


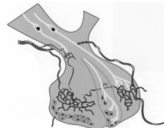
PITUITARY DISORDERS

Michael E. Herrtage
University of Cambridge

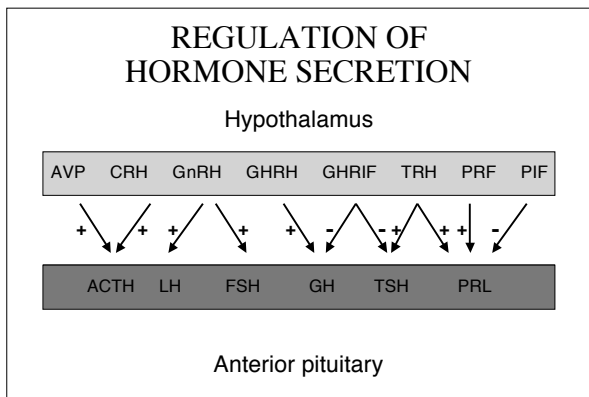


PITUITARY PHYSIOLOGY

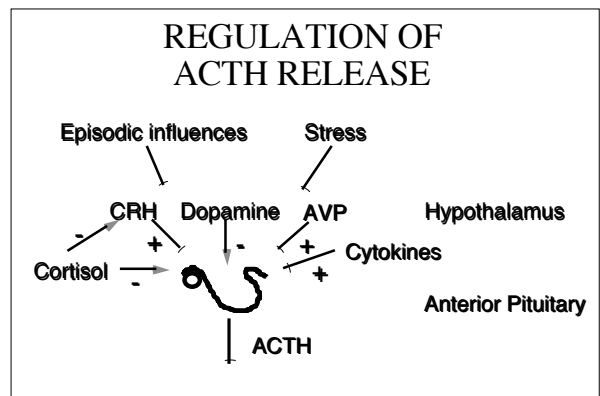
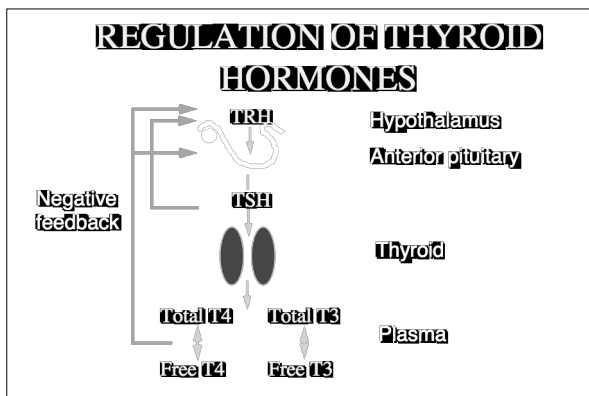
Hypothalamic hormones: **TRH CRH GHRH**
GnRH PRH Others

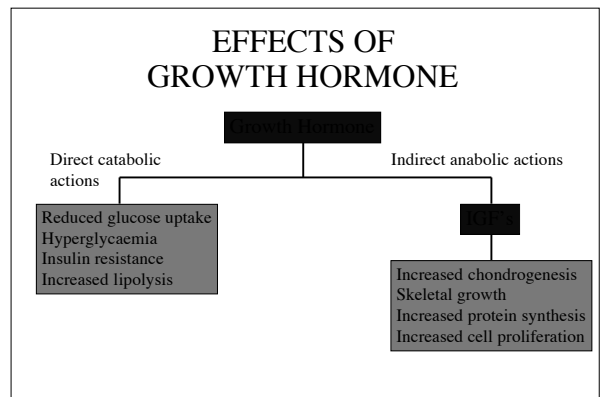
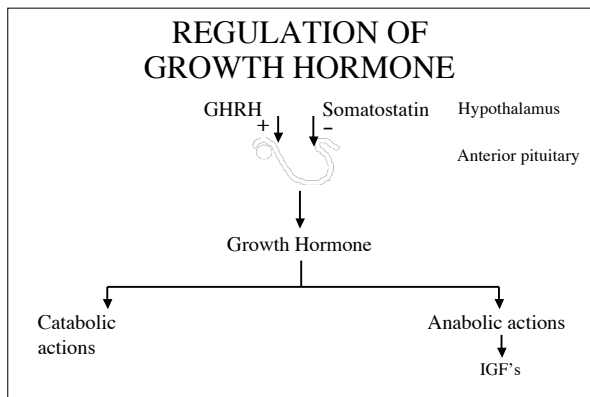
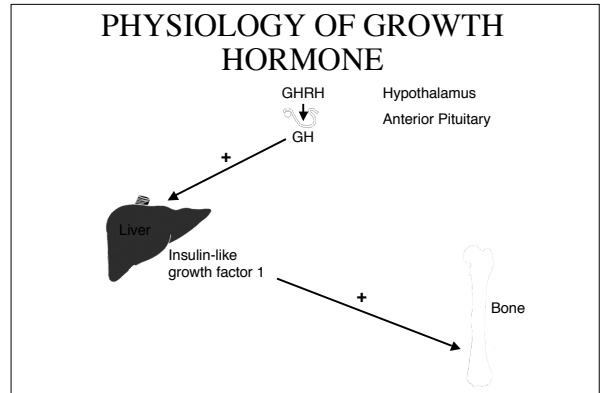
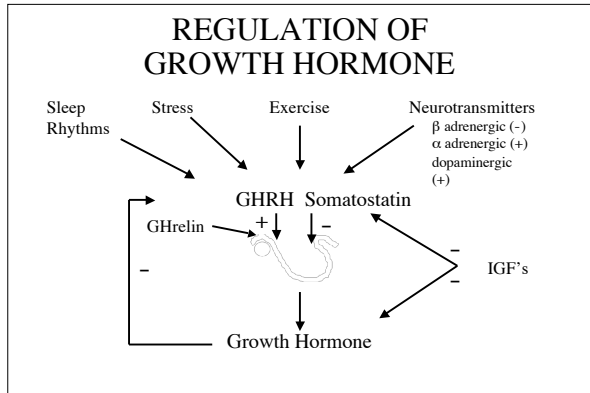


Pituitary hormones: **TSH ACTH GH αMSH Oxytocin**
FSH/LH PRL ADH



Anterior lobe hormone	Hypothalamic hormone (stimulatory)	Hypothalamic hormone (inhibitory)
TSH	TRH	
ACTH	CRH	
GH	GHRH somatotrocin	GHRIF somatostatin
FSH	GnRH	
LH	GnRH	
Prolactin	PRH	PRIF dopamine
MSH	MSRH	MSH-RIH



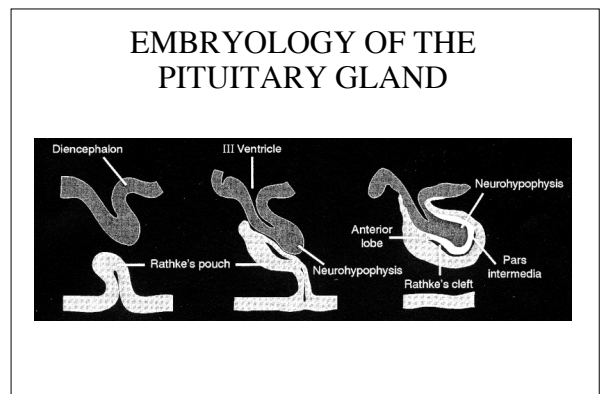


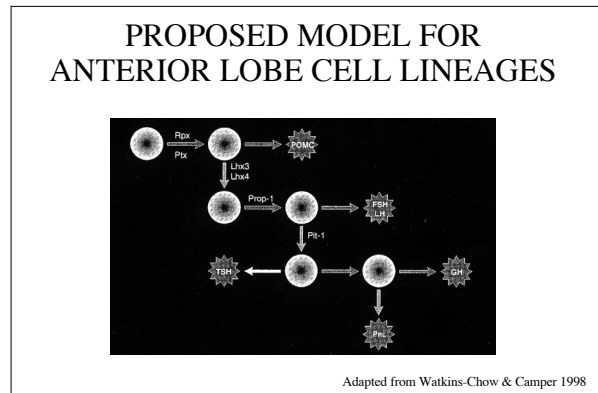
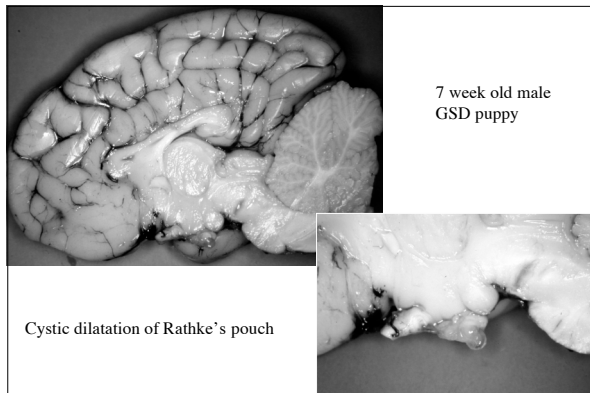
CONGENITAL PANHYPOPITUITARISM

Pituitary dwarfism

- ◆ German shepherd
- ◆ Carelian bear dog
- ◆ Toy pinscher
- ◆ Weimaraner
- ◆ Spitz

Litter brothers at 6 months of age





MUSCULOSKELETAL SIGNS

- ◆ Proportionate dwarfs
- ◆ Stunted growth
- ◆ Delayed closure of growth plates

Littermates at 6 weeks of age

MUSCULOSKELETAL SIGNS

2 weeks

6 months

MUSCULOSKELETAL SIGNS

- ◆ Delayed dental eruption
- ◆ Prognathism

18 months old GSD

MUSCULOSKELETAL SIGNS

- ◆ Immature facial features
- ◆ Square chunky contour (adult)

GSD 18 months F

GSD 2 years F

DERMATOLOGICAL SIGNS

- ◆ Retention of puppy coat
 - soft, woolly hair coat
 - lack of primary hairs



GSD 1 year M

DERMATOLOGICAL SIGNS

- ◆ Alopecia
 - bilaterally symmetrical
 - trunk, neck and proximal extremities



GSD 18 months F

DERMATOLOGICAL SIGNS

- ◆ Hyperpigmentation of the skin
- ◆ Comedones



GSD 2 years F

CONGENITAL PANHYPOPITUITARISM IN CATS



Siamese 6 months M



DSH 8 months M

OTHER SIGNS

- ◆ Reproductive signs
 - Testicular atrophy
 - Failure to cycle or abnormal cycles
- ◆ Mental dullness, aggression
- ◆ Shrill, puppy-like bark
- ◆ Clinical signs of 2° hypothyroidism
- ◆ Clinical signs of 2° hypoadrenocorticism

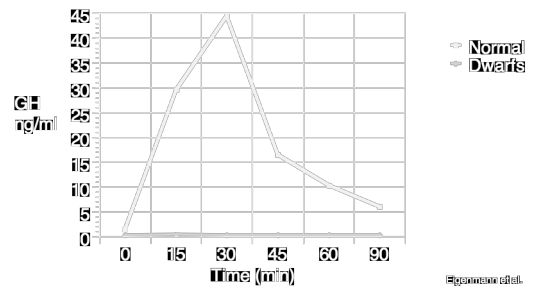
ENDOCRINE TESTING

- ◆ Basal growth hormone (GH) concentration
- ◆ Clonidine/xylazine stimulation
- ◆ Insulin-like growth factor 1 (IGF1)
- ◆ Thyroid function tests
- ◆ Adrenal function tests
- ◆ Gonadal function tests

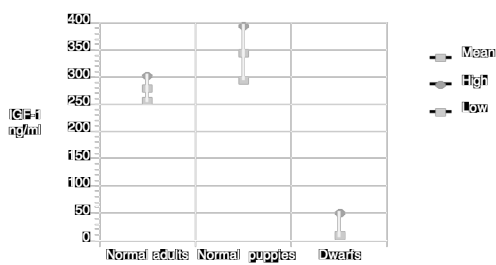
GROWTH HORMONE STIMULATION TEST

- ◆ Collect blood into EDTA, centrifuge and store frozen until assayed
- ◆ Inject IV either clonidine (Catapres®) 10 µg/kg (max. 300 µg) or xylazine (Rompun®) 100 µg/kg
- ◆ Collect second sample into EDTA after 20 min and centrifuge and store frozen

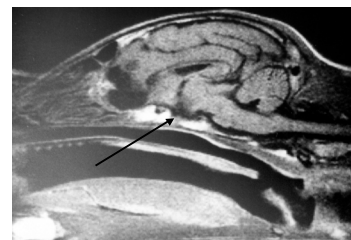
GROWTH HORMONE RESPONSE TO CLONIDINE



IGF-1 CONCENTRATIONS



MRI OF THE BRAIN OF A PITUITARY DWARF



GSD 6 month M with CDI

TREATMENT OF HYPOPITUITARISM



GSD 2 year F

After 6 months T4 therapy

TREATMENT OF HYPOPITUITARISM



GSD 8 months

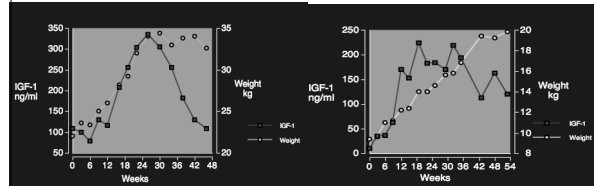
GSD 30 months

TREATMENT OF HYPOPITUITARISM

- ◆ Progestogen therapy
 - proligesterone (Delvosteron®)
 - 10 mg/kg by subcutaneous injection
 - every 3 weeks
 - monitor IGF1 concentrations
- ◆ Potential adverse effects
 - CEH, pyometra
 - acromegaly, diabetes mellitus

Jake

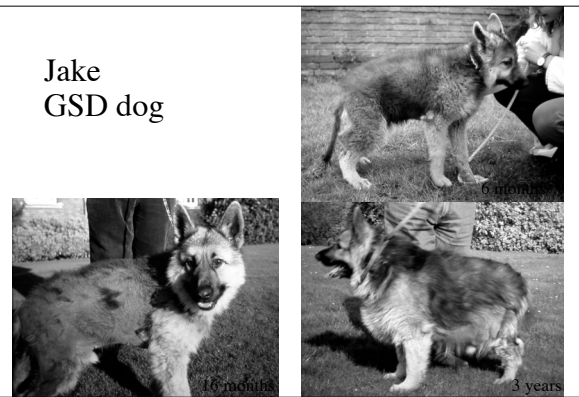
Tara



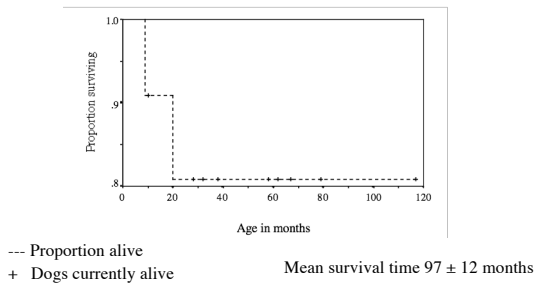
Tara
GSD bitch



Jake
GSD dog

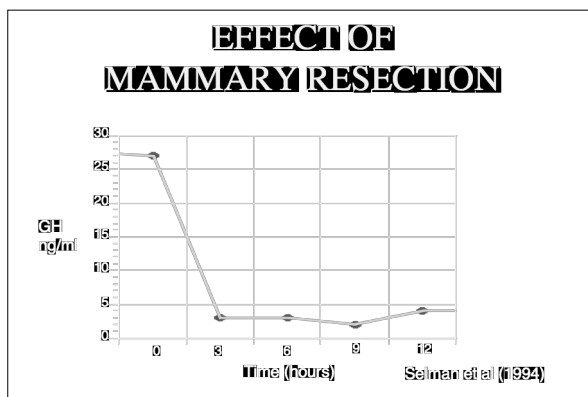
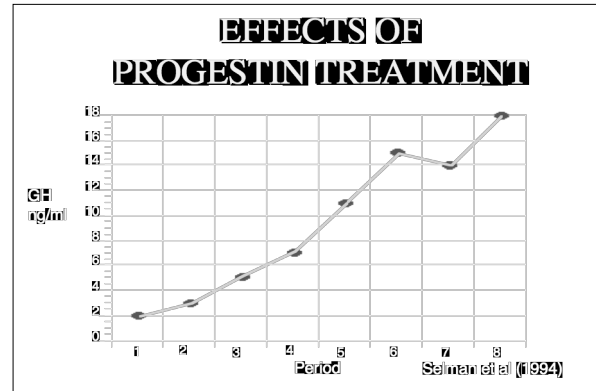
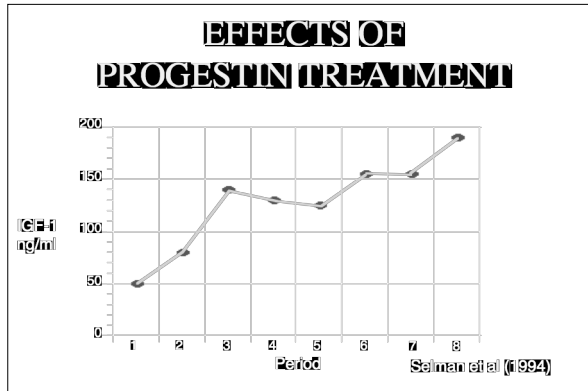


Kaplan-Meier survival curve for 11 pituitary dwarf dogs



AETIOLOGY OF ACROMEGALY

- ◆ Progesterone-induced acromegaly most common cause in bitches
- ◆ Progestogen-induced acromegaly in bitches or dogs
- ◆ Pituitary neoplasia in cats
- ◆ Hypothalamic neoplasia




- ### CLINICAL SIGNS OF ACROMEGALY
- ◆ Anabolic, IGF-induced
 - Respiratory
 - Dermatological
 - Conformational
 - ◆ Catabolic, GH-induced
 - Polyuria/polydipsia
 - Polyphagia
 - ◆ CEH/pyometra
 - ◆ Neoplasia-induced

- ### CLINICAL SIGNS OF CANINE ACROMEGALY
- ◆ Older intact bitches
 - ◆ Polyuria/polydipsia
 - ◆ Polyphagia
 - ◆ Hepatomegaly

CLINICAL SIGNS OF CANINE ACROMEGALY

- ◆ Inspiratory stridor, panting, exercise intolerance
- ◆ Enlargement of the head, abdomen, limbs and paws



GSD treated with a progestogen

CLINICAL SIGNS OF CANINE ACROMEGALY

- ◆ Increased interdental spaces



Labrador 12 years female

CLINICAL SIGNS OF FELINE ACROMEGALY



CLINICAL SIGNS OF FELINE ACROMEGALY

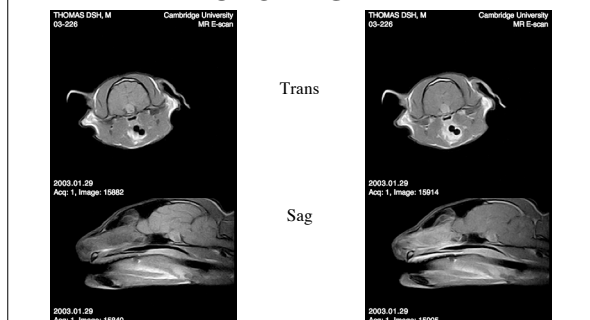


DSH 14 years Mn

LABORATORY FINDINGS IN ACROMEGALY

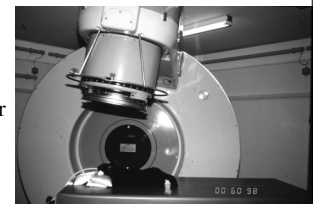
- ◆ Hyperglycaemia/glycosuria
- ◆ Insulin resistance (> 2 iu/kg per injection)
- ◆ Increased liver enzymes (ALP, ALT, AST)
- ◆ Hyperphosphataemia
- ◆ Increased growth hormone concentrations
- ◆ Increased IGF1 concentrations

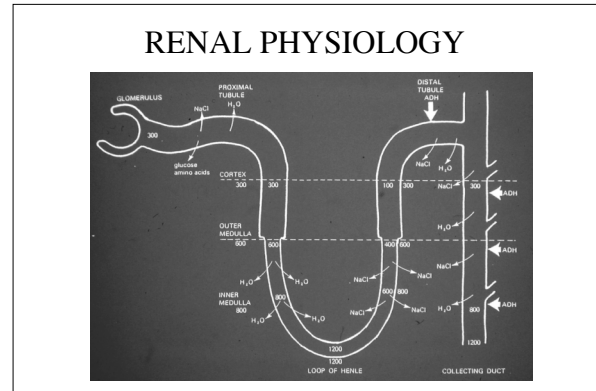
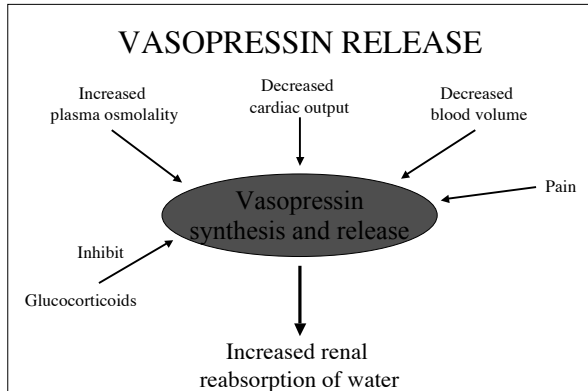
DIAGNOSTIC IMAGING FOR ACROMEGALY



TREATMENT OF ACROMEGALY

- ◆ Withdrawal of progestogens and/or ovariectomy in the bitch
- ◆ Pituitary irradiation with megavoltage radiation using a linear accelerator or cobalt-60 source





- ### DIABETES INSIPIDUS
- ◆ Central diabetes insipidus
 - Partial or total failure to synthesis or release vasopressin (ADH)
 - Cause: neoplasia, trauma, inflammation, idiopathic
 - ◆ Nephrogenic diabetes insipidus
 - Partial or total failure of the kidneys to respond to vasopressin (ADH)
 - Cause: renal medullary fibrosis, tubular necrosis, nephrocalcinosis, idiopathic

- ### PRIMARY (PSYCHOGENIC) POLYDIPSIA
- ◆ Functional lack of vasopressin due to over-hydration
 - ◆ Reduced renal concentrating power due to decreased medullary hypertonicity (medullary washing out effect)

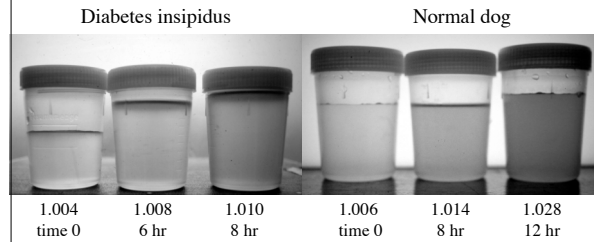
- ### CLINICAL SIGNS OF DIABETES INSIPIDUS
- ◆ Severe polyuria - often nocturia and/or urinary incontinence
 - ◆ Severe polydipsia - search for water, > 200 ml/kg/day
 - ◆ Secondary features - dehydration, anorexia, weight loss, CNS signs

- ### LABORATORY FINDINGS IN DIABETES INSIPIDUS
- ◆ Urinary specific gravity is LOW
 - 1.001 - 1.005
 - ◆ Urine osmolality is low
 - 50 - 200 mOsm/kg
 - ◆ Plasma osmolality is high
 - normal 275 - 300 mOsm/kg
 - ◆ Water deprivation test
 - ◆ ADH response test

WATER DEPRIVATION TEST

- ◆ Patient requires careful monitoring
 - Do not perform if renal function is compromised
 - Stop if patient loses > 5% body weight
- ◆ Collect urine (and plasma if measuring osmolality)
 - Weigh patient
 - Withdraw food and water
- ◆ Collect urine (and plasma) after 6 to 8 hours and then at 2 hourly intervals
- ◆ Stop if patient concentrates urine > 1.020 or loses if it loses 5% body weight

WATER DEPRIVATION TEST



DIFFERENTIATION OF DIABETES INSIPIDUS AND PRIMARY POLYDIPSIA

Parameter	Before water deprivation	After water deprivation		
	DI and PP	CDI	NDI	PP
<i>Urine</i>				
U vol ml/24h/kg	>50	>50	>50	>50
U SG	<1.010	<1.010	<1.010	<1.025
U Osm	<300	<300	<300	<700

DIFFERENTIATION OF DIABETES INSIPIDUS AND PRIMARY POLYDIPSIA

Parameter	Before water deprivation	After water deprivation		
	DI and PP	CDI	NDI	PP
<i>Plasma</i>				
P Osm	290-310	>310	>310	±310
U:P Osm	<1.0	<1.0	<1.0	2-3
ADH response	<1.0	>1.0	<1.0	>1.0

TREATMENT OF DIABETES INSIPIDUS

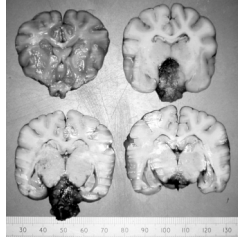
- ◆ Desmopressin (DDAVP)
 - injection, nasal drops, tablets
- ◆ Thiazide diuretics
 - Hydrochlorothiazide or bendroflumethiazide
 - Paradoxical effect due to natriuretic action reducing ECF and therefore GFR
 - Urine volume reduced by up to 50%
 - Urine SG unchanged

TREATMENT OF DIABETES INSIPIDUS

- ◆ Chlorpropamide
- ◆ Carbamazepine
- ◆ Non-steroidal anti-inflammatory drugs
- ◆ No therapy

PITUITARY TUMOURS

- ◆ Primary neoplasia
 - Functional
 - Non-functional
 - Benign
 - Malignant
- ◆ Secondary neoplasia



CLINICAL SIGNS OF PITUITARY NEOPLASIA

- ◆ Dull, depressed and listless
- ◆ Anorexia, vomiting
- ◆ Aimless wandering, head pressing
- ◆ Staring, apparent blindness
- ◆ Ataxia, incoordination

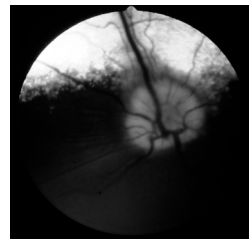


CLINICAL SIGNS OF PITUITARY NEOPLASIA

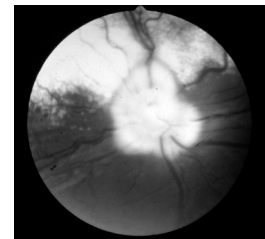
- ◆ Head tilt, circling
- ◆ Seizures
- ◆ Functional tumours
- ◆ Non-functional tumours may damage the rest of the pituitary
- ◆ Polydipsia, adipisia



CLINICAL SIGNS OF PITUITARY NEOPLASIA



Papilloedema



Pseudopapilloedema

DIAGNOSTIC IMAGING Contrast radiography



Cavernous sinus



Normal cavernous sinus venogram

DIAGNOSTIC IMAGING Contrast radiography

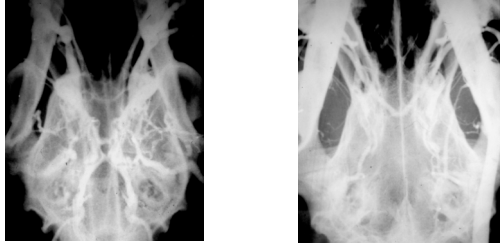


Cavernous sinus venography



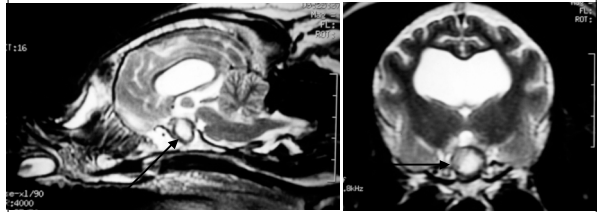
Normal cavernous sinus venogram

DIAGNOSTIC IMAGING Contrast radiography



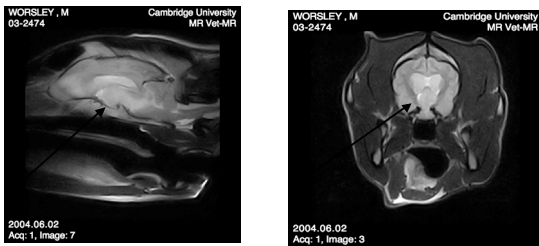
Normal cavernous sinus venogram Chow pituitary tumour

DIAGNOSTIC IMAGING CT / MR imaging



T2W scans of a Bulldog with a pituitary macroadenoma

DIAGNOSTIC IMAGING CT / MR imaging



T2W scans of a Dalmatian with a pituitary macroadenoma

Any questions?



WATER DEPRIVATION TEST

Diabetes insipidus



1.004 1.008 1.010
time 0 6 hr 8 hr

Normal dog



1.014 1.040
time 0 8 hr