

CORTICOSTEROIDS

GLUCOCORTICOIDS

MINERALOCORTICOIDS



Steroids

- **VETERINARY STEROIDAL DRUGS:**

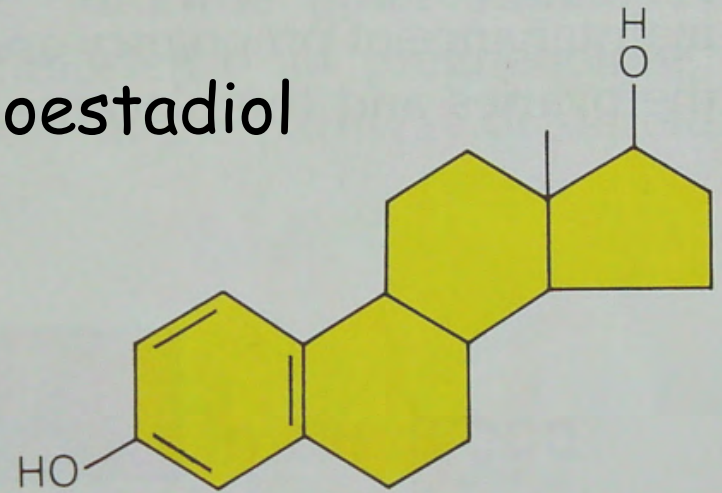
- GLUCOCORTICOIDS

- SEX HORMONES

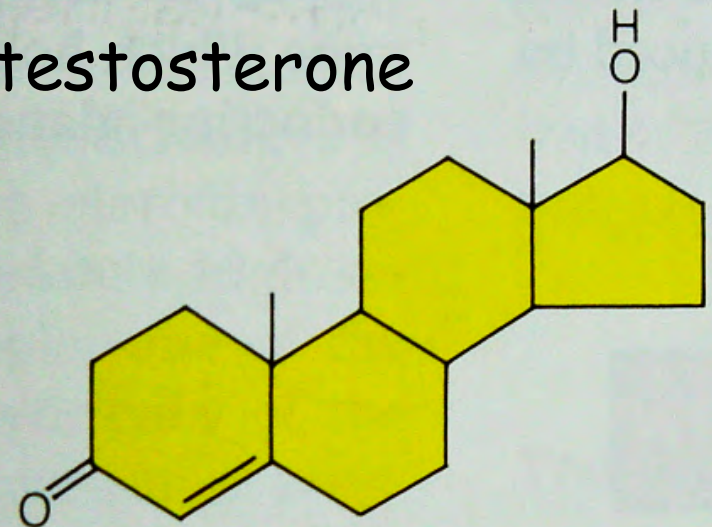
- ANAESTHETICS

- ANABOLIC STEROIDS

oestadiol

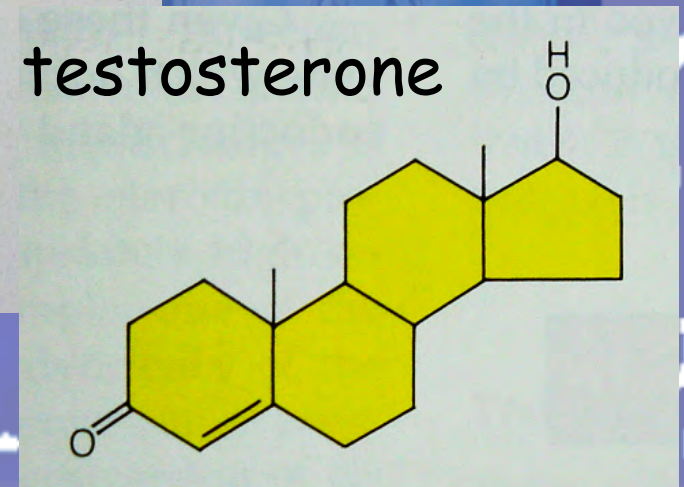
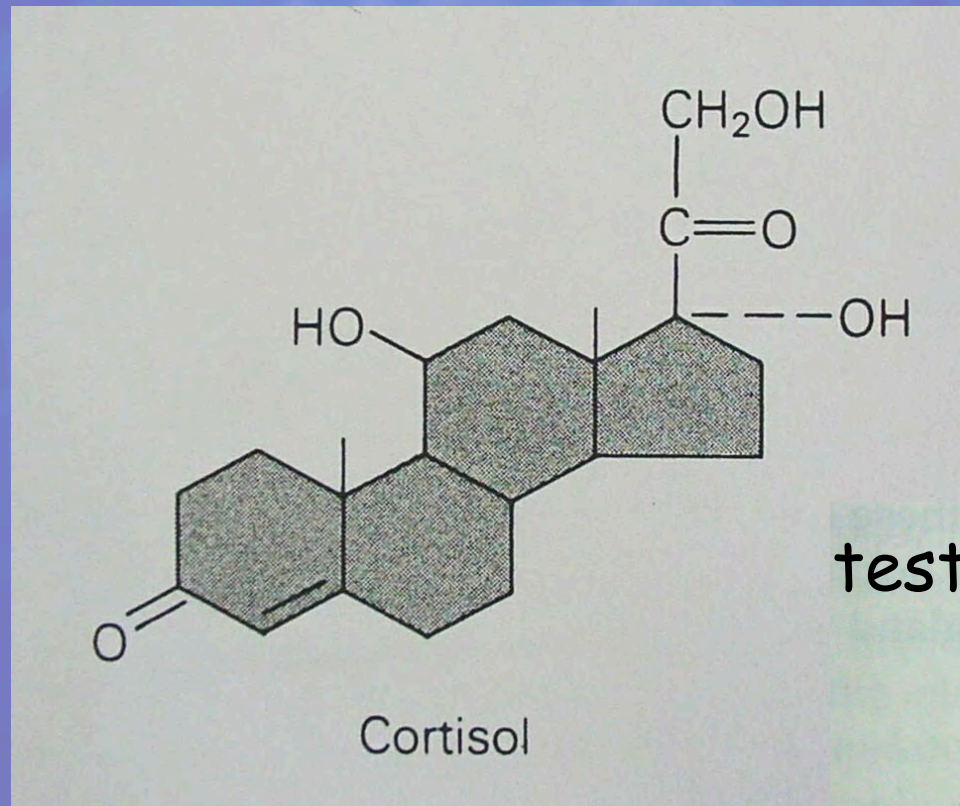


testosterone



Steroids

CORTISOL STRUCTURE



Corticosteroids

GLUCOCORTICOIDS

Hydrocortisone (Cortisol)

Prednisone and Prednisolone

Dexamethasone

MINERALOCORTICOIDS

Aldosterone

Fludromethasone -



Glucocorticoids

Corticosteroid	Sodium Retention	Anti-inflammatory
Endogenous		
Aldosterone	3000	?
Corticosterone	15	0.3
Cortisol	1	1
Synthetic		
Hydrocortisone	1	1
Prednisolone	0.8	4
Dexamethasone	0	25
Flumethasone	0	700



STEROIDAL MECHANISM OF ACTION

Transcriptional regulation

Steroid Receptor interactions



Glucocorticoid Effects

- **Energy Metabolism**
 - insulin antagonism
 - gluconeogenesis
 - lipolysis
 - protein catabolism



Glucocorticoid Effects

- **HAEMATOLOGICAL EFFECTS:**
- **INCREASED PLASMA:**
 - PCV and RBC lifespan
 - neutrophils
 - glucose
 - urea nitrogen
 - cholesterol
 - clotting time



Glucocorticoid Effects

- **HAEMATOLOGICAL EFFECTS:**
- **Decreased plasma**
 - lymphocytes
 - eosinophils
 - basophils
- **Decreased extravascular margination**
- **Depress serum thyroxine?**



Glucocorticoid Effects

- **Water and Electrolytes -**
 - ↓ calcium absorption (gut)
 - ↓ calcium absorption (bone)
 - ↑ calcium excretion (kidney)
 - polydipsia
 - polyuria
 - ↑ GFR



Glucocorticoid Effects

- **IMMUNOLOGICAL EFFECTS**

- numerous
- use extreme care with infectious disease -



Glucocorticoid Effects

- **CARDIORESPIRATORY SYSTEM**
 - Chronotropic
 - Inotropic
 - Catecholamines
 - ↑ Beta adrenoreceptors



Glucocorticoid Effects

- **CENTRAL NERVOUS SYSTEM**
 - Mental dependency
 - Euphoria
 - Hunger
 - Depression
 - ↓ pyrexia



Glucocorticoid Effects

- **SKIN -**
 - Increased calcification
 - Thinning and weakening of connective tissue



Glucocorticoid Effects

- **MUSCULOSKELETAL SYSTEM**

- ↓ osteoclast activity
- ↓ growth
- Depletion of cartilage matrix
- Osteoporosis



Glucocorticoid Effects

- **MUSCULOSKELETAL SYSTEM**
 - Muscular weakness
 - Muscle atrophy -



Glucocorticoid Effects

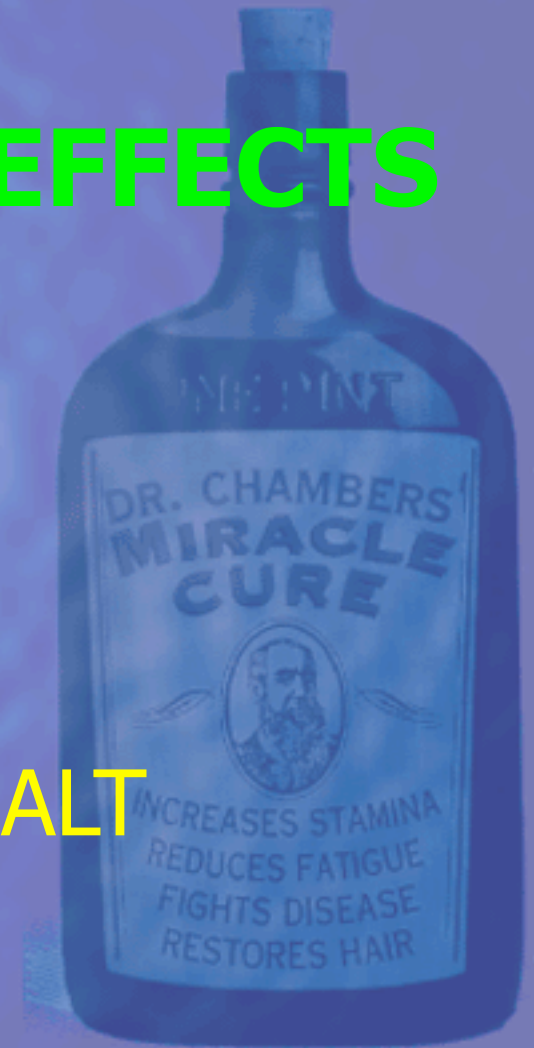
- **REPRODUCTIVE EFFECTS**

- Foetal maturation
- Teratogenic -
- Induce abortion
- Induce parturition -
- Inhibit spermatogenesis
- Inhibit ovulation



Glucocorticoid Effects

- **GASTROINTESTINAL EFFECTS**
 - Ulcerations
 - Fatty liver
 - Pancreatitis
 - Liver enzymes ↑ eg serum ALT



Anti-inflammatory Effects

- **Lipocortin**
 - inhibits phospholipase A -
- **Inhibit COX2 synthesis**
- **Lysosomal membrane stability**



Anti-inflammatory Effects

- **CELLULAR EFFECTS:**
 - Inhibition of leukocytes
 - Inhibition of inflammatory mediators
 - Interfere with catabolic enzymes
 - Suppress granulation tissue production -



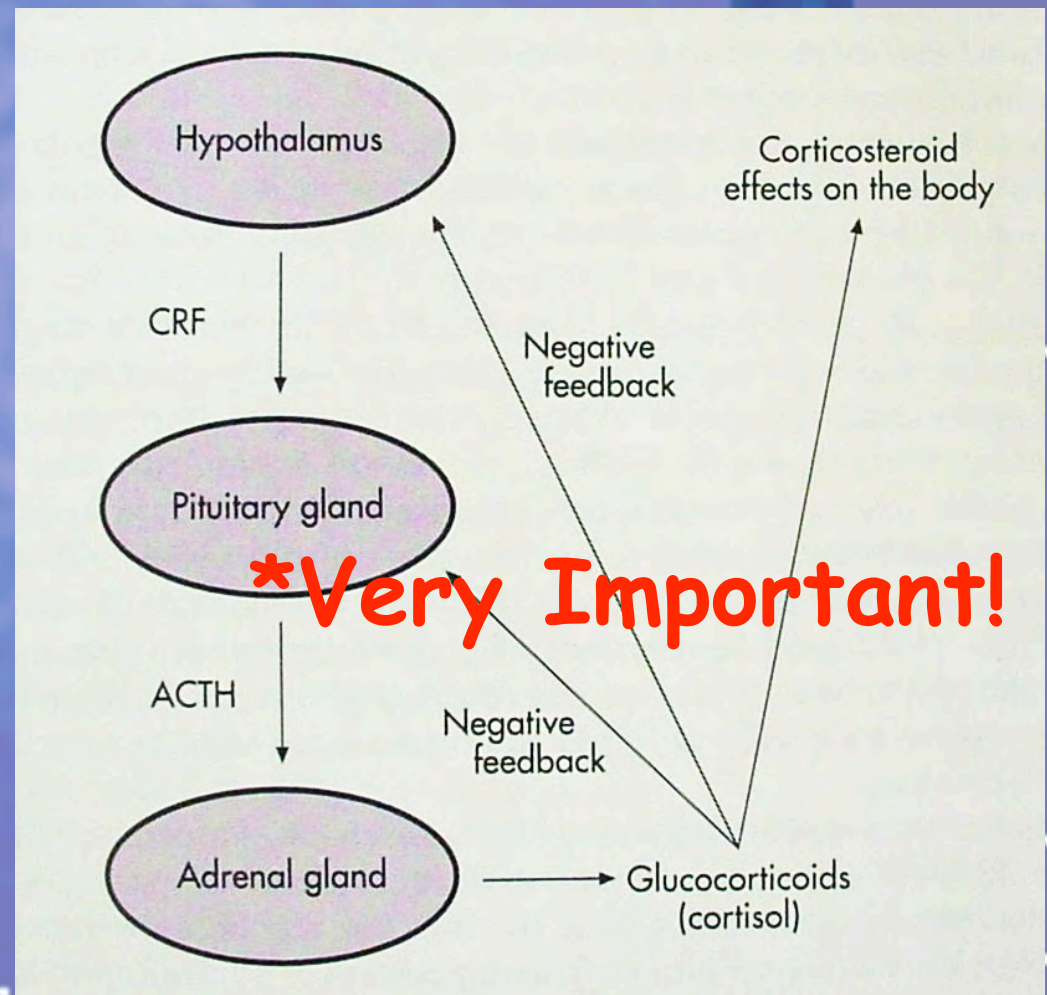
Immunosuppressive Effects

- **Dose related effect**
- **Duration of activity related effect**
 - short to medium acting
 - long acting



Hypothalamic-Pituitary-Adrenal Axis (HPA)

Negative Feedback



Corticosteroids

- **CLINICAL USES:**

- ALLERGIES
- INFLAMMATION
- IMMUNOSUPPRESSION
- PARTURITION INDUCTION
- ENDOCRINE FUNCTION TESTS
- THERAPY FOR ADDISON'S DISEASE
- TRAUMA/SHOCK THERAPY

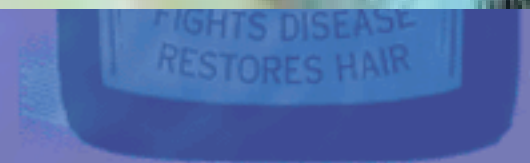
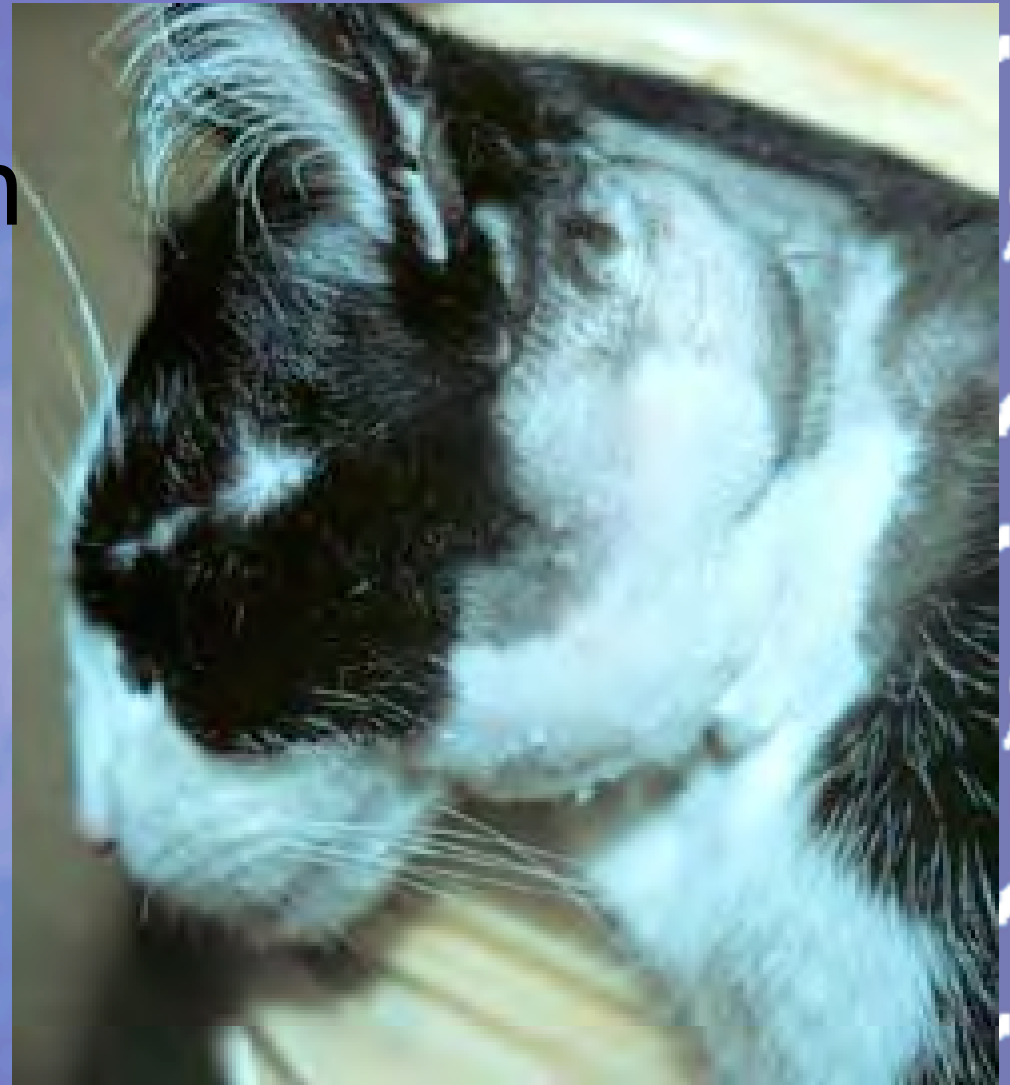




Induction of parturition



Immunosuppression cat with lymphoma





Cervical instability – Doberman breed

ALLERGY MANAGEMENT

- **Flea allergy**
- **Contact allergy**
- **Atopic conditions**
- **Inflammatory bowel disease**



TRAUMA ASSOCIATED INFLAMMATION

- Cerebral
- Spinal
- Ligamentous
- Capsular
- Synovial
- Muscular





Traumatic injuries



Glucocorticoid Anti-inflammatory Potencies

- Cortisol
- Prednisone
- Dexamethasone



Glucocorticoid Duration of Activity

- **SHORT ACTING:**

- cortisone, hydrocortisone
- Prednisone, prednisolone

- **INTERMEDIATE ACTING:**

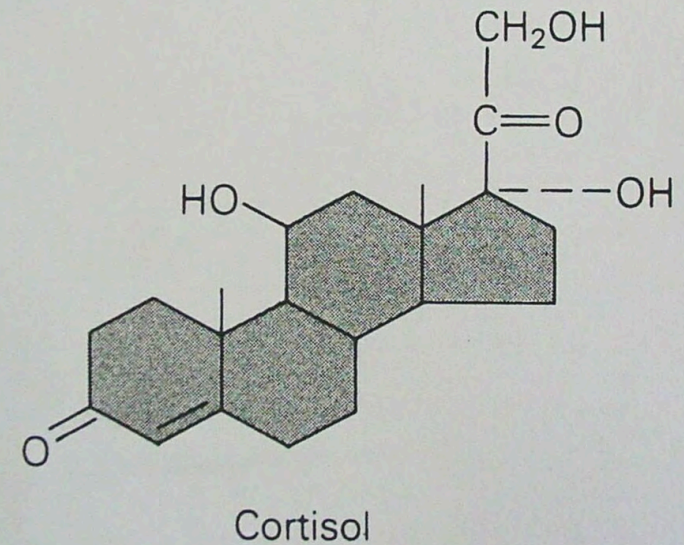
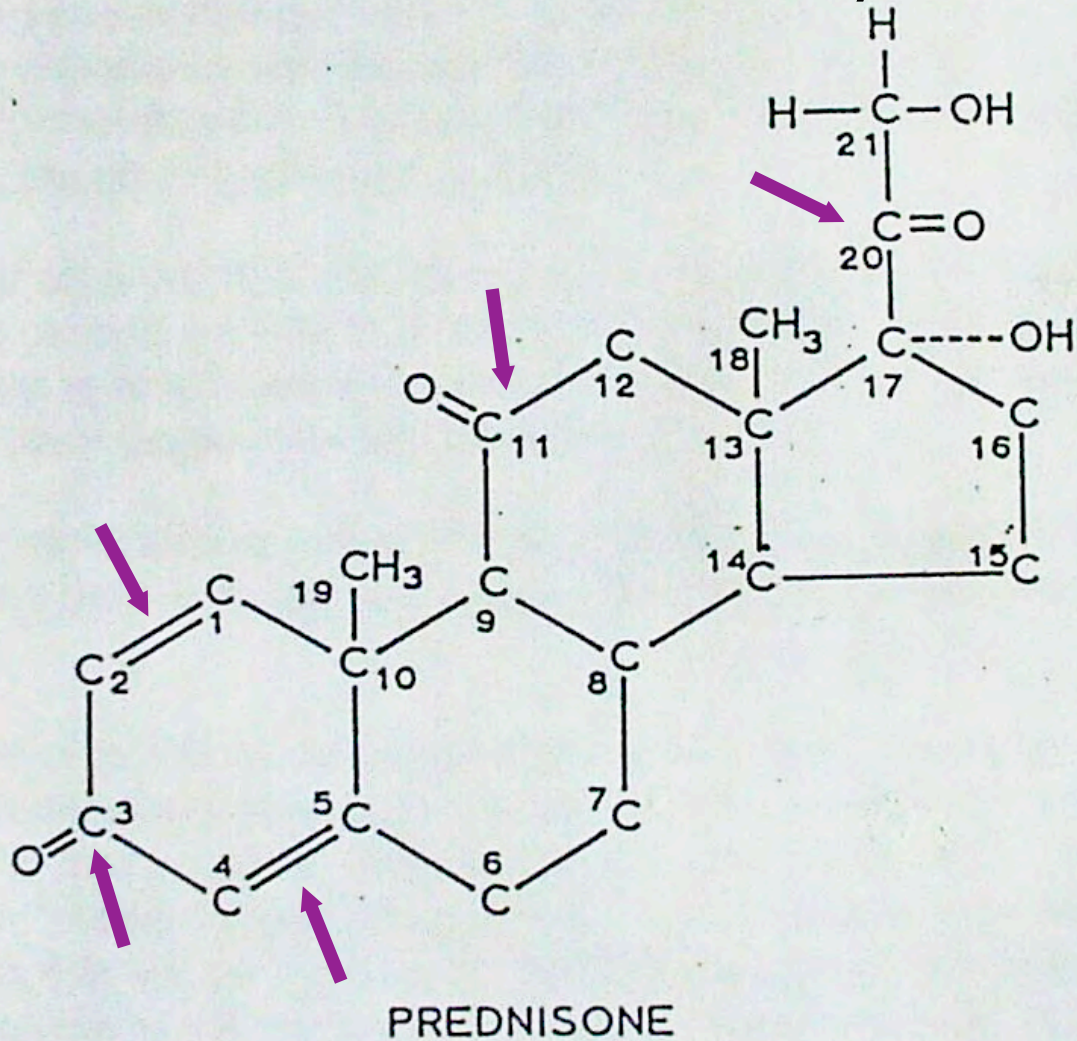
- methylprednisone, triamcinolone

- **LONG ACTING:**

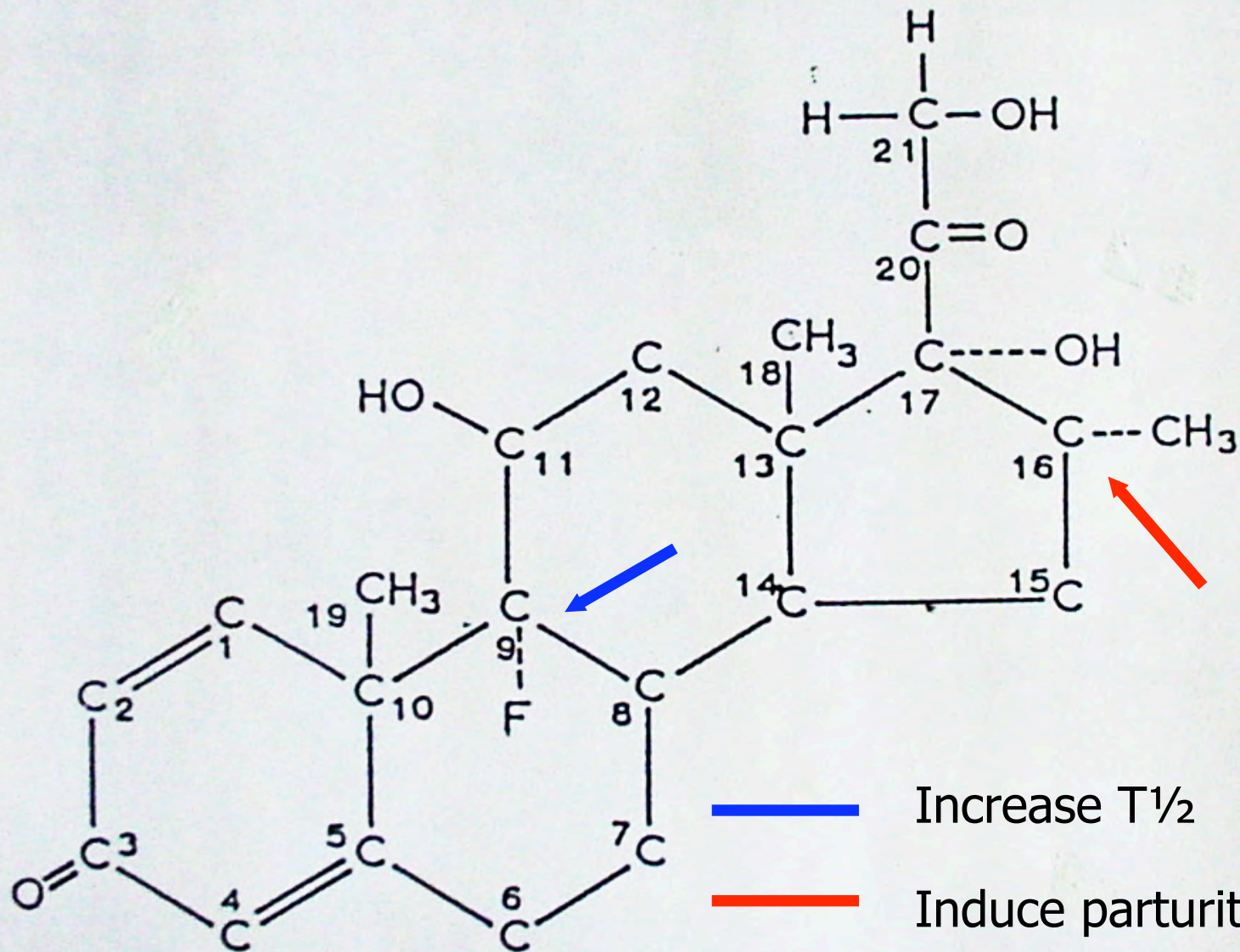
- dexamethasone
- Betamethasone



← Essential for activity



INCREASES STAMINA
REDUCES FATIGUE
FIGHTS DISEASE
RESTORES HAIR



- Increase $T_{1/2}$
- Induce parturition

DEXAMETHASONE

STRUCTURE-ACTIVITY RELATIONSHIPS

- **BASE** (relatively insoluble salts/esters)
 - short
 - intermediate
 - long acting
- **BASE-COMPOUND** (succinate, phosphate)
 - Increased solubility
- **FORMULATION** (topical, suspensions, tab)
 - physical characteristics



BASE

(relatively insoluble salts/esters)

- **BASE (relatively insoluble salts/esters)**

- **Oral corticosteroids:**

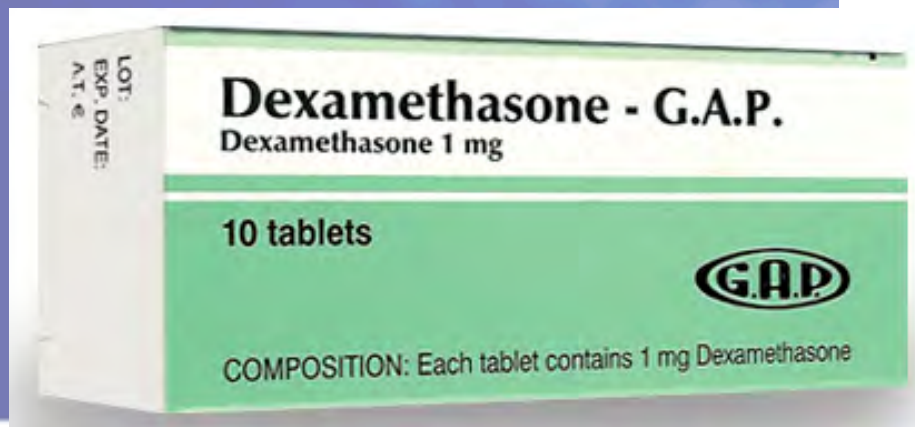
Apo-Prednisone

Methylprednisone

Dexamethasone

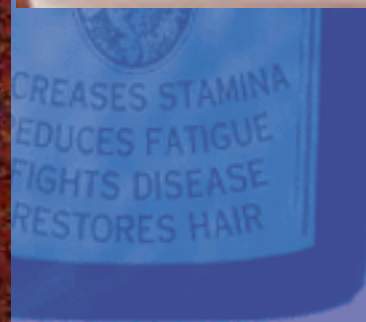
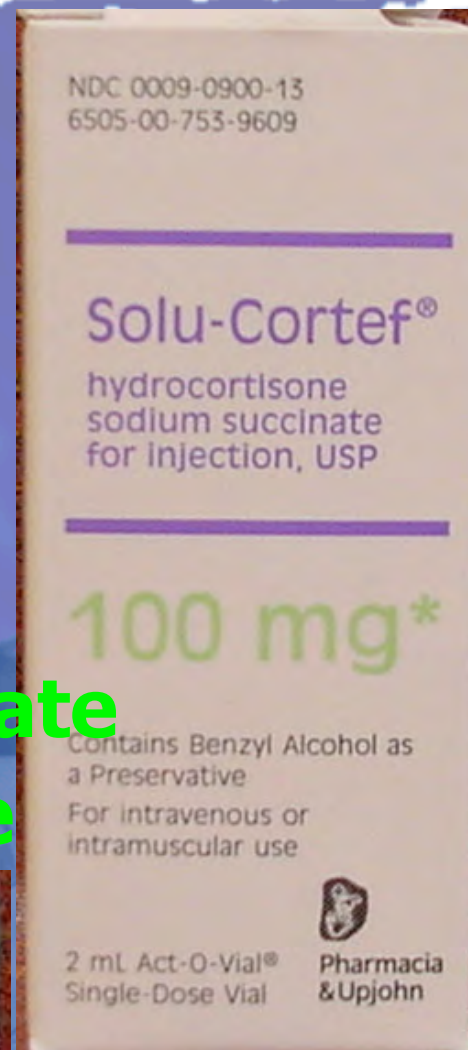
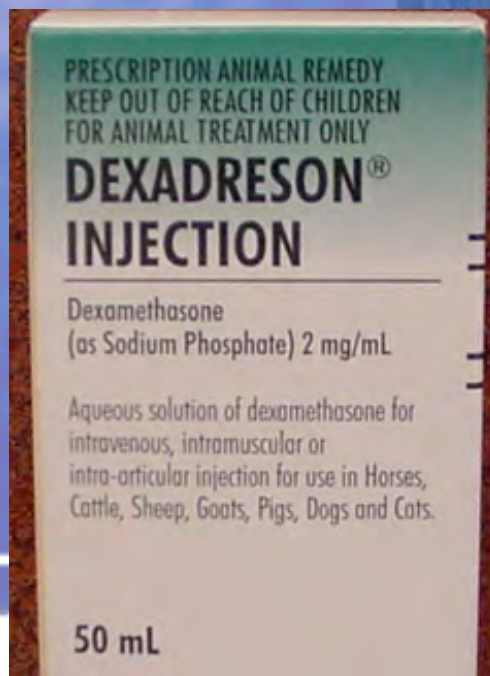


Medrol
Methylprednisolone



BASE-COMPOUND (succinate, phosphate) Increased solubility

- **BASE-COMPOUND**
- **Injectable Corticosteroids**
 - Hydrocortisone sodium succinate
 - Methylprednisolone sodium succinate
 - Dexamethasone sodium phosphate



STRUCTURE-ACTIVITY RELATIONSHIPS

- **BASE-COMPOUND** (phosphate and phenylpropionate)
 - Increased duration of action
 - Up to 8 days ?



(topical, suspensions, tab) physical characteristics



PHARMACOKINETICS

- **ABSORPTION**
- **FORMULATION & ROUTE DEPENDENT**
 - aqueous (IV, SQ, IM)
 - intermediate absorption
 - polyethylene glycol
 - long acting/depot
 - poor solubility in water



PHARMACOKINETICS

- **DISTRIBUTION**
- **DEPENDENT ON CORTICOSTEROID**
 - bound to proteins
 - transcortin
 - albumin
 - widely distributed



PHARMACOKINETICS

- **METABOLISM**

- Plasma/fluids hydrolyse most
- Hepatic metabolism of prednisone

- **ELIMINATION**

- Urinary excretion



SELECTION OF CORTICOSTEROIDS

- **COST**
- **ROUTE OF ADMINISTRATION**
- **ONSET OF EFFECTS**
- **DURATION OF EFFECTS**
- **MINERALOCORTICOID EFFECTS**
- **ANTI-INFLAMMATORY POTENCY**
- **HPA AXIS EFFECTS**



CONTRA-INDICATIONS

- **DIABETES MELLITUS**
- **CATABOLIC DISEASE**
- **INFECTIONS**
- **VIRAL INFECTIONS-CORNEAL
ULCERS**
- **YOUNG ANIMALS**
- **PREGNANCY**
- **SURGERY**



DRUG INTERACTIONS

- **MICROSOME INDUCTION**
- **DEPLETION of POTASSIUM (diuretics)**
- **INCREASE DRUG TOXICITY (digitalis)**
- **INSULIN ANTAGONISM**
- **DECREASE METABOLISM (cyclophosphamide)**
- **INHIBITS ACTIVATION (erythromycin)**
- **GASTRIC ULCERATION (NSAIDs)**



ADVERSE EFFECTS

- **STRESS LEUKOGRAM**
- **HEPATIC enzymes increase**
- **Serum THYROXINE depressed**
- **PU/PD/POLYPHAGIA**
- **CLEFT PALATE**
- **ABORTION (C16 modified)**
- **PEPTIC AND GASTRIC ULCERATION**



ADVERSE EFFECTS OF LONG TERM THERAPY

- Infection
- Myopathy
- Behavioural Changes
- Osteoporosis
- Poor Growth
- Calcinosis Cutis
- Hyperpigmentation and Thin Skin
- Collagen Diseases

Dogs are generally more sensitive than cats



GLUCOCORTICOID THERAPY

- **Taper the dose!**
- **Wean the animal off slowly**
 - the longer the course of therapy,
the longer the weaning off period



Doses

- **Anti-inflammatory doses**
- **Immunosuppressive doses**
- **Dose: dog vs cat**
- **Dexamethasone**
 - cat about 1/2 dog dose (generally)
- **Prednisone/prednisolone**
 - cat twice the dog dose (generally)



MINERALOCORTICOID EFFECTS

- **ADRENAL CORTICAL INSUFFICIENCY**
- **DOCP - desoxycorticosterone (injectable)**
- **FLUDROCORTISONE (oral use)**
 - Increased extracellular fluid
 - Sodium retention
 - Potassium and hydrogen ion loss
 - Increased glomerular filtration rate



Cushing's Syndrome

- **IATROGENIC**

- Excessive use of glucocorticoids

- **PITUITARY**

- Excessive production of ACTH

- **ADRENAL**

- Tumours or hyperplasia



Cushing's Syndrome

TREATMENT

- MITOTANE
 - Cytotoxic Effects On Z. Fasciculata and Reticularis
- SELGELINE
 - MONOAMINE OXIDASE B INHIBITOR



Glucocorticoid Effects

SUMMARY (need to know about)

- USES
- POTENCY AND DURATION
- SIDE EFFECTS
- CONTRAINDICATIONS
- DOSES

