

## 1 Anti-cancer Drugs

## 2 principles

- objective
  - to prolong useful life – not cure
- treatment
  - surgery
  - radiotherapy
  - chemotherapy
  - (euthanasia)

## 3 chemotherapy indications

- non resectable tumours
  - generalised
  - metastatised
- delay metastasis
- adjunct to surgery
- treating relapses

## 4 7 yr old Boxer

- swollen submandibular lymph nodes
- anorexia
- weight loss
- lethargy

## 5 further tests

- bloods
  - haematology
  - biochemistry
- lymph node biopsy

## 6

## 7 diagnosis

- lymphoma

## 8 lymphoma treatment

- 38 protocols for dogs published
- all empirical
- no comparative trials
- combinations
  - increase effectiveness
  - reduce side effects

## 9 COP protocol

- cyclophosphamide
- vincristine (Oncovin)
- prednisolone

## 10 induction

- cyclophosphamide 50mg/m<sup>2</sup> 4d
- vincristine 0.7mg/m<sup>2</sup> iv once
- prednisolone 1mg/kg twice daily
- repeat for 8 weeks

## 11 maintenance

- cyclophosphamide 50mg/m<sup>2</sup> every other day
- vincristine 0.5mg/m<sup>2</sup> iv every other week
- prednisolone 1mg/kg every other day of every other week

## 12 lymphoma treatment

- complicated
- expensive
- unpleasant for animal
- potentially dangerous
- temporary

## 13

## 14 cancer cells

- inactivation of tumour suppressor genes
  - mutation?

- activation of oncogenes
  - viruses
  - mutation
  - translocation
  - inflammation???


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16  cancer cells

- uncontrolled proliferation
- loss of function
  - lack of differentiation
- invasiveness
  - new blood supply
- metastases

17  cancer cells

- very similar / the same as normal cells
  - interference with apoptosis
  - telomerase
  - overexpression of some surface receptors?

18  drug strategies

- interfere with DNA
  - apoptosis
- interfere with mitosis
- interfere with blood supply
  - angiogenesis inhibitors
    - MMP inhibitors
    - FGF inhibitors

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20  general actions of drugs

- most interfere with DNA synthesis

- not specific for cancer cells – will kill any rapidly dividing cells
  - bone marrow
  - gut mucosa
  - germ cells
  - hair follicles
- not possible to kill all cancer cells
- normal cells recover faster

## 21 general side effects

- vomiting and diarrhoea
- bone marrow suppression
- alopecia
- impaired wound healing
- sterility
- teratogenesis
- plus specific side effects

## 22 dosage

- body surface area

## 23 drugs

- alkylating agents
- antimetabolites
- cytotoxic antibiotics
- plant alkaloids
- sex hormones / antagonists
- odds & ends

## 24 alkylating agents

## 25 alkylating agents


- nitrogen mustards
  - cyclophosphamide
  - chlorambucil
  - melphalan

- similar to alkylating agents
  - cisplatin
  - carboplatin
  - nitrosureas

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27  antimetabolites


- folate antagonists
  - methotrexate
- pyrimidine analogues
  - fluorouracil
  - cytarabine (cytosine arabinoside)
- purine analogues
  - mercaptopurine (azathioprine)
  - thioguanine

28  antibiotics

- doxorubicin
- bleomycin
- dactinomycin

29  plant alkaloids

- vincristine
- vinblastine
- taxol (paclitaxel)
- etoposide

30  sex hormones

- oestrogens
  - ethinyloestradiol
- anti-androgens
  - delmadinone
  - (GnRH analogues)
- anti-oestrogens

- tamoxifen
- anastrozole

### 31 others

- crisantaspase (asparaginase)
- mitotane
- radioactive iodine

### 32 drug resistance

- many mechanisms
  - P glycoprotein
- use combinations
- not usually treated in veterinary medicine

### 33 protocols

- usually combinations
- large doses with intervals?
- supportive therapy
- monitor side effects

### 34 supportive therapy

- analgesics
  - NSAIDs
- anti-emetics
  - ondansetron
  - metaclopramide
- appetite stimulants
  - diazepam
- anabolic steroids

### 35 the future???

- angiogenesis inhibitors
- specific cell targetting – MCA
- oncogene antisense oligonucleotides
- oncogene transduction blockers

- suppressor gene therapy
- telomerase inhibitors
- exogenously sensitised lymphocytes

### 36 handling drugs

- wear protective clothing – gloves & mask
- use fume cupboard for mixing drugs
- avoid spillage or leaks
- avoid breaking tablets up
- dispose of faeces and urine by burning
- pregnant women should not handle drugs / animals being treated
- keep animals away from children

### 37 handling drugs

- OSH guidelines cover vet use
- buy injections already made up
- hospitalise animals

### 38 anti-cancer drugs

- seek advice before using and check latest protocol
- remember the aim is to prolong useful life
- handle drugs with great care