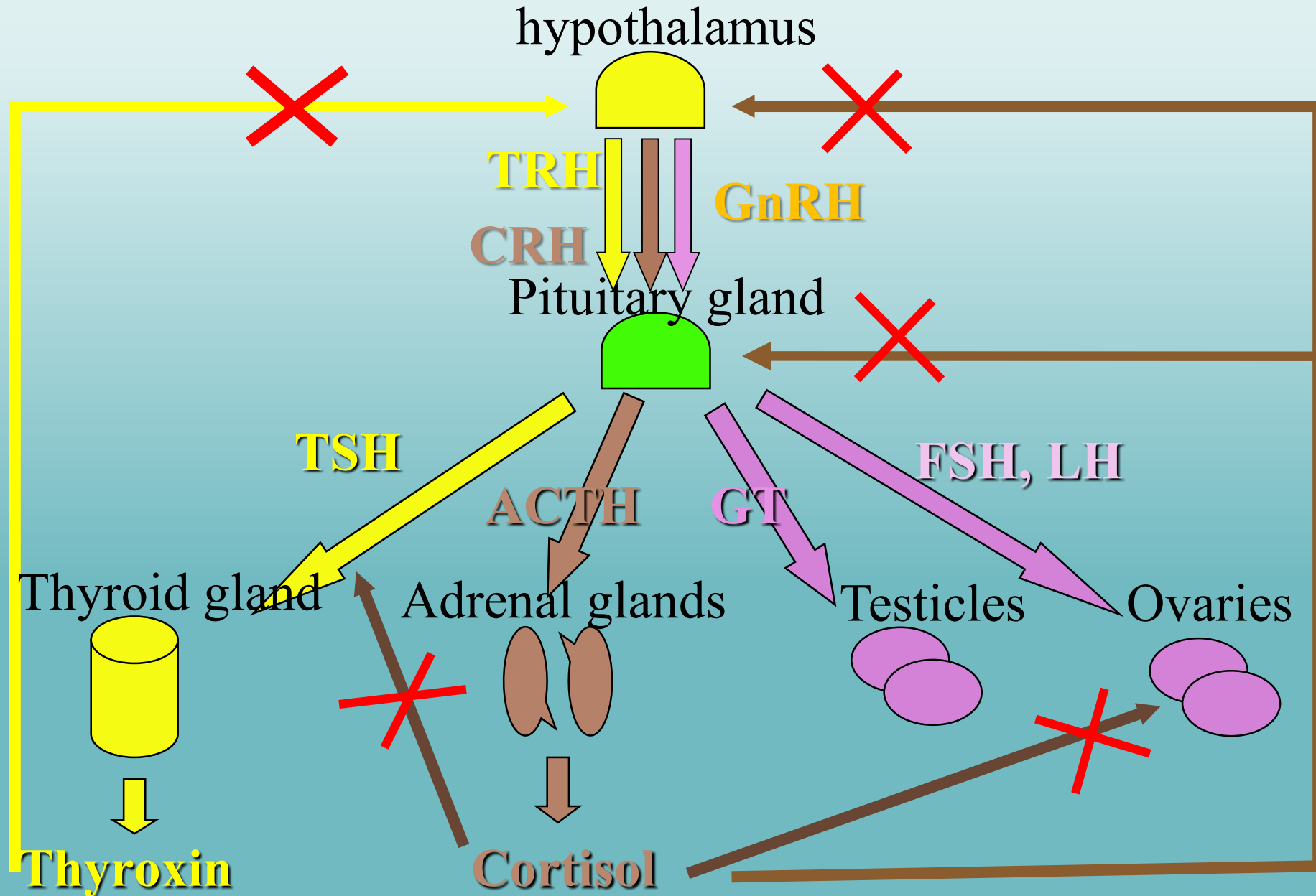
How to distinguish self-induced alopecia from spontaneous?



Common features of endocrinopathies

■ Age of onset	≥ Middle age
■ Congenital endocrinopathy	– dwarfism
■ Pruritus	Absent (?)
■ Systemic signs	+
■ Blood tests changes	±
■ Breed predisposition?	+
■ Gradual progress	+
■ Spontaneous remission	–

Regulation of hormone secretion



Thyroid hormones

- Metabolically active – T₃
- Prohormone – T₄
- Stimulated by pituitary TSH
- Regulation is by negative feedback - the more thyroxine, the less TSH.

Causes of hypothyroidism



Giant schnauzer



Gordon setters

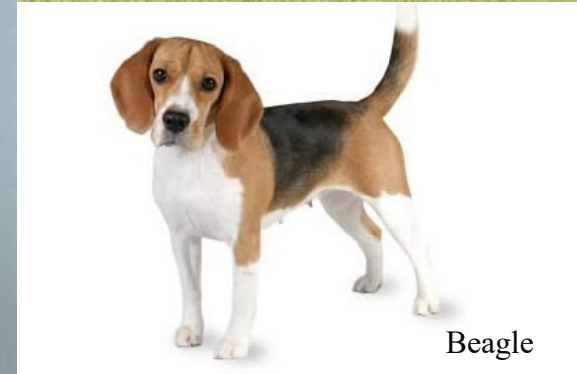


Golden Retriever

- Autoimmune lymphocytic thyroiditis (95%)
 - Possibly associated with DLA class II allele
- Idiopathic atrophy
- Not associated with a lack of iodine!
- It occurs mostly in dogs!
 - Described in some cats - extremely rare !!!
 - In cats without alopecia
- Rare central hypothyroidism - schnauzer
 - Lack of TSH \pm dwarfism.



Hovawart



Beagle



Shih tzu

Thyroid hormone effects:

- Anagen initialization
- Increase hair growth rate
- Enhance wound healing
- Stimulation of protein synthesis
- Impact on the development of lymphoid tissue, neutrophil and lymphocyte function.

Hypothyroidism

- **"Telogenization of hairs"**
- **Reduced hair growth rate**
- **Wound healing delay**
- **Deposition of glycosaminoglycans**
- **Decreased skin immunity**

- **Anagen initialization**
- **Increase hair growth rate**
- **Enhance wound healing**
- **Stimulation of protein synthesis**
- **Lymphoid tissue, neutrophil and lymphocyte function development**

Hypothyroidism

- Alopecia on friction areas
- Slow / no regrowth of hairs
- Oedema, myxedema
- Skin infections
 - Pyoderma
 - Malassezia dermatitis / otitis
- Demodicosis

- "Telogenization of hairs"
- Reduced hair growth rate
- Wound healing delay
- Deposition of glycosaminoglycans
- Decreased skin immunity

Hypothyroidism - systemic signs



- Sleepiness
- Obesity
- Bradycardia
- Neurological (rare)
- Sexual cycle disturbance (rarely), gynecomastia
- Rare:
 - Insulin Independent diabetes mellitus
 - Acromegaly.



When to think about hypothyroidism?

- Recurrent pyoderma without signs of underlying allergy
- Recurrent Malassezia dermatitis / otitis
- Generalized adult-onset demodicosis in dogs
- Diffuse spontaneous alopecia (without pruritus)
- Cornification defects (secondary).

Diagnostics. Changes in the blood.

- CBC, changes:
 - Non-regenerative anemia \pm
- Chemistry:
 - Cholesterol 
 - Triglycerides 

Diagnostics. Tests.

- Total thyroxin (tT4) ↓
- Free thyroxin (fT4) (by equilibrium dialysis!) ↓
- TSH (species specific!)** ↑ or normal!
- Cholesterol ↑
- Basal plasma growth hormone* ↑
- Function test:
 - TSH stimulation test (\pm plasma growth hormone after 45 min*)
- Central hypothyroidism diagnostics:
 - TSH stimulation test + TRF stimulation test.

What can temporarily reduce thyroxine level?

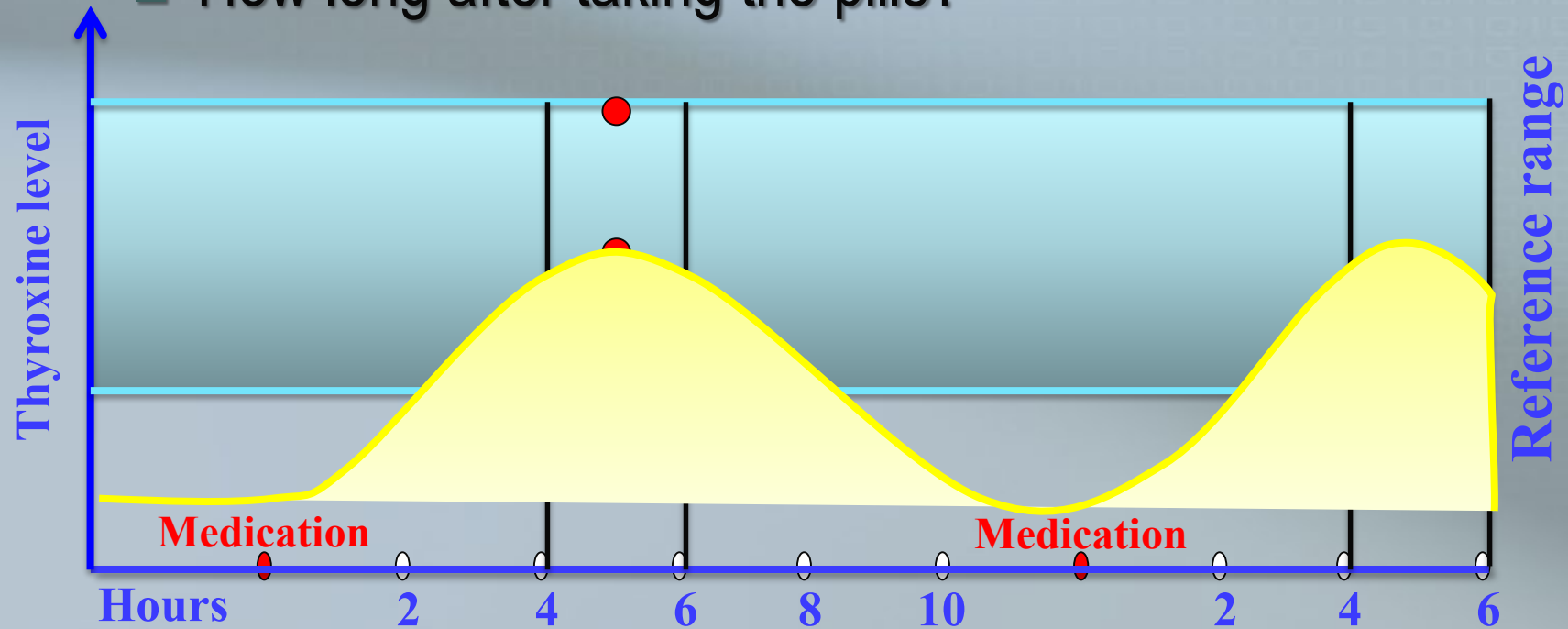
- Corticosteroids
 - Exogenous (history!)
 - Endogenous (Cushing's syndrome)
- Anticonvulsant drugs
- Sulfonamides (Biseptol)
- Aspirin and other NSAIDs
- Severe inflammation (pyoderma!)
- Furosemide
- Dopamine
- Diazepam ...

Treatment

- Levothyroxine - the initial dose - 10-15 mcg/kg BID (SID?)
 - There are liquid forms - once a day.

Dose adjustment

- Should all patients have the same dose?
- How to understand which dose is sufficient?
- When to measure the hormone level?
- How long after taking the pills?



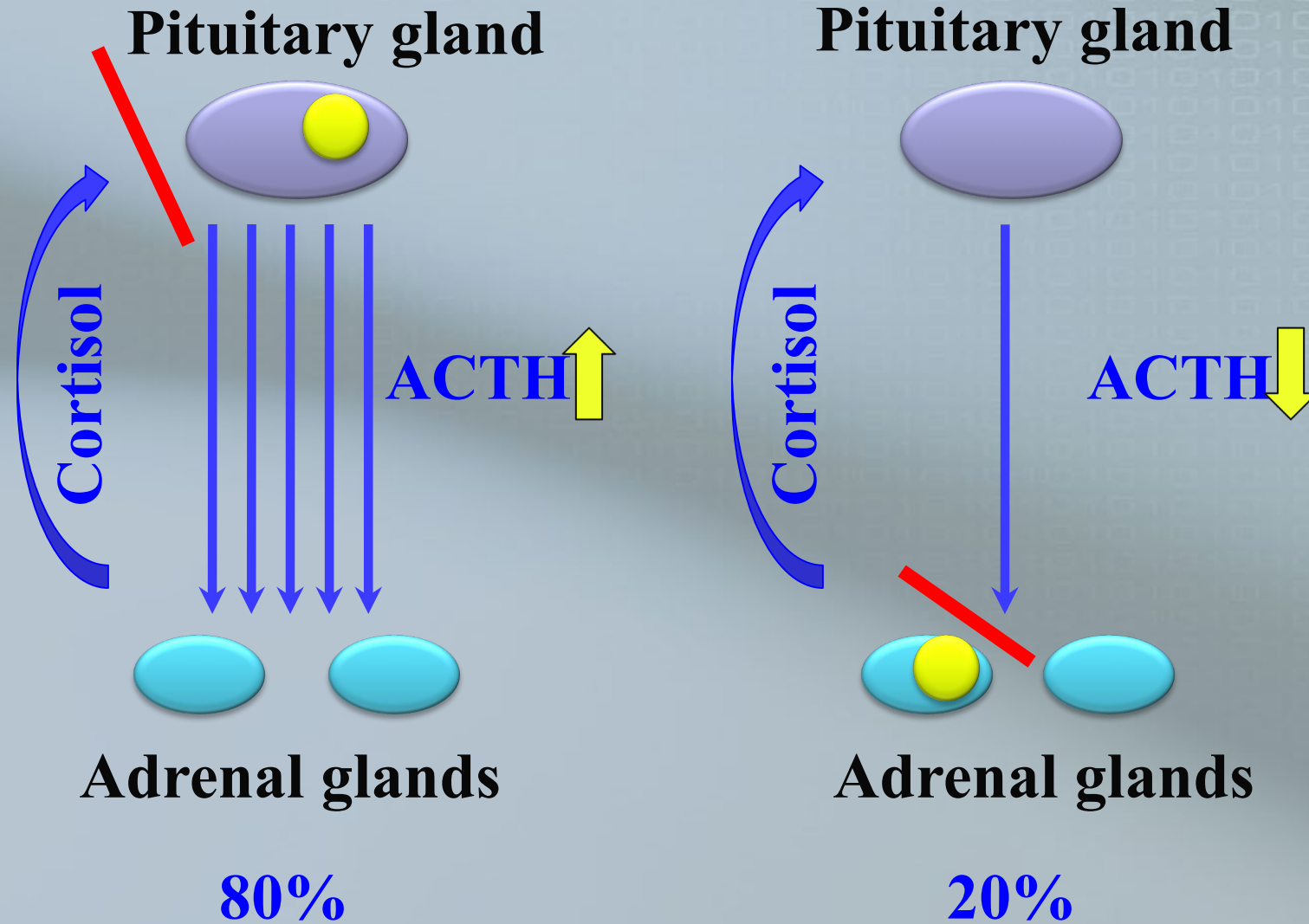
When to expect the clinical effect of the treatment?

- In 2 weeks
 - Increase activity
- In 2-3 months
 - Hair regrowth
- In 2-4 months
 - Reducing obesity
- How long to treat?
 - Life long.

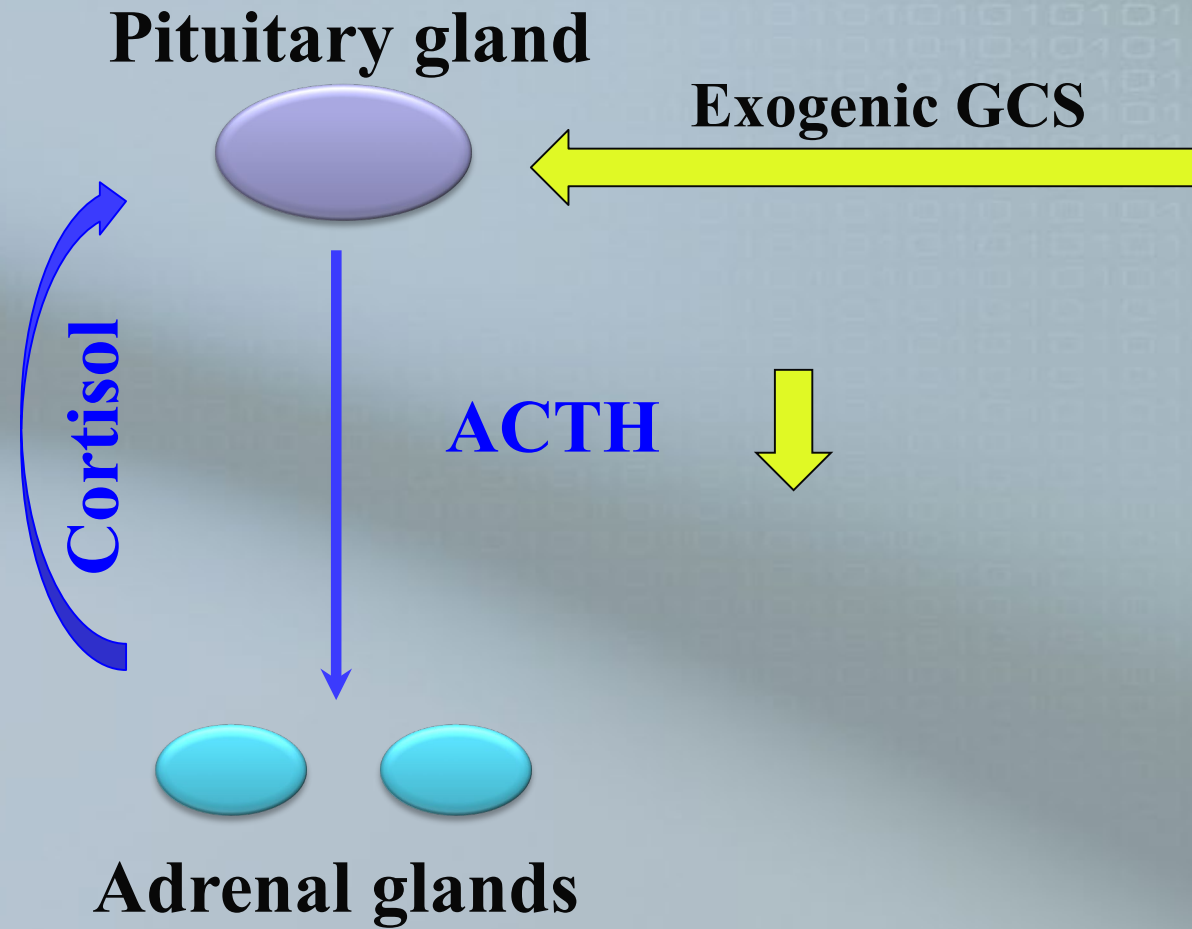
Glucocorticosteroids (GCS) ... terminology

- Cushing's syndrome
 - Complex of symptoms caused by an increase GCS level in the blood
- Cushing's disease
 - Central hyperadrenocorticism
- Hyperadrenocorticism
 - The disease caused by increased production of GCS by the adrenal glands
- Iatrogenic Cushing's syndrome
 - Not iatrogenic hyperadrenocorticism!

Spontaneous hyperadrenocorticism (HAC)



Iatrogenic Cushing's syndrome



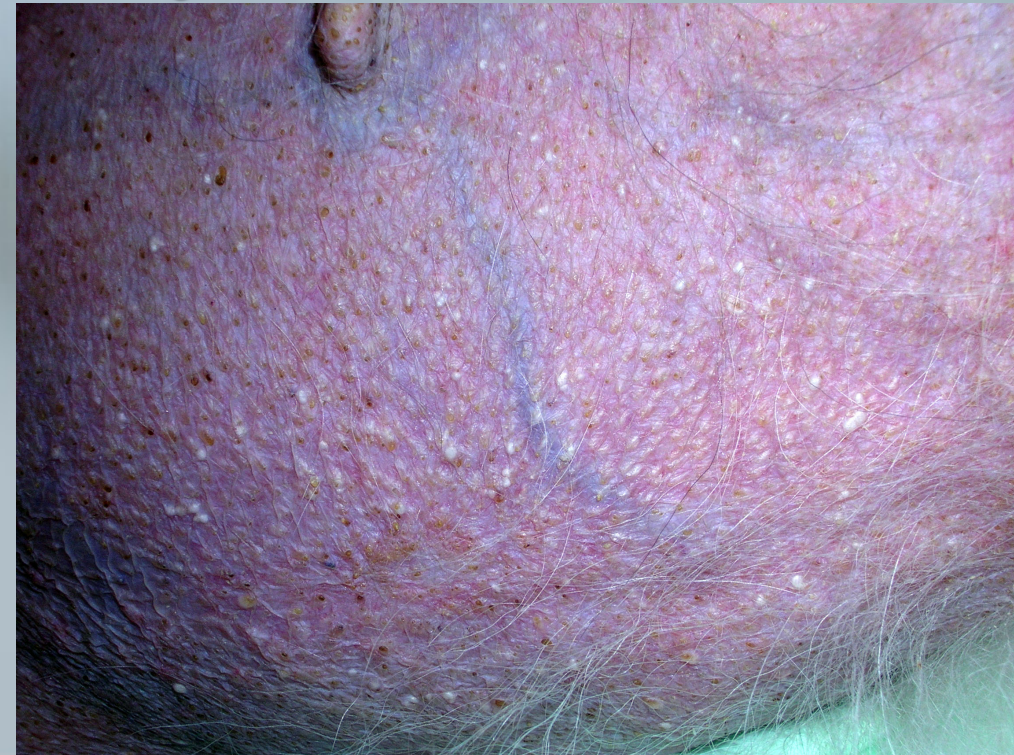
GCS, effects

- Inhibit anagen
- Reduce skin thickness
- Cause atrophy of the sebaceous glands and hair follicles
- Reduce fibroblast proliferation and synthesis of collagen
- Slow down wound healing
- Cause mineralization of the skin
- Suppress immunity.

Hyperadrenocorticism (HAC)

- **Inhibit anagen + cause glands and follicles atrophy**
- **Decrease skin thickness**
- **Reduce fibroblast proliferation and synthesis of collagen**
- **Slow down wound healing**
- **Cause mineralization of the skin**
- **Suppress immunity**

- Alopecia, dry skin, comedones
- Skin atrophy
- Skin and vessels fragility – hemorrhages
- Poor wound healing + "melting scars"
- Calcinosis cutis
- Skin infections
 - Pyoderma
 - Malassezia dermatitis
- Demodicosis.



Systemic signs

- Polydipsia / polyuria
- Polyphagia
- Weight gain
- Pot-belly
- Inhibition of the sexual cycle (no estrus)
- Phlebectasia
- Muscular atrophy
- Change hair / skin colour.

When should we think about HAC?

- Calcinosis cutis
- Recurrent pyoderma without signs of primary allergy
- Recurrent Malassezia dermatitis
- Generalized adult-onset demodicosis
- Presence of systemic signs
- Diffuse spontaneous alopecia (without pruritus)
- Skin atrophy / fragile skin syndrome in cats.

HAC diagnostics: CBC

■ CBC:

- Neutrophilic leukocytosis
- Lymphopenia
- Eosinopenia
- Erythrocytosis
- Thrombocytosis

■ Urine:

- Proteinuria
- Reduced specific gravity
- Infections
- Glycosuria
- Calcium crystals.

■ Chemistry:

- Alkaline phosphatase ↑ (dogs only)
- Glucose ↑
- ALT ↑
- AsT ↑
- Cholesterol ↑
- Triglycerides ↑
- Urea ↓ ???
- Phosphorus. ↑

HAC diagnostics: visualization

- Ultrasound - one or both adrenal glands are enlarged
- Hepatomegaly ???
- CT / MRI - adrenal / pituitary neoplasms.

HAC diagnostics: tests

- Urine Cortisol / Creatinine ratio
- Low dose dexamethasone test
- ACTH stimulation test
- High dose dexamethasone test.

Urine Cortisol / Creatinine ratio

- High sensitivity ~ 90%
 - From 100 Cushing patients, 90 will be positive.
- Low specificity ~ 40%
 - Only 40 out of 100 non-Cushing patients will be negative for the test.
- Allows to EXCLUDE HAC, if negative
- If positive - DOESN'T CONFIRM HAC – additional tests are needed.

Urine Cortisol / Creatinine ratio

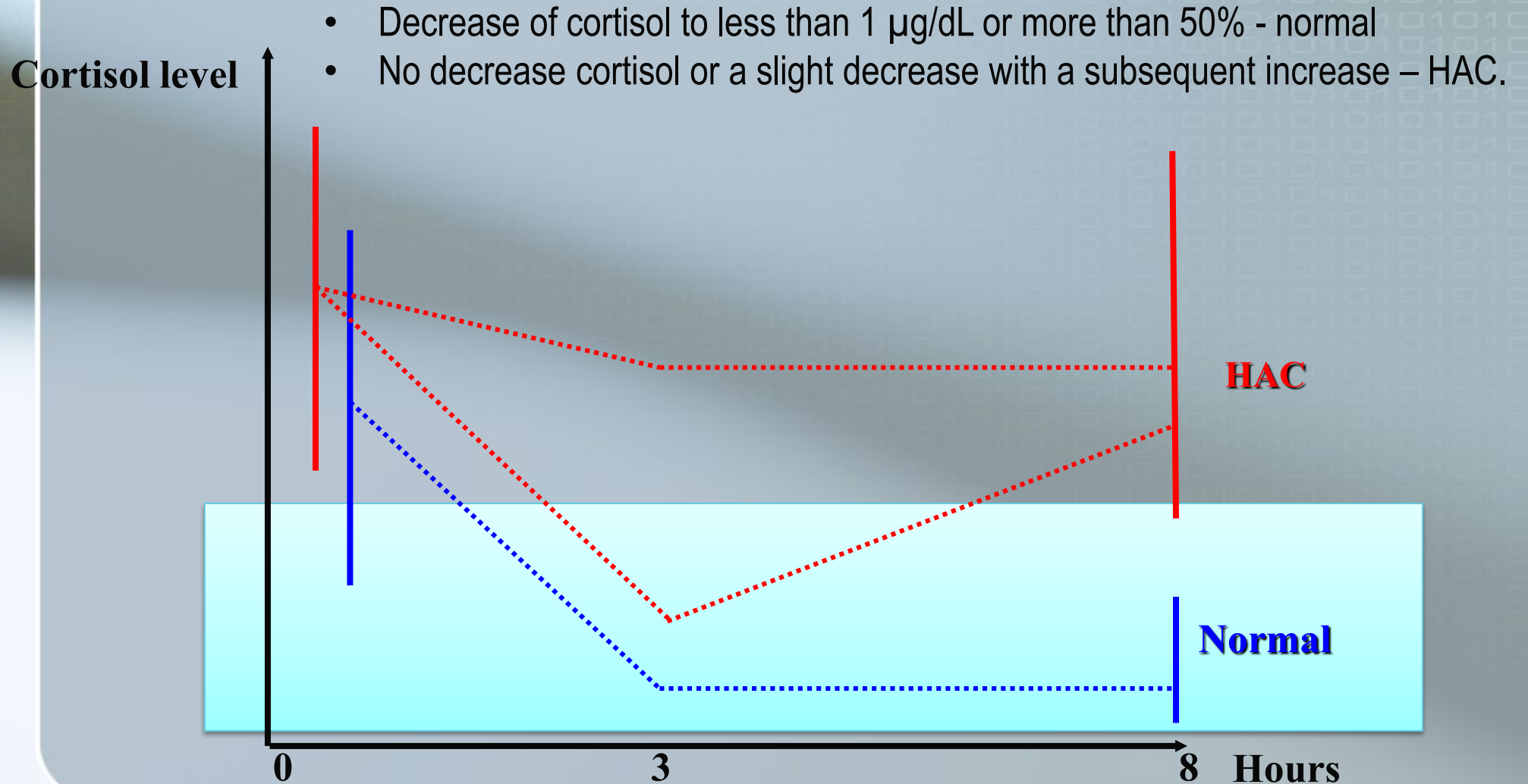
- Collect urine in the morning (first serving)
 - Not earlier than 6 days after stress
 - Not earlier than 3 days after stress 3 days in a row
- Keep refrigerated.

Low dose dexamethasone test (LDD)

- 0 Blood cortisol sample
+ IV dexamethasone 0.01 mg/kg
- 4 After 3-4 hours – test for cortisol
- 8 After 8 hours – test for cortisol.

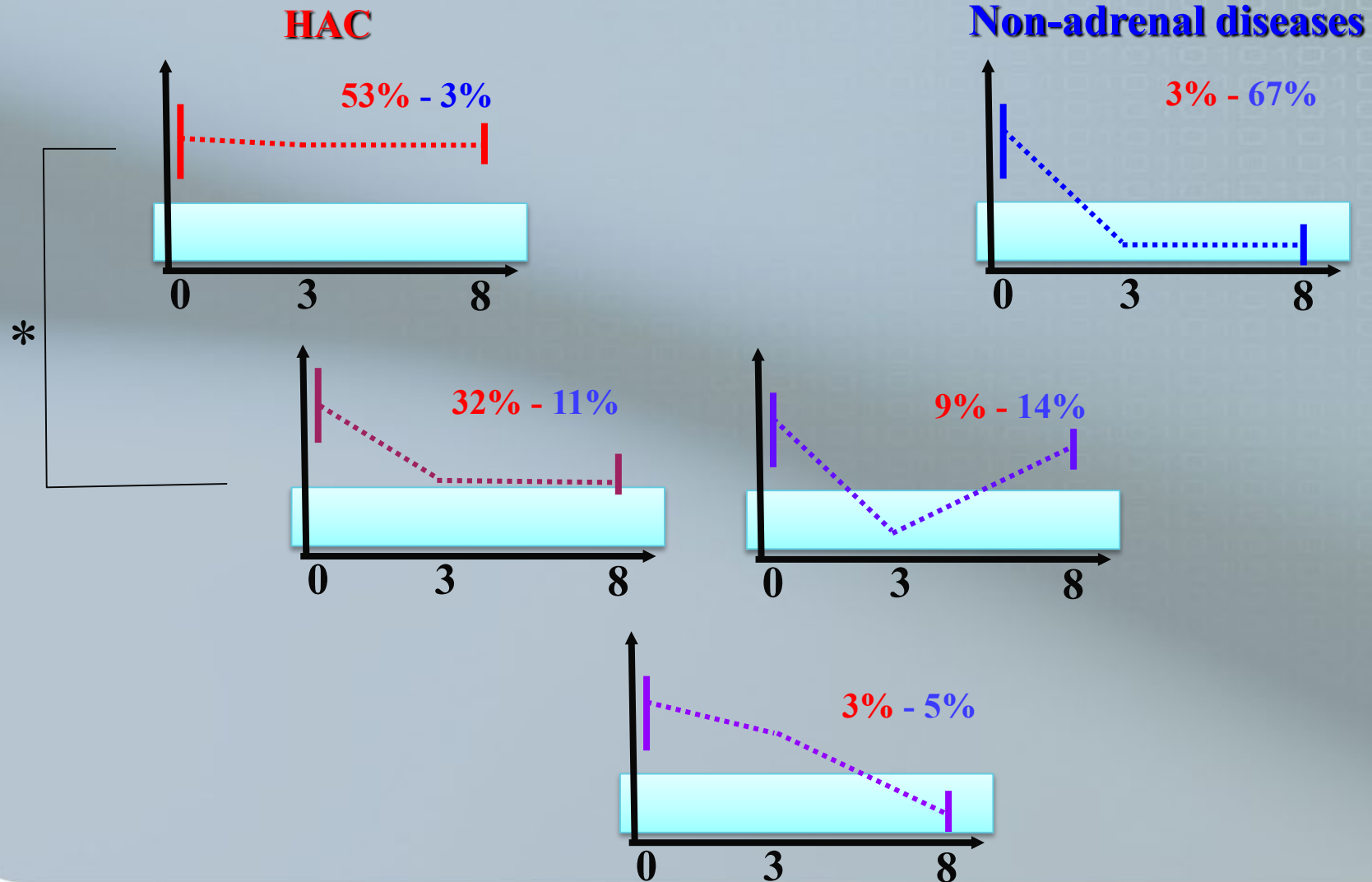
LDD – results evaluation

(J. Ramsey, J. Ristis. Diagnosis of canine hyperadrenocorticism. In Practice, 2007)



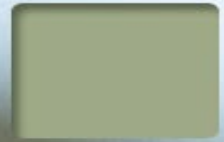
LDD – results evaluation – retrospective study of 123 cases.

Bennaim, Shiel, Forde and Mooney. Journal of Veterinary Internal Medicine, 2018.



HAC therapy

- Ketoconazole ??? (5-25 mg/kg BID, Lien, 2008)
- Lysodren (mitotane, o, p'-DDD) (25-50 mg/kg SID) – destroys adrenal tissue
- Trilostane (~ 3 mg/kg) – blocks GCS synthesis
- Adrenalectomy
 - Unilateral (temporary replacement therapy)
 - Bilateral (permanent replacement therapy).



Part 2

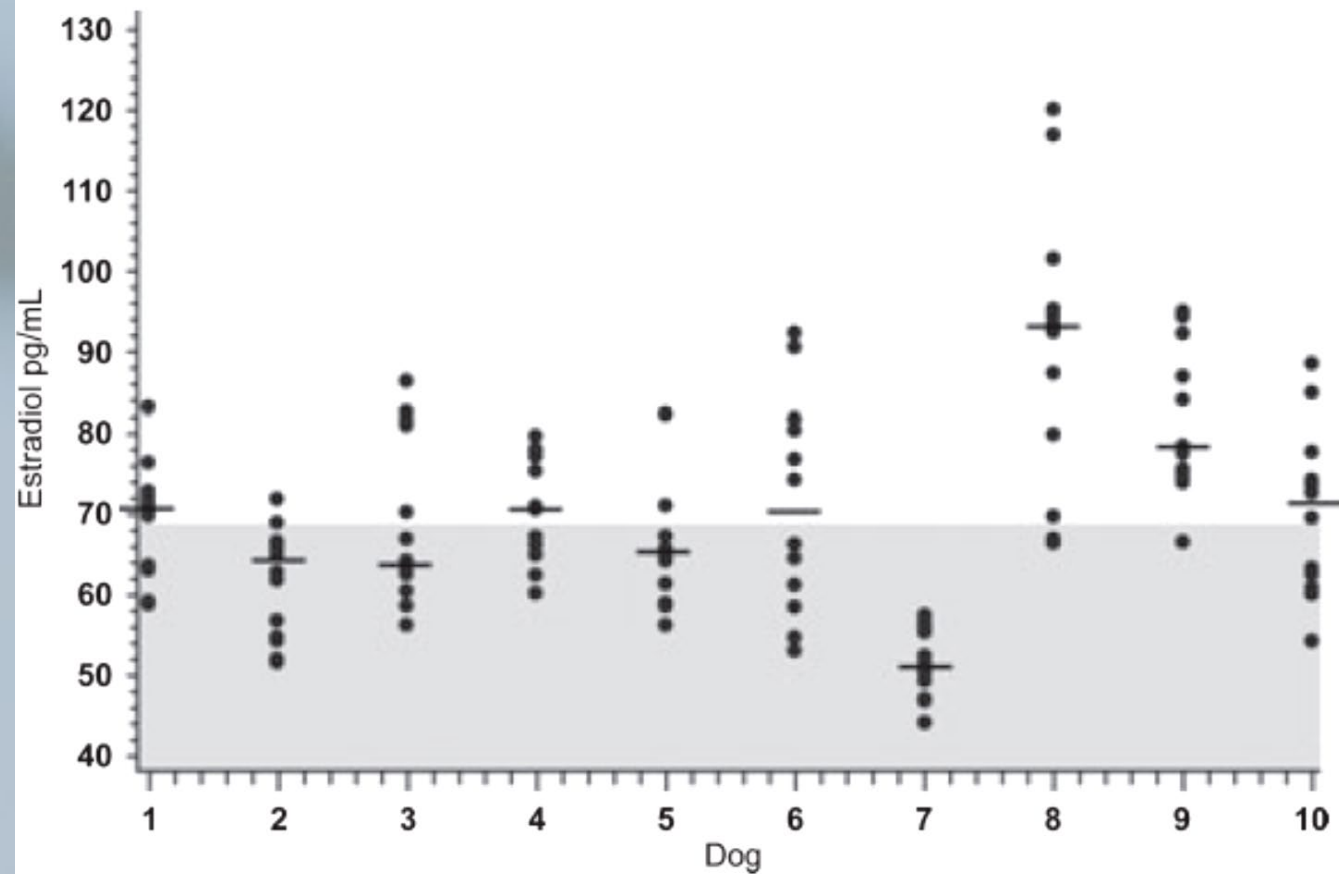
Sex hormones-related alopecia

Alopecia associated with sex hormones

- The rarest
- Can be associated with gonads or adrenal glands
- Usually are not diagnosed by hormone levels in the blood.

Variability of estradiol concentration in normal dogs

Linda A. Frank*, Rebekah Mullins* and Barton W. Rohrbach[†]



Alopecia associated with sex hormones

- The rarest
- Can be associated with gonads or adrenal glands
- Usually are not diagnosed by hormone levels in the blood.
- More often affected areas are: caudal thighs, abdomen, neck, sides.
- Hyperpigmentation of the skin.

Estrogen-related alopecia

- Feminization syndrome of male dogs
 - Cryptorchids are 8-10 times more often affected!
- Hyperestrogenism of intact females (in dogs).

Diagnostics

- Linear preputial dermatitis!!!
- Palpation of the testicles
- Ultrasound / CT / MRI of the testicles
- Estrogen level CAN be increased
 - Usually anti-Mullerian hormone is elevated
 - There is no difference in estradiol-17 β
(Holst et al 2015)
- CBC – non-regenerative anemia
- Cytology / biopsy.

«X alopecia»

- Castration-responsive alopecia
- Growth hormone-responsive alopecia
- «Pseudo-Cushing's syndrome»
- Testosterone-responsive alopecia
- Black skin disease
- Biopsy-responsive alopecia
- ...

«X alopecia», diagnostics

- Signalments, mostly breed and age
- Rule out hypothyroidism +/- HAC ???
- Sex hormones are in normal limits (ACTH-stim 17-HP↑)
- Skin biopsy???

«X alopecia», treatment

- No breeding!
- No treatment?
- Castration
- Melatonin 3 mg BID-TID
- Suprelorin / deslorelin (GnRH agonist)
 - No proven efficacy in female dogs
- Trilostane (~3 mg/kg)
 - Monitor cortisol level, sudden death risk!
- Dermaroller
- Finasteride or Osaterone acetate (Yposane)?