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2  Steroids

- VETERINARY STEROIDAL DRUGS:
  - GLUCOCORTICOIDS
  - SEX HORMONES
  - ANAESTHETICS
  - ANABOLIC STEROIDS

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5  Glucocorticoids

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7  Glucocorticoid Effects

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

8  Glucocorticoid Effects

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

9  Glucocorticoid Effects

- HAEMATOLOGICAL EFFECTS:
  - Decreased plasma
    - lymphocytes

- eosinophils
- basophils
- Decreased extravascular margination
- Depress serum thyroxine?

## 10 Glucocorticoid Effects

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

## 11 Glucocorticoid Effects

- IMMUNOLOGICAL EFFECTS
  - numerous
  - use extreme care with infectious
  - disease –

## 12 Glucocorticoid Effects

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

## 13 Glucocorticoid Effects

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

## 14 Glucocorticoid Effects

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

## 15 Glucocorticoid Effects

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

## 16 Glucocorticoid Effects

- MUSCULOSKELETAL SYSTEM
  - Muscular weakness
  - Muscle atrophy –

## 17 Glucocorticoid Effects

- REPRODUCTIVE EFFECTS
  - Foetal maturation
  - Teratogenic –
  - Induce abortion
  - Induce parturition –
  - Inhibit spermatogenesis
  - Inhibit ovulation

## 18 Glucocorticoid Effects

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

## 19 Anti-inflammatory Effects

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

## 20 Anti-inflammatory Effects

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

## 21 Immunosuppressive Effects

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

## 22 Hypothalamic–Pituitary–Adrenal Axis (HPA)

- Negative Feedback

## 23 Corticosteroids

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

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27  ALLERGY MANAGEMENT

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

28  TRAUMA ASSOCIATED INFLAMMATION

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

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30  Glucocorticoid

Anti-inflammatory Potencies

- Cortisol = 1
- Prednisone = 4
- Dexamethasone = 25

31  Glucocorticoid

Duration of Activity

- SHORT ACTING:
  - cortisone, hydrocortisone
  - Prednisone, prednisolone
- INTERMEDIATE ACTING:
  - methylprednisone, triamcinolone
- LONG ACTING:
  - dexamethasone
  - Betamethasone

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34  STRUCTURE–ACTIVITY  
RELATIONSHIPS

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

35  BASE

(relatively insoluble salts/esters)

36  BASE–COMPOUND

(succinate, phosphate)

Increased solubility

37  STRUCTURE–ACTIVITY  
RELATIONSHIPS

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

## 38 FORMULATION

(topical, suspensions, tab)  
physical characteristics

## 39 PHARMACOKINETICS

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

## 40 PHARMACOKINETICS

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

## 41 PHARMACOKINETICS

- METABOLISM
  - Plasma/fluids hydrolyse most
  - Hepatic metabolism of prednisone
  -
- ELIMINATION
  - Urinary excretion

## 42 SELECTION OF CORTICOSTEROIDS

- COST
- ROUTE OF ADMINISTRATION

- ONSET OF EFFECTS
- DURATION OF EFFECTS
- MINERALOCORTICOID EFFECTS
- ANTI-INFLAMMATORY POTENCY
- HPA AXIS EFFECTS

#### 43 CONTRA-INDICATIONS

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

#### 44 DRUG INTERACTIONS

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

#### 45 ADVERSE EFFECTS

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



## 46 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

## 47 GLUCOCORTICOID THERAPY

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

## 48 Doses

- Anti-inflammatory doses
- Immunosuppressive doses
- Dose: dog vs cat
  - Dexamethasone
    - cat about  $\frac{1}{2}$  dog dose (generally)
  - Prednisone/prednisolone
    - cat twice the dog dose (generally)

## 49 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

## 50 Cushing's Syndrome

- IATROGENIC
  - Excessive use of glucocorticoids
- PITUITARY
  - Excessive production of ACTH
- ADRENAL
  - Tumours or hyperplasia

## 51 Cushing's Syndrome

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

## 52 Glucocorticoid Effects

- SUMMARY (need to know about)
  - USES
  - POTENCY AND DURATION
  - SIDE EFFECTS
  - CONTRAINDICATIONS
  - DOSES