

Anti-Cancer Drugs

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7 yr old Boxer

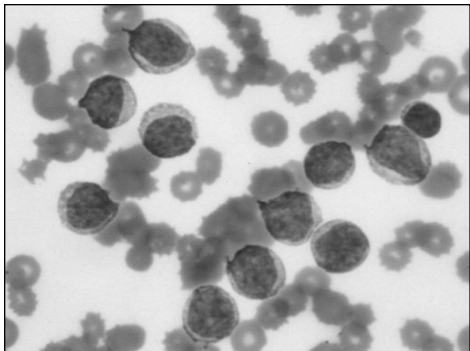
- swollen submandibular lymph nodes
- anorexia
- weight loss
- lethargy

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further tests

- **bloods**
 - haematology
 - biochemistry
- **lymph node biopsy**

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diagnosis

- lymphoma

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principles of treatment

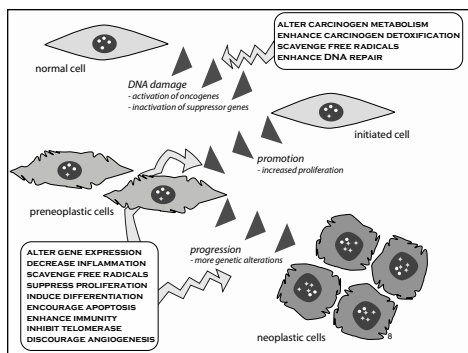
- **objective**
 - to prolong useful life - not cure
- **treatment**
 - surgery
 - radiotherapy
 - chemotherapy
 - (euthanasia)

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chemotherapy indications

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

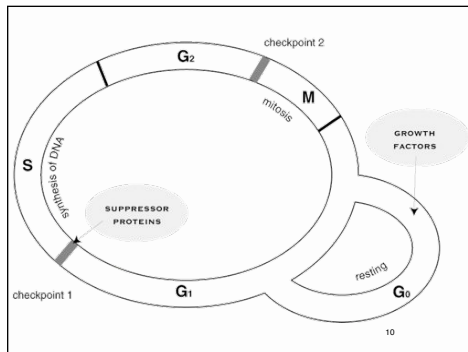
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cancer cells

- **inactivation of tumour suppressor genes**
 - mutation?
- **activation of oncogenes**
 - viruses
 - mutation
 - translocation
 - inflammation???

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cancer cells

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

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cancer cells

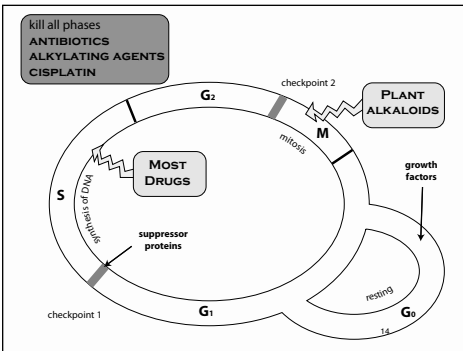
- **very similar / the same as normal cells**
 - interference with apoptosis
 - telomerase
 - overexpression of some surface receptors?

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drug strategies

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

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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**

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general side effects

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

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dosage

- body surface area

$$= \frac{W^{0.67}}{10} \text{ m}^2$$

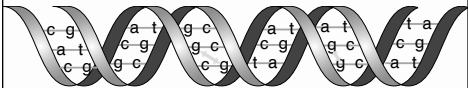
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drugs

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

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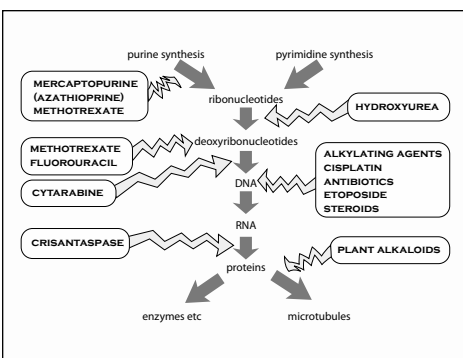
alkylating agents



alkylating agents

- **nitrogen mustards**
 - cyclophosphamide
 - chlorambucil
 - melphalan
- **similar to alkylating agents**
 - cisplatin
 - carboplatin
 - nitrosureas

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antimetabolites

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

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antibiotics

- doxorubicin
- bleomycin
- dactinomycin

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plant alkaloids

- vincristine
- vinblastine
- taxol (paclitaxel)
- etoposide

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sex hormones

- **oestrogens**
 - ethinylloestradiol
- **anti-androgens**
 - delmadinone
 - (GnRH analogues)
- **anti-oestrogens**
 - tamoxifen
 - anastrozole

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others

- **crisantaspase (asparaginase)**
- **mitotane**
- **radioactive iodine**

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drug resistance

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

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protocols

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

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supportive therapy

- **analgesics**
 - NSAIDs
- **anti-emetics**
 - ondansetron
 - metoclopramide
- **appetite stimulants**
 - diazepam
- **anabolic steroids**

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the future???

- **angiogenesis inhibitors**
- **specific cell targeting - MCA**
- **oncogene antisense oligonucleotides**
- **oncogene transduction blockers**
- **suppressor gene therapy**
- **telomerase inhibitors**
- **exogenously sensitised lymphocytes**

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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**

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handling drugs

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

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lymphoma treatment

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

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COP protocol

- **cyclophosphamide**
- **vincristine (Oncovin)**
- **prednisolone**

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induction

- **cyclophosphamide 50mg/m²
4d**
- **vincristine 0.7mg/m² iv once**
- **prednisolone 1mg/kg twice
daily**
- **repeat for 8 weeks**

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maintenance

- **cyclophosphamide 50mg/m²
every other day**
- **vincristine 0.5mg/m² iv every
other week**
- **prednisolone 1mg/kg every
other day of every other week**

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lymphoma treatment

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

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anti-cancer drugs

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

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