Parasiticidal Drugs

Anthelmintics

Drug	Method of Action	Notes
Benzimidazoles		
Binds to parasite β-tubulin of microtubules → disrupts cell shape, division, motility, absorption. Also binds mammalian tubulin but quickly dissociates ↑ drug-parasite exposure time correlated w/ efficacy Not water-soluble so comes in pastes, suspensions, granules Poor oral bioavailability – but we want it in gut lumen anyway (not good for systemic parasite tx)		Broad spectrum: GI + lung nematodes; some cestodes and trematodes (not 1st choice) High margin of safety; differences in activity dto PK not PD Extensive hepatic CYP metabolism (1st pass) and also metabolized in lung, intestines Metabolites have varying activity levels
Fenbendazole (Panacur, Safe-guard)	Kills wide range of nematodes (especially adult GI worms, lungworms - strongyles, ascarids, whipworms, hookworms, pinworms) Has claim for cestodes (*Taenia)* in dogs	Licenced for use in horses, cattle, swine, dogs Used off-label in small ruminants + turkeys, reptiles In cats, used for nematodes (esp. lungworm) + *Giardia*
Fenbental	Fenbendazole pro-drug	Product is Drontal Plus for dogs (also includes pyrantel, praziquantel)
Albendazole (Valbazen)	Oral suspension for cattle Indications: adult flukes *(F. hepatica)* – limited efficacy, adult tapeworms, same GI + lung roundworms as FBZ	Is more expensive, not often used Possible teratogenic in early gestation (don't use w/i 21 days of breeding)
Triclabendazole (Fascinex)	Active against adult + juvenile flukes: *F. hepatica*, also *F. gigantca, F. magna, Paragonimus*	Available only via emergency drug release
Macrocyclic Lactones		
Activates (opens) glutamate-gated Cl- channels → Cl- enters cell, hyperpolarization – flaccid paralysis of worm pharyngeal and somatic muscles (can't eat/move) At high concentrations, may bind to similar GABA receptors Considered endectocides: kill internal + external parasites - active against nematodes & arthropods (but not *Demodex* or adult heartworm), minimal activity against cestodes & trematodes Lipophilic so absorbed orally/transcuticular by the parasite Produced by fermentation of *Streptomyces* in the soil Withdrawal times can be long dto 1-3 week T1/2 Must apply to skin, not hair. Also is flammable, so careful w/ branding. Decrease efficacy at cold temps 2 categories: *Avermectins* = ivermectin, salamectin, eprinomectin, doramectin. *Milbemycins* = moxidectin, milbemycin		PK determines efficacy more so than potency Good bioavailability, high distribution Products are oral, topical or injectable for animals, also will groom though so topical = oral Toxicity associated w/ GABA stim if gets into CNS (esp. in ABCB1 mutants) → ataxia, seizures. Treatment is supportive care +/- lipid emulsion Hepatic metabolism, excreted by bile/feces Resistance increasing in horses/cattle, worst in sheep – esp for cyasthostomes & small strongyles. Mechanism = parasite efflux pumps + changes in Glu-gated Cl- channels Can persist in feces and contaminate environment
Ivermectin (Ivomec), generics	Formulations based on species: Oral drench = sheep, oral paste = horses, pour-on = cattle, injectable = cattle/sheep/swine, oral premix = swine, oral tablets = dogs	Oldest, most used. NOT FOR DAIRY COWS!! (milk residues) Small doses (3-6% of normal dose) used in dogs for heartworm prevention (Heartgard)– safe in ABCB1 mutants
Eprinomectin	Eprinex = Pour-on product for daily cattle Long-Range = extended release SC injection; 4-5mo activity but 4-mo meat withdrawal period.	No milk withholding time ∴ only one for dairy NOT FOR DAIRY COWS! Also very expensive
Doramectin (Dectomax)	Injectable for cattle/swine, pour-on version used to exist	Similar parasite spectrum to ivermectin
Salamectin (Revolution, Dolmectin)	Monthly cat/dog topical for fleas, mites (but not *Demodex)*, nematodes, heartworm prevention	Less affinity for P-gp than ivermectin, so somewhat safer for ABCB1 mutants Possible use against sea lice in salmonid aquaculture
Moxidectan	Cydectin: pour-on for beef/dairy cattle Quest/Quest Plus (+ praziquantel): oral gel for horses Advantage Multi: moxidectin + imidacloprid ProHeart 6: sustained release injection for dogs	Same as ivermectin + questionable efficacy against lice Nematodes +/- tapeworms GI nematodes, HW prevention, fleas, ear mites HW prevention (for 6 months)
Milbemycin	Milbemax: monthly tablets for cats (+ praziquantel) Interceptor: tablets for dogs/cats Sentinel: tablets for dogs (+ lufrenon) Trifexis: tablets for dogs (+ spinosad)	HW prevention, GI nematodes + tapeworms Same but no tapeworm efficacy (no praziquantel) HW prevention, GI nematodes plus fleas HW prevention, GI nematodes plus fleas
Other Anthelmintics		
Piperizine (Diethylenediamine)	Anticholinergic activity at parasite NMJs, probably hyperpolarization of NMJs → leads to flaccid paralysis, swept out of host GI tract For large roundworms (not effective on migrating larvae)	Sold in feed and pet stores, not clinics Very old OTC dewormer for chickens, turkeys, swine, horses, dogs, cats (not ruminants, lack of efficacy) Safe, but can cause GI or neuro signs. Water additive for food animals, tablets for dogs/cats
Diethylcarbamazine (Decacide)	Tablets for dogs/cats for HW prevention, ascarids	Related to piperazine, but daily administration (rarely used)
Pyrantel	Depolarizes NMJ; nicotinic agonist → leads to spastic paralysis Pamoate salt in paste/suspension: Drontal/Drontal Plus (+ praziquantel, febantel): dogs/cats Dolpac (+ oxantel, praziquantel): dogs HeartHard Plus (+ ivermectin): dogs Exodus: oral paste for horses Strongid: oral for horses, EDLU for small animals (cheap) Tartrate salt in solutions for drinking water: Pro-Banminth premix: For *Ascaris suum* in swine	Nematodes but maybe some cestodes at high doses Resistance in horses to small strongyles Very safe (toxic dose is 7x normal dose) Similar drugs: morantel, oxantel

Other Anthelmintics			
	Emodepside Topical	Induces intracellular signal transduction in parasite pharynx and body wall muscle → flaccid paralysis Profender (+ praziquantel) for cats	For roundworms, hookworms, tapeworms Very safe incl. pregnant queens, just mild GI signs P-gp substrate → drug interactions
	Praziquantel	↑ Ca2+ in the intracellular fluid → spastic paralysis Droncit is just praziquantel, but is also found in other products also containing anti-nematode drugs (see above)	For cestodes (tapeworms) in dogs, cats, horses, cattle etc. P-gp substrate
	Epsiprantel (Cestex)	Unknown, likely similar to praziquantel For tapeworms in dogs/cats	Poor oral bioavailability, but using for GI worms anyway Likely very safe, used in young animals. No drug interactions
	Nitroscanate (Lopatol)	For roundworms, hookworms, some tapeworms Tablets for dogs	Only available in CAN ($$$) not USA Poor GI absorption ADE: mainly vomiting; is safe in pregnant and young dogs
	Melarsomine (Immiticide)	Arsenic-like, mechanism unknown Used in dogs to kill adult heartworms	Deep IM injection in epaxial muscles L3-L5 2x, 1d apart Narrow therapeutic window – emboli, immune rxn; NASTY! Painful on injection
	Closantel (Flukiver)	For tx of *Haemonchus contortus* (Barber Pole worm) infection in sheep and lambs	Not for lactating sheep, long 49d withdrawal time EDLU for flukes in cattle/sheep (not labelled for flukes in NA)
	Monepantel (Zolvix) **Derquantel**	Act on nACh-Receptor (nematode-specific so very low toxicity for mammals) Gets all GI nematode stages, even hypobiotic stages	Not available in CAN Oral drench for sheep available elsewhere in world

Coccidiostats & Antiprotozoal drugs

Drug	Method of Action	Notes
Coccidiosis Therapies		
Sulfon amides **Sulfaquinoxaline** **Sulfamethazine**	Analogue of PABA; interrupts folate synthesis → antibacterial + anti-coccidial effects Oral solution for poultry Oral bolus or solution for calves, sheep, poultry	Used for cases of clinical dz associated w/ coccidiosis
Potentiated Sulfas **Quinnoxine-S**	Also inhibits a 2nd step in folate synthesis (dihydrofolate reductase) Sulfa + pyrimethamine Sulfa + trimethoprim is also affective against coccidia	For poultry Available in CAN but not licensed for this use
Amprolium (Amprol, AmproMed)	Thiamine analogue (anti-metabolite) For prevention of coccidial dz but not effective if clinically effected	Oral solutions + feed mixes available for poultry and calves At high doses can affect mammalian thiamine → thiamine deficiency → polioencephalomalacia. Tx w/ thiamine ASAP
Ionophores	Na/K pump activation & disruption of electrolyte balance in bacterial/protozoans → osmotic damage in myocytes Also affects metal cation transport into cell → osmotic damage Good for coccidiosis prevention, not great for tx of clinical disease Generalized inhibitory activity against all coccidial stages	Old drug; still very commonly used as coccidial prophylaxis in poultry and cattle Coccidiostat in broilers/turkeys, calves, sheep, rabbits Toxicity can be significant in HORSES & dogs – keep away from medicated feeds for other spp.
Monensin	Registered for cattle; ↑ feed efficiency, ↑ wt gain, ↓ bloat on legumes Also selectively kills Gram + bacteria (ex. *Strep bovis*) → ↑ propionate & ↓ methane production ↓ fecal shedding of *Mycobacterium avium paratuberculos*is in mature cattle in high-risk Johne's disease herds ↓ incidence of rumen lactic acid production after grain overload	Dairy-specific claims: aid in preventing subclinical ketosis when lactating, ↓ milk fat, minimize loss of BCS during lactation. Used widely.
Others **Decoquinate** (Deccox) **Robenadine** (Robenz) **Clopidol** (Coyden) **Diclazuril (**Clinicox) **Zoaline** (Zoamix)	 Hydroquinolone class Guanidine class Pyridinol class Triazine class Nitrobenzamine class	
Toltrazuril (Baycox)	Interferes w/ nuclear division and mitochondrial functioning Used to ↓ shedding and for tx of clinical infection Used in lambs (tx, prevention) , piglets (tx), calves (prevention, tx) Forceris: injection for piglets that includes iron	Long withholding time (48-70d) before can go to slaughter Oral suspension EDLU in puppies/kittens uncommonly for tx coccidiosis EDLU also used to control of coccidiosis in poultry
Ponazuril (Marquis)	Toltrazuril metabolite For tx of protozoal Equine Protozoal Myeloencephalitis (ECM) in horses (*Sarcosystis neurona)*	Oral formulation used over several weeks – well tolerated
Halofuginone (Halocur, Halagon)	Mechanism unknown Aids in reducing clinical signs of *Cryptosporidium parvum* in newborn calves	Low safety margin → diarrhea, melena (also signs on cryptosporosis to cause hard to determine!) Given orally for 1st 7d of life 20d withdrawal period (careful w/ veal calves)
Clindamycin	Lincosamine (macrolide) category of antimicrobials Tx of clinical toxoplasmosis and *Neospora* infxns in small animals	High volume of distribution – good concentration reached in CNS
Benzimidazoles **Fenbendazole** **Febantel** **Albendazole**	Used for tx of *Giardia* infections	
Metronidazole (Flagyl)	Human antimicrobial for anaerobic infections, used for *Giardia*	

Pesticides

→ Regulated differently and have a Pest Control Product (PCP) number instead of a DIN
→ No EDLU allowed! Also must dispense the entire package so client has the info label as well
→ Thinner margins of safety than drugs.
→ Only topical effects for pesticides, no systemic absorption (unlike drugs)
→ Given via ear tag, collars (only for parasites near head), immersion baths, topical dusts, shampoos, premises applications

Drug	Method of Action	Notes
Acetylcholinesterase Inhibitors		
Organophosphates	Irreversible binding to AChE (wears off when new AChE produced) Highly toxic to mammals also (muscarinic, then nicotinic effects) → delayed neuropathy days to weeks after use	Environmental concerns Diazinon ear tags used to control horn flies/face flies in cattle
Carbamates	Reversible competitive inhibitor of AChE Less toxic to mammals, but still pretty toxic	Carbaryl dusting powder used for mites, fleas, lice, ticks (some), flies in various food animals
Amitraz	Inhibits monoamine oxidase Used for tx of *Demodex,* prevention of ticks	Toxicity dto α2 receptor activation if oral or excessive topical exposure
Pyrethrins/Pyrethroids **Permethrin** **Cypermethrin** **Cyfluthrin**	Most act on Na+ channels (remain open) or other neurotransmitter effects Highly lipid soluble – topical formulations stay in stratum corneum and not absorbed systemically	Chrysanthemum plant extracts (pyrethroids = synthetic) TOXIC to cats – dto grooming and poor glucuronidation
Neonicotinoids		
Imidacloprid	Like nicotine, but stable and persists longer → activates insect nicotinic receptors (not vertebrate) → first depolarizes neuron (Na+ channels open) but then stops neural transmission bt upsetting Na+/K+ balance Topical for tx of larval fleas and lice in dogs/cats (some tick activity)	Crosses BBB b/c not ionized at physiological pH Environmental risk – may be contributing to bee decline Minimal absorption but surface translocation over skin Considered very safe for animals Advantage multi: (+ moxidectin) K9 Advantix: (+ permethrin, pyriproxyfen)
Nitenpyram (Capstar)	Oral tablet (DIN) flea adulticide in dogs/cats Given daily if fleas observed on animal	Rarely used but works well and is safe. 100% oral bioavailability Effective against Fipronil-resistant fleas (not in CAN)
Insect Growth regulators		
Methoprene **Pyriproxifen**	Analogues of hormones affecting larval development No effect on adult insects, arrests the larvae at larval state Not that efficacious – takes weeks to see effects	Not sold at clinics, but pet stores as flea collars and spot tx Generally little toxicity in mammals Often included w/ other adult insect pesticides
Insect Development Inhibitors		
Lufenuron	Inhibits chitin synthesis/utilization – stops exoskeleton development Used to control fleas at egg and larval stages Used in dogs/cats and also in aquaculture for sea lice	Program: for cats, monthly oral suspension or SC injection that lasts 6mo Sentinel: tablets for dogs (+ milbemycin)
Spinosad	Nicotinic ACh receptor agonist Used for flea control in dogs/cats, some ticks if large doses used	Derived from actinomycete soil fungus Significant drug rxn w/ MLs (P-gp inhibitor)
Isoxazoline		
Fluralaner **Afoxolaner** **Sarolaner** **Lotilaner**	GABA and glutamate-gated Cl- channel (not in mammals) antagonists Lack of hyperpolarization → excess neural activity (opposite of MLs) For control of fleas, ticks and some activity against mites (*Demodex)* Neurological adverse events – contraindicated if previous hx of seizures Watch for transfer to owners petting the animal if topical	All classified as drugs (DIN), not pesticides Products for dogs include: Bravecto: Fluralaner, topical or oral tablet, every 3mo NexGard: Afoxolaner, monthly tablet Simparica Trio: (Sarolaner, moxidectin, pyrantel) monthly tabs Credelio: Lotilaner, monthly tablet
Phenylpyrazoles		
Fipronil (Frontline)	Blocks Cl- movement through GABA and glutamate-gated channels	Not available in CAN, widely used in USA

Antifungals

Drug	Method of Action	Notes
Amphotericin B	Binds to sterols (ergosterol) in fungal cell membrane → alters permeability and L+ leaks out → disturbs osmotic balance Broad antifungal spectrum, no effect on bacteria Used for invasive fungal infections in dogs, cats, horses Tx of Aspergillosis, Blastomycosis, *Cryptococcous, Candida*	Old drug, but still used sometimes. Human product IV only, so only given in hospitals. Not 1st line therapy Mammalian cells have sterols (cholesterol) so animal toxicity is likely Very toxic in cats: nephrotoxic (↓ GFR, direct tox; irreversible w/ prolonged use), anorexia, vomiting, anemia
Systemic Azole Antifungals		
Ketoconazole	Binds to cytochrome P450 enzyme complex and inhibits synthesis or ergosterol → damages fungal cell membrane Also impacts mammalian P450 enzymes → compromises liver function, ↓ synthesis of steroid hormones, ↓ cholesterol synthesis Time-dependant efficacy (longer administration – better); concentration independent BID dosing half the dose is more effective even though labels say SID Resistance is an issue dto ↓ drug influx or ↑ efflux, also fungus can change its synthesis pathways for ergosterol to circumvent effects	Human products - Oral tablets, suspensions, topical creams/shampoos Can be used to tx hyperadrenocorticism (but not best tx) Significant drug interactions (ex. cyclosporin is $$, give ketoconazole to ↓ dose needed b/c will enhance effect) Tx of mycotic infections dto yeast (*Malassezia),* systemic fungi (Coccidioidomycosis, Blastomycosis, Histoplasmosis, Cryptococcosis) and dermatophytes Cheaper than most other antifungals ADEs = rare but include hepatotoxicity (esp. cats) so monitor liver enzymes and watch for drug interactions, GI (nausea, vomiting, anorexia; less if given w/ food)
Itraconazole (Itrafungol, Sporanox)		Itrafungol = only vet product; oral solution for tx of dermatophytosis caused by *Microsporum canis* in cats Sporanox is the human product; oral capsules Expensive, but safer and more effective than most Don't used compounded products! Absorbed better when acid in stomach so give w/ food High V_D – accumulates in hair/skin Also used for Blastomycosis (dogs), Cryptococcus (cats) and guttural pouch mycosis, nasal aspergillosis and fungal keratitis (horses)
Fluconazole		Human product; very expensive Penetrates well into tissues, crosses BBB Less hepatic metabolism (mostly excreted by urine) so better in patients with liver dz. Safe (w/ mild GI side effects) Good for Candida, Cryptococcus, Coccidioides, limited against Blastomycosis, Histoplasma, Sporothrix, no activity for *Aspergillus*
Voriconazole		Human product; fluconazole derivative Broader spectrum but likely not safe in cats Not used now but maybe in future
Topical Azoles		
Miconazole	Licensed for topical use against superficial skin/ear mycotic infections in small animals Products often include an antibiotics & steroid Systemic use leads to rapid hepatic enzyme induction (↑ drug clearance) and serious adverse evets	Vet product = Surolan
Clotrimazole		Vet products = Otomax, Aurizon, Mometamaxx
Enilconazole	For dermatophytes in dogs and horses Animals washed with a diluted solution – considered very safe	Imaverol - Not currently available
Miscellaneous Antifungals		
Terbinafine (Osurnia, Claro)	Inhibits enzymes involved in ergosterol synthesis	Topical gel for skin/ear dermatophytes in dogs/cats
Iodophors (Betadine)	Works by drying out the surface → desiccates the cells	
Silver sulfadiazine	Inhibits DNA replication, cell membrane function	Found in Baytril Otic (+ enrofloxacin)
Griseofulvin	Disrupts structure of fungal cell's mitotic spindle → cells can't divide Only effective against *Trichophyton, Epidermophyton* and *Microsporum spp.* Used for dermatophytosis in dogs, cats, horses Absorption highly variable (↑ when given fatty meal)	Not available in CAN anymore Hepatic metabolism + elimination → drug interactions T1/2 is shorter in dogs/cats than humans, so vet med requires higher doses ADRs common, esp in cats: hematological abnormalities (aplastic anemia, leukopenia, pancytopenia), teratogenicity, anorexia, depression, vomiting, diarrhea

Anesthesia Drugs

General overview:

- → Unconsciousness = isoflurane, sevoflurane, propofol, alfaxalone, ketamine
- → Analgesia = opioids, NSAIDs, local anesthetics, ketamine, α2 agonists
- → Muscle relaxation = high doses of anesthetics, peripheral neuromuscular blockers, drugs that act on SC to reduce muscle tone (benzodiazepines, guaifenesin, α2 agonists)

Pre-medications

Drug	Method of Action	Notes
1. Phenothiazines	Anti-dopaminergic: post-synaptic DA blocker in CNS, inhibits release of DA	Calms, reduced anxiety, anesthetic sparing OD can cause catalepsy & extrapyramidal signs, muscle rigidity Hypotension via α1 receptor blockade → vasodilation (non-reversible, can last 8h) Reduces sensitivity of resp centre to pCO2 → slight reduction in RR, no change in blood gas Anti-emetic dto effect on CRTZ (best to give 20min before opioids) Anti-arrhythmic – blocks α1 in the myocardium, increases the [EPI] needed to induce arrythmias
Acepromazine	Mild sedation when used alone – no analgesia! Slow time to onset of effects (up to 30min) Used in dogs, cats, horses (beware rare penile damage), but not exotics or ruminants Usually combined w/ opioids, sometimes α2 agonists 30-40% anesthetic sparing effect; can decrease inhalant dose Dose-dependent duration and **hypotension** (use low doses & give fluids +/- ephedrine, don't use if hypovolemic or hemorrhagic Disturbs thermoregulation centrally + via cutaneous vasodilation (↑ thermal loss) → hypothermia Very little respiratory effects Can be used to control emergence delirium during recovery. No longer contraindicated for seizure-prone patients Strains of boxer dogs may be sensitive & collapse dto vasodilation/bradycardia – tx w/ anticholinergics	
2. Butyrophenones	Combo of anti-dopaminergic, anti-adrenergic, and GABA-mimetic activity in the RAS of brain	Less predictable than phenothiazines Tend to cause excitement before sedation occurs Less cardiorespiratory depression and thermoregulation interference than phenothiazines
Azaperone (Stresnil)	Used in swine	
Fluanisone (Hypnorm)	Used in mice, rats, rabbits, guinea pigs	
3. Benzodiazepines	Enhance the affinity for and/or action of GABA → decreases activity in RAS	Anti-convulsant, anxiolytic/sedative (not always; can cause excitement), **No analgesia,** muscle relaxation (dto depression of SC interneurons), retrograde amnesia If given orally has significant 1st pass metabolism effect Avoid using along IV; can cause excitement/aggression in young, healthy animals Better combined w/ mu-opioids IV or IM. Used alongside ketamine to ↓ its muscle rigidity effects. Minimal CV effects Minimal respiratory effects; some depression dto relaxation of respiratory muscles and reduced response to high pCO2 Can be pre-med or used as co-induction technique w/ injectables: give ¼ to ½ of injectable, then all the benzo, then titrate remaining injectable to effect - good if need to ↓ amount of induction agent or if there's no time for premed (emergency) → *Neurolept-analgesic induction* = benzo + potent opioid (fentanyl/sufentanil). Used for high risk severely debilitated parents. Slow 2-5 min induction, is anesthetic sparing, can cause bradycardia + resp depression.
Diazepam	Adheres to plastic syringes – so use within 12h of drawing up. Also sensitive to light degradation Propylene glycol carrier, so painful and unreliable absorption if given IM (IV only) Active metabolites prolong the effect Crosses placenta and remains in fetus – don't use for C-sections unless antagonist (flumazenil) is available	
Midazolam	2-3x more potent than diazepam Given IM, IV, intranasal, transmucosal. Becomes highly lipophilic once in pH>4 Inactive metabolites so shorter duration Used in exotic anesthesia for reliable sedation – can cause excitement in dogs/cats esp if young/healthy	
Flumazenil *benzo antagonist*	No side effects. Useful for exotics. 30-60min duration IV, IM Increases muscle tone to normal → improves ventilation	
4. Alpha-2 agonists *See P&A notes for full list*	Activate α2 (and α1) receptors Interact with imidazoline receptors	Highly lipophilic Anxiolysis/sedation, anti-convulsant, CNS depression, neuroprotectant (decreases intracranial blood volume), muscle relaxation, analgesia Anesthetic sparing Promotes diuresis via ADH suppression α1 effects = CNS stimulation: arousal, excitement, restlessness (unwanted; new drugs α2 specific) CV effects = peripheral **vasoconstriction** → ↑ BP → baroreceptor → reflex bradycardia. Afterload is high so heart can't ↑ SV, so overall causes ↓ CO even if BP looks good. Also may ↓ contractility and is pro-arrhythmic. Resp effects: RR may ↓ – compensated for by ↑ tidal volume. Blood gasses unchanged. In horses, IV xylazine vasoconstrictive effects last 2-3min, HR should come back up within 5 min In dogs, dexmedetomidine vasoconstrictive phase can persist. HR remains low, should come back up when inhalant introduced, but if too low check BP; if hypertensive – partially reverse w/ antagonist; if hypotensive – use an anticholinergic
Atipamezole (Antisedan) *α2 antagonist*	Antagonizes α2 receptors	Reverses α2-mediated anesthesia and analgesia. IM only Can cause muscle tremors, tachycardia, transient hypotension, panting, V/D, over-alertness
5. Behaviour Modifiers		
Trazadone	Serotonin antagonist + reuptake inhibitor Some α1 blocking action	Shouldn't interfere w/ later anesthesia. Can be combined w/ an opioid Possible hypotension Can give PO before visit
Gabapentin	Unclear; inhibits Ca channels → less glutamate released in CNS	Routinely used for epilepsy and tx of chronic pain

Injectable Anesthetics

- → When used as sole anesthetic, need high doses → profound CV + resp depression (so use in combination)
- → Not well tolerated by: debilitated, hypovolemic, endotoxemic patients or those w/ renal or hepatic dz
- → Mostly used for induction but also for maintenance and in emergencies to top up rapidly if animal wakes
- → IV route is best to achieve surgical anesthetic plane rapidly and bypass stages 1 and 2
- → Modern injectable anesthetics have an anesthetic effect lasting 4 – 10min
- → If using infusions, beware of context-sensitive T1/2: Time for [drug] in plasma to ↓ by 50% after discontinuing a CRI dto accumulation
- → When using to induce, titrate to effect in small animals but give large animals the whole dose. Can reduce dose by 20-80% depending on the premedication used
- → Induction apnea following rapid bolus dose can lead to poor uptake of maintenance inhalant and poor transition to surgical plane. Must assist ventilation until spontaneous ventilation returns

Drug	Method of Action	Notes
Propofol a substituted phenol	Acts on $GABA_A$ receptors in CNS to produce anesthesia (solution is ~~yellow~~ white colour)	Onset 40-90sec (but can see in 10sec) and lasts 5-10min. Give slowly over 1-2mins to reduce the chance of post-induction apnea Extrahepatic sites of metabolism: kidneys, lungs, GIT → rapidly metabolized, minimal hangover Vehicle is a lipid emulsion – can grow bacteria so discard w/i 24h of opening. *PropoClear* is lipid-free formulation, *Propoflo 28* is good for 28d dto preservative but is toxic to cats CV effects: myocardial depression, vasodilation → ↓ BP, **cancels baroreceptor reflex** (so ↓BP doesn't cause an ↑ in HR). Dose-dependant. Avoid if hypovolemic or has cardiac dz. . Transiently ↓ contractility lasts 10mins Resp effects: post-induction apnea (esp if given as large bolus quickly) and cyanosis, mild bronchodilation. Dose dependant. Supplement w/ O2 and consider preoxygenating Occasionally pain upon IV injection but no damage if given perivascular Used for TIVA induction and maintenance. Co-induction: used after giving benzos or ketamine Good for C-sections, cerebroprotection (↓ CBF & cerebral metabolic rate), and patients w/ compromised liver function (extrahepatic metabolism sites) Recovery is fast and smooth. Occasionally dogs have limb stiffness, opisthotonos, twitching (may be excitement, depends on premed). Cats have delayed recovery dto poor conjugation
Alfaxalone a neurosteroid	Acts on $GABA_A$ receptors in CNS to produce anesthesia (solution is clear)	Onset 15 – 45 seconds and lasts 5–10 min. Similar effects to propofol but w/ longer shelf life Give slowly over 1-2mins to reduce the chance of post-induction apnea Rapidly metabolized → no accumulation/hangover CV effects: hypotension dto myocardial depression and some peripheral vasodilation, **baroreceptor function intact** so ↓BP → reflex tachycardia. Dose dependant. Transiently ↓ contractility lasts 10mins Good muscle relaxation, reliable sedation in cats (IM) and great in reptiles (IM) May have some analgesic properties? Used for TIVA induction and maintenance. Co-induction: used after giving benzos or ketamine No pain upon injection and no damage if given perivascular Recovery fast and quality improves w/ premed
Ketamine phencyclidine derivative	NMDA antagonist (analgesic) CNS voltage dependent Na+, K+, Ca2+ channels Depression of CNS ACh receptors Some action at $GABA_A$ receptors Depression of nociceptive cells in spinal cord Dissociative anesthetic agent → interrupts info from reaching higher brain centres	IV onset 30-90 sec and lasts 20-30 mins. Can also be given IM, SC, TM Causes muscle rigidity at high doses (so always give w/ muscle relaxers: benzos or $\alpha 2$ agonists) Cataleptiod state w/ slow nystagmus (esp in horses) Profound **analgesia** (somatic > visceral, good for wind-up pain) Sub-anesthetic doses used for reliable sedation Maintains cranial nerve reflexes; gag, swallow, palpebral and central eye in dogs/cats (no rotation) Racemic mix, S isomer is 2-4x more potent than R Hepatic metabolism produces active metabolite norketamine (but in cats excreted unchanged; avoid if renal function is compromised) CV effects: **sympathomimetic** effects that last 2-15mins = ↑ HR (↑ myocardial oxygen demand), ↑ BP (so helps w/ low BP). In critically ill or catecholamine depleted patients = myocardial depressant. Avoid in cats w/ HCM. Can also be pro-arrhythmic. Resp effects: minimal depression, post-induction apnea less likely, can cause irregular patterns like apneustic breathing (esp in horse), bronchodilation, laryngeal + pharyngeal reflexes preserved Used to 'bridge the gap' b/w induction and maintenance anesthesia Auditory and visual stimuli disturbed during recovery to cause 'emergence delirium' (esp horses – give $\alpha 2$ agonist to sedate them through recovery) Used in combinations for induction: → *Ket-Val:* ketamine/diazepam IV used to induce dogs, cats, neonatal foals, horses, calves/cattle. 30-90 sec onset, 30min anesthesia, rapid recovery. Minimal CV/resp side effects (less than $\alpha 2$/ketamine combos). Don't use for C-sections (dto diazepam) → *Xylazine + ketamine*. Good for horses/cattle IV, wildlife IM. Analgesia, muscle relaxation, narcosis but CV depression! Not for small animals → *'Kitty magic'*: Dexmedetomidine-Ketamine-Opioid. Used for cat neuters, possible resp depression, can reverse $\alpha 2$ if needed
Guaifenesin	Unclear; Selectively blocks polysynaptic reflexes in the spinal cord, reticular formation, and subcortical areas of the brain	Used in large animals for mild sedation Provides skeletal muscle relaxation via spinal interneurons. Doesn't impair breathing NOT an analgesic Rarely used alone, can be used after xylazine premed to top up sedation in horses/cattle → *Triple drip:* guaifenesin, xylazine, ketamine to maintain anesthesia High concentrations (>15%) can cause hemolysis, hemoglobinuria, urticaria Irritating to tissues if goes perivascular → inflammatory response

Inhalational Anesthetics

→ Do not accumulate and are not metabolized very much; recovery is rapid as drug is blown off by lungs. High safety margin
→ Can produce more CV depression and vasodilation than injectables. Also has slower onset so may observe excitement phase during loss of consciousness (less likely if sedated 1st)
→ Effect on brain related to partial pressure of the inhalant – not concentration! (% output varies w/ atmospheric P but partial P remains same!
→ The more fat-soluble the IH is the slower the uptake/elimination (opposite of injectable anesthetics)
→ Potency described by MAC at (% at 1atm that prevents rxn to surgical stimulus in 50% of patients; lower MAC = more potent, more lipophilic)
→ If animal has ↑ ventilation – leads to ↑ uptake; but ↑ lung perfusion actually ↓ uptake (b/c blood moves by too quick, no time for absorption) so low CO means more uptake ∴ excited animals are hard to 'mask down'
→ Rapidly eliminated drugs can cause 'emergence delirium' b/c moving through recovery stages so fast (have IV sedatives ready to go in case)
→ Always keep O2 on for ~5min after shutting vapour off to remove inhalant from patient
→ Sedation & opioid analgesics lower the dose required (esp in dogs). Also older animals require less anesthetic

Drug	Method of Action	Notes
Halogenated Ethers		
Isoflurane	Enhance inhibitory activity at GABA receptors in brain + glycine receptors in SC. Also inhibit excitatory effects at cholinergic and glutamate receptors Also depress activity at various types of Ca channels and may inhibit some Na and K channels	MAC = 1.28% in dog, 1.71% in cat, 1.31% in horse Depending on other drugs used in PIVA, induce w/ 2-4% and maintain w/ 1-2% Rapid uptake/elimination – metabolized very little by liver Pungent smelling; may elicit coughing and breath holding if inducing w/ a mask More lipid soluble than sevoflurane ∴ recovery is longer dto hangover effect Good muscle relaxation. Also relaxes SM in vessels → **vasodilation** → hypotension (esp when used w/ acepromazine, so α2 agonists are better premed if using iso). Stable HR Most commonly used inhalant Dose dependant CV depression and most resp depressive of all inhalants – may need to do IPPV
Sevoflurane		MAC = 2.4% in dog, 3.0% in cat Depending on other drugs used in PIVA, induce w/ 3-7% and maintain w/ 2-4% Not pungent smelling, more sweet smell. Used in exotics. 3x as expensive as isoflurane Dose-dependant CV depression. **Vasodilation** > myocardial depression→ hypotension likely Minimal resp depression compared to iso – animals will breathe spontaneously Can combine w/ CO2 absorber to form carbon monoxide (toxic) → can accumulate in rebreathing systems w/ low O2 flow Some liver metabolism → can produce Fl- ions which are nephrotoxic, but not big issue b/c mostly eliminated via the lungs anyway Hepatic blood flow preserved more than iso (but not too bad for either) Exothermic reaction (even fires!) if used w/ a desiccated absorber – always ensure is fresh/crumbly
Desflurane		Boiling point close to room temp; requires expensive vaporizer w/ heating unit Uncommon in vet med
Nitrous Oxide	Action on NMDA and possible opioid receptors	MAC = 188% in dog, 255% in cat (so not as potent!) Compressed liquid w/ gas above. Rapid absorption & elimination Used for analgesic properties only (NMDA antagonist, opioid agonist) – not an anesthetic in dogs/cats; used to supplement inhalant at 60% inhaled Administer w/ O_2 at minimum ratio of 2:1 N_20 to O_2 **Sympathomimetic** → helps ↑ BP, minimal other side effects Bone marrow depression if used >24h Must supplement w/ O2 for >5min to prevent hypoxemia when N_20 shut off Is a greenhouse gas so falling out of fashion and is also possible drug of abuse Don't use if patient has lung pathology

Support Drugs

Drug	Method of Action	Notes
Analgesics: **Ketamine** **μ-opioids**	Nociceptive pathways can be stimulated during anesthesia and also sympathetic NS stimulation Instead of ↑ dose of anesthetics (and ↑ side effects), it's better to provide good quality analgesia Ketamine is the only general anesthetic w/ analgesic properties. See P&A notes	
Fluids	Surgical fluid rates: dog = 5mL/kg/hr, cats = 3mL/kg/hr To replace fluids lost to evaporation, bleeding, urine production and also to offset hypotension (↑ venous return & CO)	**Isotonic crystalloid solutions (balances electrolyte):** Lactated Ringers, Normosol R/Plasmalyte **Colloids:** Starches. Larger molecules to ↑ oncotic pressure and draw fluids into vasculature. Stay in circulation longer than ~~colloids~~ crystalloids **Blood products:** whole blood, packed red cells, plasma
Respiratory Stimulants **Doxapram**	Directly stimulates the CNS and respiratory center ↑ the sensitivity of peripheral and central chemoreceptors to CO2 and O2 → ↑ tidal volume and RR	Not often used during anesthesia – best to ventilate lungs using breathing system. Used in field settings where no way to ventilate lungs manually. Also required for some laryngeal paralysis tests Increases cerebral and myocardial oxygen demand → if patient not breathing OR already hypoxemic can be detrimental Given IM, IV, buccal; onset immediate and lasts 1-2min Also ↑ BP (stimulates vasomotor centre) and ↑ plasma [catecholamines] so can cause patient to wake up if too light
Hypotension Drugs	During anesthesia, hypotension results from: ↓ CO (↓ contractility, ↓ venous return dto relaxation of great veins), vasodilation (depression of vasomotor centre) and bradycardia *Treating reduced CO* = **fluid therapy** to ↑ venous return, **β1 agonists** (catecholamine drug infusion to ↑ contractility + HR), **dobutamine** (a positive ionotrope), **epinephrine** (to ↑ contractility, reserved for CPR use) *Treating excessive vasodilation* = **α1 agonist catecholamines** (phenylephrine, NE, EPI, dopamine) to ↑ vascular tone (but beware of too much vasoconstriction that perfusion drops). Useful for vasodilatory shock, sepsis, anaphylaxis. Short acting so used as infusion → **Ephedrine** has longer 5-10min duration, can be used as bolus or infusion. Acts on adrenal glands to release endogenous NE (can become depleted though). Also some direct β1 and α1 effects *Treating bradycardia* = **anticholinergics** to prevent increase in vagal tone and also to prevent excessive drooling (not used in herbivores). Also causes some bronchodilation, ↑ BP and ↑myocardial oxygen demand/work of the heart (healthy animals only). Dilates pupils and ↓ tear production (so use eye lube). ↓ GIT motility and secretion, ↓ lower esophageal tone → more prone to regurgitation. Use when excessive parasympathomimetic action is likely (concurrent use of opioid) or if BP is already low and has become HR dependent → **Atropine:** onset is 1-2min, lasts 30-40min - ↑ HR higher than glycopyrrolate → **Glycopyrrolate**: onset is 15-20 min, lasts 2h – dries secretions more	
Neuromuscular blocking agents (NMBAs)	For procedures that require <u>no</u> muscle tone (ex. intra-ocular surgery requires medial eye) Not lipophilic ∴ don't cross BBB or placenta No sedation or analgesia properties – muscle paralysis only! So inhumane to use alone in animals. Paralyze all skeletal muscles, so must ventilate the patient and ensure full reversal before recovery **Depolarizing NMBAs**: Act similar to Ach @ NMJs but remain on receptor longer → flaccid paralysis. Broken down by plasma cholinesterase; no reversal drug available → **Succinylcholine** used to relax laryngeal muscles to allow intubation (not routinely used in animals). Fast onset (20sec), short acting in all but dogs. Used during horse euthanasia to prevent limb paddling. **Non-depolarizing NMBAs:** Competitively inhibits ACh from binding to receptor. Longer onset (1-2min), lasts 15-20 min. Can be reversed by blocking AChE to ↑ [ACh] → **Atracurium**: spontaneously broken down at body temp/pH by plasma esterases. Must store in fridge. Duration of action ↑ w/ hypothermia → **Rocuronium:** Duration doesn't change w/ body temp. May ↑ HR on administration. Liver metabolism Reversing the NMBAs via inhibition of AChE via **neostigmine** to ↑ [ACh]. Strongest effect at muscarinic sites, lasts 40min. May require **atropine** to prevent undesirable side effects like bradycardia, drooling, bronchoconstriction	

Drug Summary: ANS Pharmacology

Organs	Sympathetic Stim "Adrenergic" (EPI, NE)	Receptor	Parasympathetic Stim "Cholinergic"(Ach)	Receptor
Eye				
- radial muscle, iris	pupillary dilation	α1		
- sphincter muscle, iris			pupillary constriction	M3, M2
- ciliary muscle	slight relaxation (for long-distance focus)	β2	contraction	M3, M2
- aqueous humor production		β		
Glands of Head				
- lacrimal	↑ secretion (minor)	α1	↑↑ secretion (major)	M3, M2
- salivary	↑ secretion (minor) (viscous, "dry mouth" secretion)	α1	↑↑ secretion (major)	M3, M2
Lungs				
- bronchiolar SM	bronchiolar dilation	β2	contraction	M2=M3
Heart				
- SA node	↑ HR	β1>β2	↓ HR	M2>>M3
- atria	↑ contractility/conduction	β1>β2	↓ contractility/conduction	M2>>M3
- AV node	↑ automaticity/conduction	β1>β2	↓ conduction	M2>>M3
- ventricle	↑ contractility/conduction	β1>β2	↓ contractility	M2>>M3
Blood Vessels (arteries & arterioles)				
- coronary	constriction; dilation	α1, α2; β2	NO parasympathetic innervation of vessels!	
- pulmonary	constriction; dilation	α1; β2		
- skin & mucosa	constriction	α1, α2		
- abdominal viscera	constriction; dilation	α1; β2 (more α1 ∴ more constriction)		
- skeletal muscle	dilation; constriction	β2; α1 (more β2 ∴ more dilation)	dilation (only dlo drugs, not ANS)	M3, M2 in endothelium
Gastrointestinal Tract				
- motility	↓ motility	α1,α2,β1,β2	↑ motility	M2=M3
- sphincters	↑ tone	α1	↓ tone	M3, M2
- secretion	inhibition	α2	stimulation	M3, M2
Urinary Bladder				
- detrusor muscle	relaxation	β2, β3	contraction	M3>M2
- sphincters	contraction	α1	relaxation	M3>M2
Sex Organs				
- male	ejaculation	α1	erection	M3
- female			erection	M3
Skin				
- sweat glands	↑ secretion	α1	↓ secretion	M3,M2
- pilomotor muscles	erect	α1		
Adrenal Medulla	EPI secretion	N_N		
Kidney				
- renin	↑ secretion (↑blood volume ∴ ↑preload ∴ ↑contractility)	β1		
Liver				
- glycogenolysis	↑	α1		
- gluconeogenesis	↑	β2		
Spleen				
- splenic capsule	contraction	α1		
Autonomic Nerves				
Sympathetic Nerves				
- autoreceptor	inhibition of NE release	α2		
- heteroreceptor			inhibition of NE release	M2, M4
Parasympathetic Nerves				
- autoreceptor			inhibition of ACh release	M2, M4
- heteroreceptor	inhibition of ACh release	α2		

a1 receptors also can exacerbate pain

Drugs that *indirectly* affect ANS by altering neurotransmission:

Drug	Affecting Adrenergic signalling	Affecting Cholinergic signalling
Metyrosine	Inhibits L-dopa production ∴ ↓ NE synthesis	
Botulinum toxin		Interferes w/ SNAREs ∴ ↓ ACh release
Bretylium	Blocks NE release	
Black widow venom		Causes ACh leak into cleft ∴ ↑ ACh response
Amphetamine	Causes NE leak into cleft ∴ ↑ NE effects	
Cocaine	Prevents NE reuptake ∴ ↑ NE effects	
Neostigmine, Edrophonium		*Reversible* AChE inhibitor ∴↑ ACh response
Organophosphate/Carbamate Insecticides		*Irreversable* AChE inhibitor ∴↑ ACh response
MAO inhibitors	Prevent NE breakdown ∴ prolong NE response	

Cholinergic Drugs:

Type	Receptor selectivity	Name	Notes
Agonists	N=M (dirty drugs; many effects)	Acetylcholine	rapidly degraded by AChE
		Carbachol	more resistant, can be used locally
	N>>M	Nicotine	used as insecticide
	M>>N	Muscarine	toxin in *Amanita* mushroom
		Bethanechol	
		Pilocarpine	
Antagonists	M>>N	Atropine	used to stifle excessive parasym stimulation
		Ipratropium	can reverse bronchoconstriction
	$N_N > N_M >> M$	Hexamethonium	**Ganglionic blockers**; can cancel baroreceptor action
		Trimethaphan	
	$N_M > N_N >> M$	Tubocurarine	**NMJ blockers** (this is paralysis blow dart drug)
		Pancuronium	Newer drug than Tubocurarine
		Succinyl choline	*1st acts as agonist but then antagonizes*

Adrenergic Drugs:

Type	Receptor selectivity	Name	Notes
Agonists	β2 > β1 > α1=α2	Epinephrine	released from adrenals
	α1=α2 > β1 > β2	Norepinephrine	released from adrenals & nerves (warning: reflex bradycardia)
	β1=β2 >> α	Isoproterenol	used in ER to ↑HR
	D1 > β1 > β2 > α	Dopamine	used in ER for shock (vasodilates for ↑ blood flow); D1 ↑ renal perfusion
	β1 > β2 > α	Dobutamine	
	α1 > α2 >> β	Phenylephrine	used as decongestant (constriction; ↓ nasal blood flow to ↓ mucus – but can cause ↑ BP)
	α2 > α1 >> β (↓ adrenergic outflow)	Xylazine	used as sedative dto α2 activity
		Clonidine	used to ↓ BP but can cause postural hypotension
	β2 > β1 >> α	Terbutaline	
		Clenbuterol	bronchodilator (used locally to avoid systemic β effects)
		Albuterol	aka. Salbutamol; bronchodilator
	β3 > β1 >> β2 > α	Mirabegron (Myrbetriq)	β3s on detrusor; relieves overactive bladder
Antagonists			
α antagonists	α1 >>> α2	Prazosin	block vasoconstriction; used as anti-hypertensives
	α1 > α2	Phenoxybenzamine	
	α1 = α2	Phentolamine	
	α2 > α1	Tolazoline	
		Atipamezole	used to reverse α2 sedation
Mixed antagonists	β1 = β2 > α1 > α2	Carvedilol	used in heart failure b/c dilation ↓ BP, also ↓ RAAS
β antagonists	β1 >>> β2	Metoprolol	
		Acebutolol	
		Atenolol	
	β1 = β2 (can cause asthma attacks by blocking β2)	Propanolol	anti-arrythmic & anti-hypersentive (via ↓ RAAS)
		Timolol	in ophthalmic preps for glaucoma (↓ aqueous humor)

Diuretics

	Drug	Method of Action	Notes
	Loop Diuretics **Furosemide**	Inhibits Na/K/Ca symporter in ascending LOH (where 25% of Na reabsorbed) Forces retention of Na and K in the filtrate → but Na later reabsorbed Stimulates Na exchange for K in distal tubule/collecting duct → K lost to urine, Na retained in blood	"High-ceiling" – very efficacious Secondarily causes Ca and Mg (in addition to K) loss in urine (ion imbalances → muscle spasm, arrythmia) Acute and chronic (w/ monitoring) edema relief
	Thiazides **Hydrochlorothiazide**	Inhibits Na/Cl symporter in distal tubule (where 7% of Na reabsorbed) Results in naturesis → diuresis Na exchanged for K in distal tubule/duct ∴ causes less K loss than furosemide	Mostly used in human med Chronic edema therapy; heart failure
	Potassium-Sparing Diuretics **Spironolactone**	Antagonizes mineralocorticoid (aldo) receptor at CD (3% of Na reabsorbed) Prevents transcription of Na pump genes in late distal tubule/CD Prevents hypokalemia – used w/ other diuretics	Smallest effect; not often used Effective in DCM dogs and mitral valve failure Anti-steroid hormone effects (anti-estro and androgenic → ex. breast growth
	Osmotic Diuretics **Mannitol**	Draws fluid into plasma; is freely filtered at glomerulus ∴ prevents water reabsorption from proximal tubule (where 60% of Na is reabsorbed)	IV emergency use only to ↓ edema in brain Careful! Venous return can ↓ too much (↓CO)

Glucocorticoids

- Used to reduce inflammation (at low doses) – useful for allergies + musculoskeletal inflammation (but not pain!), reduce swelling
- High doses → immunosuppression; neutropenia, lymphopenia (stress leukogram)
- USE SMALLEST POSSIBLE DOSE! Anti-imflammatory at 10x physiological done, immunosuppressive at 20x, shock at 100-200x
- Blocks conversion of phospholipids to arachidonic acid ∴ ↓ prostaglandins (incl. prostacyclin), leukotrienes, Thromboxane A2
- Weak mineralocorticoid effect (↑ Na reabsorption from distal nephron, can lead to loss of K in urine)
- Suppressed HPA axis; has negative feedback on CRH (hypothalamus) and ACTH (ant pituitary) ∴ don't stop cold turkey
- Hemodynamic effects: ↑glucose → plasma volume expansion → PU/PD; ↓RCB, PCV, Hb
- Can cause hyperadrenocorticism ("Cushingoid"), muscle atrophy, delayed wound healing, GI ulceration (dto ↓ protective prostaglandins), pancreatitis, ↓GFR → acute renal damage, laminitis, abortion, polyphagia/weight gain

	Drug	Method of Action	Notes
endo	**Cortisol**	↑ blood glucose; GNG via anti-insulin effects; less glucose enters cells ↓ fat stores dto lipolysis ↓ protein stores dto proteolysis; more AAs in bloodstream	Released during chronic stress Effective ketosis relief but chronic release can cause diabetes mellitus dto anti-insulin effects (β cell burnout or receptor downregulation)
	Desoxycorticosterone (Percoten-V, Zycortol) **Fludrocortisone** (Florinef)		Treatment of mineralocorticoid deficiency in Addison's disease (hypoadrenalcorticism)
	Phosphate or succinate esters – fast acting!		
	Prednisolone sodium succinate (Solu-Delta-Cortef; vet)		IV or IM injections
	Methylprednisolone sodium succinate (Solu-Medrol; human)		
	Dexamethasone sodium phosphate (many vet products)		
	Acetate or acetonide esters – slow absorption		
	Methylprednisolone acetate (Depo-Medrol; vet) – most used in dogs/cats (skin issues); long-acting		IM, SC or intra-articular injections
	Prednisolone acetate (many generics)		
	Isoflupredone acetate (Predef 2x) – used in large animals; mineralocorticoid effects (hypokalemia)		
	Oral formulations		
	Prednisone **Prednisolone**	Pro-drug (horses and cats have poor metabolism Active form	Tablets, powder Good oral bioavailability, high volume of distribution Plasma T1/2 doesn't correlate w/ effects Hepatic metabolism
	Dexamethasone		

Antihistamines

- H1 receptor binding = SM contraction (bronchioles > GIT > urinary tract), SM relaxation (vasodilation of arterioles, capillaries → ↑ blood flow, ↓BP) Anaphylaxis → hypotension, bronchoconstriction
- H2 receptor binding = Facilitates HCl excretion from parietal cells
- H3 receptor binding = modulates NT release from CNS neurons; pruritis, pain
- H4 receptor binding = allergic/inflammatory response

- Limited efficacy for atopic dermatitis, may temporarily ↓ pruritis (but could just be sedation)
- Adjunctive therapy for anaphylaxis, insect bites (but not a replacement for epinephrine!)
- H1 blockers can also inhibit muscarinic receptors (anti-cholinergic effects → dry mouth, tachycardia, mydriasis)

	Drug	Method of Action	Notes
H1 blockers: reversible, competitive			
1st generation: Ethylene diamine family			
	Pyrilamine (Antihist, Pyrihist)		Injectable and oral formulations (contain ephedrine)
	Tripelennamine HCl		Injectable form (USA)
1st generation: Ethanoloamines			
	Diphenhydramine (Benadryl)	anti-cholinergic effects	Commonly used
	Dimenhydrinate (Gravol)	Diphenhydramine + 8-chlorotheophylline	Less common
	Clemastine (Tavist)		
1st generation: Alkylamines			
	Chlorpheniramine	Inhibits serotonin re-uptake; has anti-depressant properties	
1st generation: Piperazines			
	Trimeprazine	Anti-pruritic; for treating dermatitis	Old formulation for animal skin allergies
	Hydroxyzine (Atarax)	Human anti-pruritic, anxiolytic	
2nd generation → more selective for peripheral H1 receptors. Longer T1/2 and dosing intervals. Non-drowsy! Zwitterions ∴ can't cross BBB and enter CNS			
	Cetirazine (Zyrtec; human)		Good for ppl w/ pet allergies
	Loratidine (Claratin; human)		
Autocoids			
	Cyproheptadine (Periactin)	Blocks H1 and serotonin receptors	Used for photic head shaking in horses Weak appetite stimulant in cats
	Cromolyn sodium	Mast cell stabilizing agent	

Anti-Convulsives

	Drug	Method of Action	Notes
	Phenobarbitol (Epiphen)	Unknown; may ↓ Ach, Glutamate, NE and/or ↑ GABA HEPATOTOXICITY (cirrhosis, fibrosis, nodules) - ↑ ALT/ALP, abnormal bile acid stim test - ↓ albumin, urea, cholesterol - Induces CYP ∴ ↑ clearance rates of other CYP substrate drugs	Oral formulation Sedation, lethargy, PU/PD, ↓ T4 (transient hypothyroid) Polyphagia – DON'T use in obese patients! Temporary (10-15d) ataxia, blood dyscrasias, facial swelling, blood clotting disorders
	Potassium Bromide	2nd line drug No drug interactions (dto renal elimination) Long T1/2 → can take 6mo to reach steady state Salty treats → ↑ Cl outcompetes Br at renal tubule → ↑ Br excretion (↓ plasma [Br]) Low-salt diets → ↑ Br reabsorption, ↑ plasma [Br]	Sedation, vomiting, diarrhea, constipation, ↑ hunger/thirst, pancreatitis, temporary pelvic limb weakness/stiffness, pruritic skin lesions, behavioural changes (depression, irritability, pacing, attention seeking) NaCl can be used to reverse overdose Not recommended in cats! Induces coughing
	Diazepam (Valium)	Used to treat status epilepticus (stop seizures as they're happening) Hepatic metabolism Seizures may occur after abrupt discontinuation	Given IV (100%), rectal (50% so 2x dose), intranasal (80%) or oral (poor bioavailability) Can cause lethargy, sedation, ataxia, hyperactivity, increased appetite (wt gain)
	Gabapentin (Neurontin)	Unknown; may block Ca channels	Given in combo w/ KBr or PB in dogs Low side effects: mild sedation, ataxia
	Pregabalin (Lyrica)	Precursor to Gabapentin	Not as well proven efficacy, mild side effects
	Levetiracetam (Keppra)	Renal excretion; no drug interractions Given in combo w/ PB, KBr	Tolerance may develop 3-4h T1/2 → frequent dosing
	Zonisamide (Zonagran)	Sulfonamide-based ↓ Lipid peroxidation, scavenges free radicals May block Na or Ca channels May ↑ serotonin/dopamine neurotransmission Hepatic metabolism, renal excretion PB can lead to ↓ plasma [zonisamide]	No products in CAN, must compound Can cause sedation, vomiting, dry eye, crystalluria Has neuroprotective effects (stabilizes membranes, suppressed neuron activity) Use in seizures refractory to PB/KBr
	Imepitoin (Pexion)	Low affinity for benzodiazepine binding site of GABA receptor	Use if PB toxicity occurs
	Cannabadiol		At high doses: hyperesthesia, ataxia Issues w/ inconsistency b/w products marketed

Respiratory Drugs

	Drug	Method of Action	Notes
β-2 agonists			
- ↑ adenylate cyclase activity → ↑ cAMP → relaxation of bronchiolar SM → bronchodilation			
- β receptor activation on mast cells ↓ release of inflammatory mediators and also increases mucociliary clearance			
	Epinephrine	α1 → ↑TPR β1 on heart → ↑HR, SV, CO	Reserved for emergency use (ex. anaphylaxis) because of unspecific activity at other receptors and short T1/2
	Isoproterenol	β1 and β2 agonist; has same cardiac effects as epinephrine	Unsuitable for chronic use Administered by inhalation or injection; short duration (1h)
	Terbutaline	Similar to Isoprotenerol	Longer action (6-8h)
	Clenbuterol (Ventipulmin)	β1 ∴can cause tachycardia, muscle tremors (at high doses) Uterine relaxation Lipolysis and ↑ skeletal muscle blood flow (↑ muscle def'n; anabolic) → risk for abuse, can "improve" carcass quality	Injectable or oral, approved for horses w/ RAO Opens airways but doesn't resolve underlying inflammation; limited efficacy as sole therapy BANNED IN FOOD ANIMALS (cardiotoxic residues) Compounded versions are risky! Can have high potency! Used for acute events, not chronically
	Salbutamol, Albuterol (Ventolin; human)	Aerosol route – rapid onset, few systemic effects Chronic use → β receptor downregulation; use only acutely!	Metered dose inhaler for asthma attacks Used in cats and horses
	Salmeterol (Adavair; human)	Longer acting than salbutamol	
Methylxanthines			
- PDE inhibitors – relax bronchiolar SM, antagonize adenosine and ↑ intracellular cAMP			
- Not used much; adverse effects = cardiac/CNS stimulation, diuresis			
	Theophylline salt form = **Aminophylline**	Can ↑HR, ↑SV CytP450 metabolism ∴ [plasma] can ↑ if patient is on antibiotics, propranolol → toxicity CytP450 is induced by rifampin, phenobarbital (can ↓ [plasma], may need to ↑ dose)	Human formulations only, injectable, elixirs, tablets
	Caffeine	Causes CNS stimulation also	
	Theobromine		
Anti-cholinergics			
- Inhibits vagal-mediated bronchial SM tone (which is excessive in asthmatic patients) → bronchodilation			
	Atropine	Can cause ↑HR, mydriasis	May cause colic in horses
	Glycopyrrolate	Mostly used during anesthesia	
Glucocorticoids			
- Used in equine RAO, feline asthma, canine bronchitis (high dose, chronic oral administration)			
- ↓ debris, mucus and inflammatory cells → opens up airways w/o bronchodilators			
- See above for adverse effects! PU/PD, immunosuppression, metabolic etc			
- Give bronchodilator 1st, then steroids			
	Prednisone, prednisolone, dexamethasone		
	Fluticasone (Flovent)	Inhalant: a puffer, have choice of doses	Expensive
	Beclomethasone		
	Budesonide		
Anti-leukotriene Drugs			
- moreso used in human chronic therapy; are not bronchodilators!			
	Zafirlukast (Accolate)		No effect in cats; b/c leukotrienes don't cause bronchoconstriction
	Montelukast (Singulair)		
Antitussives (cough suppressants)			
	Opioids - μ agonists: M**orphine** **Codeine**	Suppress cough centre in medulla oblongata	 Better oral bioavailability, ↓ analgesia than morphine
	Opioids - κ agonists: **Butorphanol** (Torbutrol; dogs) **Tramadol**	Suppress cough centre in medulla oblongata Also α2 and serotonin agonist	 Oral tablets, poor bioavailability Less effective than butorphanol
	Dextromethorphan (Robitussin)	Opioid-like effects, no analgesia	May be moreso a placebo
	Guaifenesin	Loosens mucus (more viscous); easier to cough up	
	Ambroxol	Increases mucus transportability by cough	
	N-acetylcysteine	Reduces mucus viscosity	
Others			
	Ciproheptadine (Periactin)	Blocks H1 and serotonin receptors	Useful, but not as good as steroids
	Doxapram (Respiram)	A direct stimulant or respiratory centre	Used in neonates and during anesthesia

Heart Failure Drugs:

Drug	Method of Action	Notes
Pimobendan	PDE inhibitor (↑cAMP → ↑Ca sensitivity → ↑contractility; positive ionotrope) Arterial vasodilator (to ↓ afterload); removes SNS overactivation → ↑ SV/CO	Induces wellbeing/comfort, ↑ appetite ↑ survival of dogs w/ DCM or mitral valve dz Contraindicated in cats w/ HCM
Digoxin	Inhibits Na/K ATPase Positive ionotrope (↑ contraction strength/SV dto intracellular ↑Ca from exchange for ↑Na retained in cytosol) Negative chronotrope (↓HR; dto hyperpolarization) and dromotrope (↓ conduction → more time for heart to fill) AV node ↑ Parasympathetic NS tone → ↓ Sympathetic NS tone (baroreceptor)	Doesn't affect BP HIGHLY toxic Leads to ↑ peripheral perfusion (↑ renal output) Used in heart failure and arial fibrillation Side effects: death, anorexia, vomiting, diarrhea, AV block or arrythmias, hypokalemia (hyperkalemia blocks digoxin effects)
Dobutamine	β1 agonist (positive ionotrope → ↑ SV/CO)	Emergency/acute use only – given IV (can cause arrythmias)
Dopamine	D1 agonist; dilates renal arteries → ↑ urine output	
β Blockers	↓ Sympathetic NS tone → ↓ HR, ↓ BP, ↓ CO	Useful for HCM; slows/relaxes heart, inhibits renin release Useful for DCM also; inhibits renin release dto β1 block
Metoprolol **Carvedilol**	β1 selective antagonist, slows heart (↓ HR to ↑ diastolic filling), ↑CO Mixed β1, α1 antagonist	Doesn't have β2 bronchospasm effects ↓RAAS, arterial vasodilation → ↓TPR → ↓ afterload
Vasodilators		
- ACE Inhibitors **Enalapril** **Benazepril** **Imidipril**	Prevents formation of AngII by inhibiting ACE (stops ↑ in blood volume) Extends survival of DCM dogs by 92%, Not as good for cats w/ HCM	Used in heart failure/hypertension; arteriolar dilation, prevents aldosterone release. Can cause dry cough dto inhibition of bradykinin breakdown
- AT1 receptor antagonists **Valsartan** **Telmisartan**	Antagonizes Ang Type 1 receptor (usually activated by AngII; so ↓ RAAS, ↓ blood volume, ↓ preload, ↓ edema). Also arteriolar vasodilation	↓ BP but not HR Prevents aldosterone release
Nitroglycerin	Venodilator; metabolized to NO → ↓ edema, ↓ preload	Acute/severe treatment Orthostatic hypotension
Sodium Nitroprusside	Ateriolar and venodilator (also metabolized to NO; ↓ edema, ↓ preload)	Acute/severe treatment Can cause cyanide toxicity
Prazosin	α1 antagonist – mainly arteriolar, some venodilation → ↓ afterload	Old, cheap drug for heart failure, hypotension
Hydralazine	Direct arteriolar dilator (↓ Ca in SM?; causes relaxation)	Old, cheap drug for heart failure, hypotension
Sidenafil	PDE inhibitor → prevents cGMP breakdown → vasodilation in lungs, penis	

Anti-Arrythmia Drugs

Drug	Method of Action	Notes
Class 1 **Quinidine** **Procainamide** **Lidocaine**	Na channel inhibitors - ↓ Phase 0 potential Vagolytic (will ↑ HR), also α1 antagonist (neg ionotrope), K channel blocker K channel blocker, ganglionic + NMJ blockade	Used in ventricular arrythmias, esp. tachycardia. Sometimes also supraventricular arrythmias Be careful! Blocks other Na channels too
Class 2 **Metoprolol** **Propanalol** **Atenalol**	β-1 receptor antagonists - ↓ cAMP → ↓ contractility, HR (negative chronotrope, dromotrope, ionotrope) Good for HCM cats β-2 block also and Na channels	Used in supraventricular tachycardias, esp. when causes by SNS overactivation Hyperpolarizes RMP (less excitable)
Class 3 **Amiodarone** **Bretrylium** **Sotalol**	K channel inhibitor - prolong refractory period (systole), ↓ HR β-1/β-2 noncompetitive, Na blocker and Ca blocker also	Used in refractory ventricular tachycardias
Class 4 **Verapamil** **Diltiazam** **Amlodipine**	Ca channel inhibitor - ↓ contractility, ↓ HR, vasodilation (negative chronotrope for slowing spontaneous depolarization in pacemaker cells) Selective for cardiac channels – inhibits funny current, can also ↓ contractility In vasculature → vasodilation (anti-hypertensive)	Used in supraventricular tachycardias, HCM (↓ HR, BP) Hyperpolarizes RMP (less excitable)

Behaviour Modifying Drugs

Drug	Method of Action	Notes
"Antidepressants"		
Tricyclic Antidepressants		
Clomipramine (Clomicalm)	Inhibits reuptake of serotonin + NE Used as sole treatment or combine w/ anxiolytics + training Takes 4-6 weeks for therapeutic effect Side effects: Mild sedation (b/c also blocks H1 receptors), urine retention, dry mouth + constipation (anti-cholinergic), hypotension + arrythmias (adrenergic) +/- VD	Used in dogs/cats for anxiety states (separation anxiety, aggression, urine marking/spraying, generalized anxiety, excessive vocalization, phobias) and compulsive behaviours (stereotypies like lick dermatitis)
Amitriptyline (human generics)		Older drug, largely replaced by clomipramine
SSRIs		
Fluoxetine (Prozac is human formulation)	Used as sole treatment or combine w/ anxiolytics + training Takes 4-6 weeks for therapeutic effect Side effects: Mild sedation, GI irritation (reduced appetite, V/D), excessive vocalization, seizures (dto ↑ serotonin)	Also for anxiety states and phobias Transdermal has low bioavailability Good for urine spraying in cats
Paroxetine		
Sertraline		
SARI (Serotonin Antagonist/Reuptake Inhibitor)		
Trazodone (human, used off label)	Effect is dose-dependant • Low doses: mainly antagonizes post-synaptic 5HT2, H1 and α1 receptors • Higher doses: agonist for 5HT1 and possibly GABA Side effects: transient sedation and ataxia	Can be used in combo w/ other SSRIs and TCAs (start with these, add trazodone in) T1/2 = 3h Good oral bioavailability
MAOI		
Selegiline	Inhibits breakdown of dopamine, NE and serotonin Used as sole treatment Metabolized to amphetamines → so really just perks them up a bit Side effects: GI irritation (inappetence, V/D), lethargy	Approved for treatment of canine cognitive dysfunction (old senile dogs) Used previously for PD-hyperadrenocorticism Generally considered ineffective
"Anxiolytics"		
Benzodiazepines		
Diazepam (Valium)	Bind to GABA receptors and stabilize membranes Side effects: sedation, ataxia, ↑appetite, ↑ friendliness, paradoxical excitation +/- hepatic necrosis (cats) Can interfere w/ learning and memory! Animals may forget routines	For tx of anxiety states, phobias, urine spraying (not best choice tho) Oral and injectable formulations Has propylene glycol solvent → erratic absorption if IM injection. Also causes vascular irritation and pain on injection, best to give IV injection slowly Used as sole tx or combined w/ antidepressants
Midazolam		IV or IM
Alprazolam		
Clorazepate, Clonazepam		
Azapirones		
Buspirone (human generic)	5HT1 partial agonist, dopaminergic (antagonist?) effects Generally used as sole treatment Non-sedation, doesn't affect memory No CYP-mediated drug interactions Side effects: decreased inhibition (could lead to intra-species aggression) +/- V, ↑ affection, tachycardia.	Tx of anxiety states Used in cats for urine spraying (but not approved) – only useful if reason is inter-cat aggression in multi-cat houses Frequent dosing TID needed, transdermal has poor bioavailability compared to oral May disrupt cat hierarchies
Pheromones		
Feliway Classic	Feline Facial Pheromone analogue	Intended to reduce anxiety and urine spraying – no evidence
Feliway Friends	Feline Cat Appeasing Hormone analogue – the hormone produced by nursing queen to kittens	To decrease inter-cat aggression – there is evidence!
Adaptil	Dog Appeasing Pheromone	Some evidence
"Antipsychotics"		
Phenothiazine tranquilizers		
Acepromazine (Atravet)	Dopamine (D2) antagonist Labelled for non-specific sedation Side effects: HYPOTENSION, extrapyramidal signs, muscle rigidity, penile prolapse (horse), ataxia, prolapsed 3rd eyelid, CYP-mediated drug interactions Antihistaminic (dogs) and weak cholinergic (cats)	Oral and injectable; poor oral efficacy Hypotension risk increased if used w/ α2 agonists If extrapyramidal signs arise – tx w/ diphenhydramine to block H1 (anti-cholinergic)
Chlorpromazine		
Flupromazine		Drug of abuse in horses
Butyrophenone tranquilizers		
Azaperone (Stresnil)	Inhibition of dopamine and NE in CNS; poorly understood	Sedative approved in pigs Given IM to reduce aggression Also used for wildlife immobilization

Other drugs for CNS modulation:			
	Mirtazepine (Remeron)	Nonadrenergic (possible $\alpha 2$ inhibition), specific serotonergic (agonist for 5HT1) antidepressant (NaSSA) Antagonist for: 5HT2, 5HT3, H1 A human antidepressant See: Appetite drugs	Also used to increase appetite via serotonin modulation (5HT2) Anti-nausea, anti-emetic May vocalize more and seek attention
	Dextromethorphan (Robitussin)	NMDA antagonist (reduced glutamate effect), but has excitatory effects in CNS • May activate sigma receptors (alter 5HT) or activate AMPA receptors	Antitussive
	Reserpine	NE reuptake inhibitor Can lead to Ne depletion → HYPOTENSION which may last for several weeks after single use	Potentially fatal interactions if other hypotensive drugs used also, like $\alpha 2$ agonists

Beware of:

Serotonin Syndrome: too much serotonin in CNS dto using combo of TCAs, SSRIs +/- MAOIs, Tramadol. Signs are autonomic (tachycardia, hypertension, hyperthermia, diarrhea), neurological (tremors, myoclonus, hyperreflexia), mental (restlessness, paradoxical anxiety, confusion, agitation, coma), other (metabolic acidosis dto myoclonus, renal failure, DIC).

Tx: only supportive therapy: IV fluids, external cooling +/- Diazepam

Extrapyramidal signs: dopamine imbalance (Dopamine:Ach balance) – involuntary muscle movements that look like seizure. Most likely dto phenothiazines or metoclopramide

Tx: IV diphenhydramine: H1 blocker w/ anticholinergic effect

GIT drugs: Appetite

Drug	Method of Action	Notes
To decrease appetite		
Dirlotapide (Slentrol)	Microsomal triglyceride transfer protein inhibitor → results in ↓ lipoprotein/chylomicron assembly; less fat absorbed into lacteal from enterocytes. More fat stuck in enterocyte → satiety signal (via peptide YY)	Wt loss is via ↓ food intake (not less fat absorption!) Side effects: anorexia (too far), emesis, loose stools, elevation in liver enzymes (can cause hepatic lipidosis in cats)
Orlistat (Xenical; human)	Pancreatic lipase inhibitor ↓ dietary fat digestion/absorption	Low oral bioavailability but works in lumen anyway Side effects: fatty/oily stool
Appetite stimulants		
Anabolic Steroids		
Testosterone	Labelled for use in chronic illness w/ wt loss, debilitated or androgen deficient horses	Controlled drug Propionate salt injectable form
Methyltestosterone/estradiol (Geri-Tabs) **Stanozolol** (Winstrol V) **Boldenone undecylenate** (Equipose)		Similar use but older, discontinued drugs
Benzodiazepines		
Diazepam	GABA-induced effects & central inhibiton of satiety centre in hypothalamus (don't realize they've eaten more) Side effects: see CNS drugs	Used as appetite stimulant for cats Idiosyncratic effects
Oxazepam		
Others		
Cyproheptidine (Periactin)	Blocks H1 receptors but also blocks serotonin 5HT2 → blocks sense of satiety	Used as appetite stimulant for cats Only works in 20% of cats Also for pruritis – see: Antihistamines
Mirtazepine (Remeron)	Nonadrenergic (possible $\alpha 2$ inhibition), specific serotonergic (agonist for 5HT1) antidepressant (NaSSA) Antagonist for: 5HT2 → increased appetite 5HT3 → anti-nausea, anti-emetic H1 → possible sedation effects, not used for this though A human antidepressant	Oral (Remeron, human generics) or transdermal (Mirataz) Don't use compounded formulations May vocalize more and seek attention Hepatic metabolism, renal secretion – can accumulate in cats w/ repeated doses if have renal or liver dz Polyphagia noted within 8-36h
Megesterol acetate (Ovaban)	Synthetic progestin Anti-estrogen + glucocorticoid activity → causes adrenal suppression	Old drug formerly used to stimulate appetite and promote wt gain in dogs – no longer available
Glucocorticoids	Effect dto inherent activity of steroids (cortisol-like effect) or secondary to being 'perked up'	Polyphagia is common side effect (dogs < cats) Transient effect (days – weeks) Used in palliative + oncology cases

GIT drugs: Emesis and Ulcers

Drug	Method of Action	Notes
Emetics – used after toxin ingestion (<4h is ideal)		
Apomorphine	Dopamine agonist in CRTZ (activates the emetic centre in medulla)	90% effective emetic for dogs (less so for cats) Modified opioid given IV or in conjunctiva Other opioids may also induce vomiting
α2 agonists **Xylazine** **Dexmedetomidine**	Stimulates CRTZ	Given IM 50% efficacy in cats >50% efficacy in cats
Syrup of Ipecac	GI irritation → vomiting	Used in kids, less so in vey med
Hydrogen Peroxide	Stimulates pharyngeal receptors	Used in dogs; owners can do at home
Anti-Emetics - for motion sickness, parvo, gastroenteritis, chemo, uremia, hairballs		
Phenothizines **Acepromazine** **Chlorpromazine**	Antagonizes dopamine, inhibits CRTZ or emetic centre directly Antihistaminic (dogs) and weak cholinergic (cats) Side effects: see CNS drugs	Injectable and powder, beware pyramidal signs
Anti-cholingergics **Atropine, Scopolamine**	Block cholinergic afferent pathways from GIT/vestibular systems to emetic centre	Minimal efficacy as anti-emetics in vet med + lots of side effects
Antihistamines **Diphenhydramine** (Benedryl) **Dimenhydrinate** (Gravol)	Blocks cholinergic (cats) and histaminic (dogs) nerve transmission of vestibular system to emetic centre	Anti-nausea effects – may be due to a mild sedation
Metoclopramide	Inhibits dopamine in CNS, Inhibits 5HT3 receptors in CRTZ → Stimulates 5HT4 → prokinetic effect. See: GIT drugs	Injectable Doesn't cause sedation like phenothiazines do Used in small animals but variable PK Beware extrapyramidal signs
Serotonin Agonists **Ondansetron** (Zofran) **Dolasetron** (Anzemet) **Granisetron** (Kytril)	Inhibit 5HT3 receptors on vagal nerve & CRTZ Used in parvovirus pups and in chemotherapy; cytotoxic drugs release serotonin from enterochromaffin cells Not as useful for motion sickness-induced vomiting	All are human drugs, injectable Extremely expensive Lots of ondansetron generic human products
Maropitant (Cerenia)	Neurokinin (NK1) receptor antagonist; blocks binding of Substance P (tachykinin) in the emetic centre Side effects: can cause bone marrow hypoplasia in young pups (not used in parvo dogs <16w) May also have analgesic + anti-inflammatory effects by blocking Substance P – may reduce inhalational anesthesia	For acute vomiting and motion sickness Oral (dogs, cats off label) and injectable (dogs/cats) Most efficacious of this list when used in chemo esp. Cisplatin, same effectiveness as others for parvo
Drugs Affecting Gastric Secretion		
Proton Pump Inhibitors		
Omeprazole (Gastrogard)	Inhibit K/H pumps at apical border of parietal cells → less HCl Reduced gastric acid can lead to hypergastrinemia (body overcompensates) → mucosal cell hyperplasia, rugal hypertrophy, carcinoids – so taper off slowly Can minimise CSF production to reduce intracranial pressure (maybe inhibits carbonic anhydrase?)	Can treat or prevent ulcers (remove = relapse) Short T1/2 but long effect (irreversible inhibition) Be careful w/ long term use CYP enzyme inhibitor Gastrogard is an expensive horse product, there's compounded options but may be less efficacious
H2 receptor antagonists		
Cimentidine (Tagamet)	H2 receptor blocker → blocks parietal cell HCl secretion Limited evidence of efficacy in dogs/cats – use PPIs instead None licenced for vet use. Lots of human generics available Lipid soluble, orally absorbed but low in horses/ruminants CYP inhibition	Don't give w/ food or antacids Maybe prokinetic?
Ranitidine (Zantac)		Maybe prokinetic?
Famotidine (Pepsid)		Can be given w/ food or antacids Not prokinetic
Antacids		
AlOH, MgO, MhOH, CaCO3	Neutralize HCl to form water + a neutral salt Usually not absorbed systemically	Cheap and short acting Ex. Tums, Rolaids etc. No vet approved products
Sucrasulfate	Dissociates in gastric acid to sucrose octasulfate (coats the ulcer) + AlOH Increases mucosal PGE synthesis	Few ADRs in normal patients, may interfere w/ absorption of other drugs
Misoprostol	A synthetic PGE analogue → stimulates HCO3 and mucus secretion, increases musical blood flow, decreases vascular permeability, increases cellular proliferation + migration More prevention than tx; limited efficacy	Used as preventative for NSAID-induced ulcers in dogs Doesn't stop methylprednisone-induced GI hemorrhage

GIT drugs: Motility

Drug	Method of Action	Notes
Prokinetic drugs		
Metoclopramide	Inhibits D2 receptors in CNS → peripheral prokinetic effect – ↑ gastric and upper duodenal opening, ↑ gastroesophageal tone Inhibits 5HT3 receptors in CRTZ → anti-emetic Stimulates 5HT4 → prokinetic effect Can ↑ prolactin secretion (dto dopamine effects)	Injectable Used in megaesophagus, post-op GDV to restore motility. Also some use in hairballs, chemotherapy, parvovirus, stimulate horse small intestine motility Before using, make sure there's no GI obstruction!!! Beware extrapyramidal signs
Domperidone	Peripheral dopamine antagonist No known affect on 5HT receptors No BBB penetration – no CNS rxns	Limited efficacy as GI prokinetic Approved for horses in USA to treat mare agalactia w/ no prokinetic effect, in CAN use human generics
Cisapride	5HT4 agonist (↑ ACh in myenteric neurons) 5HT3 antagonist (so less anti-emetic than Ondansetron) Like metoclopramide but more effective No approved vet or human formulations, compounded only Can cause arrythmias and CYP drug interactions	Used in cats w/ megacolon to ↑ SM motility in stomach, intestine, colon Used in dogs to ↑ gastroesophageal sphincter tone, for delayed emptying and small bowel motility disorders (not megaesophagus) Given to horses IV to prevent ileus post-surgery
Erythromycin	Prokinetic side-effects Activates motilin receptors in stomach and small intestine	Doesn't affect distal GIT in small animals, maybe in cattle/horses. Can cause diarrhea in horses dto flora disturbance
H2 antagonists **Cimentidine** (Tagamet) **Ranitidine** (Zantac)	Mechanism not well understood; maybe inhibits AChE? Increases gastric emptying	
Lidocaine	Suppresses sympathetic tone + has direct stimulatory effects on SM of intestine	Used in horses IV to prevent post-op ileus
Anti-diarrhea drugs • Fluid therapy is most important to prevent dehydration + acidosis! Also electrolytes (Na, Cl +/- P), acid/base tx (IV bicarb to correct acidosis)		
Protectants **Kaolin-Pectate** **Activated Charcoal** **Bismuth Subsalicylate**	 (Kaopectate) Minimizes toxin absorption from GIT (Pepto-bismol) Bismuth (coating) and aspirin (anti-PGE)	All are temporary fixes
Hyoscine butylbromide (Buscopan)	Anticholinergic → ↓ intestinal motility/secretions Can cause transient tachycardia and ↓ gut sounds (can make a colic look surgical even if it's not!)	But few cases of diarrhea are dto "hypermotility" – may make it worse → stovepipe effect Labelled for non-surgical colic in horses
Opioids ~~**Loperamine**~~ **Loperamide** (Imodium) **Diphenoxylate** (Lomotil) **Paregoric**	Act on μ (and other?) receptors in GIT → anti-secretory/ant-motility ↓ propulsive contractions and ↑ segmentation contractions → overall constipating effect Increases tone of GIT sphincters	In theory, no other opioid effects Don't use w/ infectious diarrhea (don't want to ↑ absorption of pathogens) or in known ABCA-1 deletion dogs Meant for transient diarrhea
Antimicrobials	If diarrhea is dto known bacterial dz	Can cause diarrhea dto change in flora May result in carrier animals
NSAIDS **Meloxicam** **Ketoprofen** **Flunixin**	 Label claim for diarrhea (w/ oral fluid therapy) At high doses Only when blood is present in feces	Risk of renal damage w/ concurrent dehydration Used in calf scours
Treatment of constipation: don't use prokinetics, can be dangerous + worsen blockages		
Lubricants **Mineral oil**	 Cattle, horses. Add white petroleum jelly for cat hairball tx	Vet product is Laxatone (fancy Vaseline)
Stimulant Laxatives **Phenolphthalein** (old Exlax) **Senna** (new Exlax) **Bisacodyl** (Ducolax)	Inhibit Na/K ATPase → leads to electrolyte loss in lumen and extra fluid loss	Too potent! Crazy diarrhea
Hyperosmotic laxatives **Sodium phosphate enemas** **Lactulose** **PEG: polyethylene glycol**	Draw fluid into GI lumen to stimulate motility	NOT for use in cats! Can cause hyperphosphatemia
Bulk laxatives **Hydrophilic colloids** (Metamucil)	Non-absorbed cellulose material ↑ bulk of fecal material → triggers defecation response Can also use fibre: prunes, pumpkins	
Stool softeners **Dioctyl sodium (or Ca) sulfosuccinate**	↑ water accumulation in feces	
Probiotics	May change gut flora (but diet may be better way to do this) Effects maybe dto short chain FA production or stimulation of the enteric immune system?	No adverse effects

GIT drugs: Misc

Drug	Method of Action	Notes
Tx for chronic colitis/IBD		
5-amino-salicylic acid	Aspirin derivative; NSAID effects but poor absorption (the point - so it accumulates at mucosal layer of intestine)	Symptomatic tx for chronic colitis Still risky in cats
Sulfasalazine	Anti-LOX activity, ↓ IL-1, ↓ PGE synthesis, oxygen radical scavenging activity	Sulphapyridine derivative
Antimicrobials **Metronidazole** **Tylosin**	Useful to ↓ inflammation via altering flora Controversial, mechanism largely unknown	Helpful but not best choice
Glucocorticoids **Prednisone/Prednisolone** **Budosenide** (Entocort)	Immunosuppression	 More efficacious than metronidazole Used for Crohn's dz + inhalant bronchodilator
Other immunosuppressives **Azathioprine** **Chlorambucil** **Cyclosporine** (Atopica)		 For dogs w/ IBD unresponsive to steroids
Tx for pancreatic conditions		
Pancrealipase (Pank-Aid)	Supplement of exocrine pancreas enzymes (lipase, amylase, proteases) for tx of exocrine pancreatic insufficiency $$$$	Mix w/ food before giving to dog to start breakdown Giving with gastroprotectants (PPI/H2 antagonists) to ↑ stomach pH means less enzymes digested in stomach → more make it to duodenum
Octreotide (Sandostatin)	Synthetic somatostatin analogue → inhibits secretion of gastrin, secretin, VIP, motilin, glucagon, insulin Inhibits acid and pepsin production, intestinal motility, GI blood flow	Tx for pancreatitis but not a recognized therapy Does not replace supportive therapy (fluids, anti-emetics!)
Tx of hepatitis – none are that effective		
SAMe	s-adenosylmethionine Increases hepatic concentrations of glutathione (antioxidant often deficient in severe hepatic dzs). Helps produce and regulate hormones and maintain cell membranes	Nutritional supplement for hepatocytes Give on an empty stomach; food reduces bioavailability
Urso-deoxycholic acid (Ursodiol)	Impairs cholesterol uptake + synthesis from hepatocytes → less chol in bile → reduced hepatotoxic effects of bile acids	Can aid in clearing cholesterol gallstones Limited side effects
Others: glucocorticoids, colchicine, penicillamine + trientine, zinc, antioxidants, milk thistle		
Tx of copper toxicosis		
Copper Chelators **D-penicillamine** **Trientine** **Zinc**	GI signs (esp. V). Breed issue w/ West Highland Terriers Safer than penicillamine Blocks intestinal Cu absorption	 Associated w/ pyridoxine (B6) deficiency Only compounded available GIT signs common

Hematology Drugs

Drug	Method of Action	Notes
RBC drugs		
Erythropoietin (EPO, Epoetin)	Stimulates erythrocyte generation, normally produced in kindey peritubular interstitial cells	Injectable only – is protein so would degrade in GIT Used for anemia dto CKD, myelodysplasia, performance-enhancing Takes too long to work to be effective for IHMA
Darbepoietin-α	Hyperglycosylated recombinant human erythropoietin analogue	Results in ↓ clearance, longer T1/2 → less frequent dosing
Pentoxifylline (Trental, Navicon)	Oral methylxanthine derivative → lowers blood viscosity and improves RBC "deformability" Alters immune response: ↓ production of pro-inflammatory cytokines → ↓ adhesion & aggregation of leukocytes	Previously used in horses for navicular disease Dogs: has been used for dermatomyositis, vasculitis, atopic dermatitis, ulcerative dermatitis of collies
Antithrombotic Drugs		
Anticoagulants		
Calcium Chelators: **Sodium citrate, sodium oxalate, EDTA, sodium fluoride**	Good for blood collection, blood storage; not used as anticoagulant drugs	
Heparin (many ending in __parin)	Produced by mast cells Inactivates Factors IX, X, XI, XII (along with antithrombin), prevents conversion of prothrombin to thrombin, prevents conversion of fibrinogen to fibrin, prevents stabilization of fibrin clots (inhibition of factor XIII)	Moreso used in human med Used in multiple types of antithrombotic drug IV or SC
Coumarin derivatives **Dicoumarol, warfarin**	Interfere with vitamin K-dependent coagulation factors (1972)	Long-term oral administration may be required Dose modification based on observed PT
Thrombolytics **Streptokinase, tPA**	Enhance fibrinolysis by stimulating conversion of plasminogen to plasmin	tPA = tissue plasminogen activator Used in DIC
Drugs affecting platelets **Aspirin, Clopidogrel**	↓ platelet activation	Not really used in vet med for this, sometimes for IMHA dogs

Chemotherapy Drugs

- Goal is tx not cure; cure is rare. Narrow therapeutic window.
- PK and doses aren't well known, most drugs are human. Dosed based on body surface area (mg/m^2) not body wt (mg/kg); BSA correlates better w/ metabolic rate which is lower in larger animals; risk is overdose to small dogs
- Tx is hard; cancer cells develop resistance ∴ protocols include multiple drugs
- Three classes: 1) Cycle nonspecific: kills cells at all phases, 2) Cycle specific: spares resting cells at G_0, 3) Phase specific: kills cells only in specific stages

Drug	Method of Action	Notes
Alkylating agents: bind b/w DNA bases → crosslinking → abnormal base pairing → prevents DNA replication/RNA transcription → death • Cell cycle nonspecific but most active in replication phases (G1 + S) → toxic to rapidly growing cells (incl. bone marrow, hair, GI epi)		
Cyclophosphamide (Procytox)	Used for carcinomas, sarcomas, feline lymphoproliferative dzs, mammary carcinoma, lymphoma ADRs= done dependant neutropenia, maybe thrombocytopenia (marrow suppression delayed but prolonged in cats), V/D, alopecia	Prodrug; hepatic metabolism converts it to active compounds Dogs w/ ↓ liver function may need higher dose Acrolein, one of the active compounds, causes hemorrhagic (sterile) cystitis in 30% of dogs – can minimize w/ furosemide and mesna
Chlorambucil (Leukeran)	Less potent and less toxic than cyclophosphamide	Used moreso for immunomodulation; see immunosuppressives Expensive, only used in small animals
Melphalan	Very bone marrow toxic	Used in plasma cell tumors, myeloma
Ifosfamide	Can cause hemorrhagic cystitis Hepatic activation to active form (acrolein)	Used for sarcomas, lymphoma
Nitrosoureas: also crosslink (alkylate) the DNA		
CCNU (Lomustine) **BCNU** (Carmustine) **Methyl-CCNU** (Semustine)	Lipid soluble ∴ good oral bioavailability Enters cells passively (no efflux pump resistance!) Crosses BBB – may be used in brain tumors. Also for lymphoma, mast cell tumors etc.	Causes neutropenia (nadir @7d), can cause leukopenia
Streptozocin (Zanosar)	Used for insulinomas as is toxic to pancreatic β-cells	ADEs= renal tubular necrosis (use w/ IV fluid diuresis), can cause type 1 diabetes, vomiting is common in dogs
Platinum-based drugs: binds to DNA bases w/ platinum ion → inhibits DNA synthesis (max effect in S phase) • Used for solid tumors: osteosarcomas, carcinomas, mast cell tumors		
Cisplatin (Platinol)	ADEs = nephrotoxicity ∴ use IV diuresis b4 administration, in cats can cause rapid fatal pulmonary edema – don't use! V/D	Dosed every 3-4 weeks Part of multimodal approach w/ surgery Effective intra-lesionally for sarcoids + other skin tumors in horses
Carboplatin (Paraplatin)	Less nephrotoxic than cisplatin Causes thrombocytopenia	2nd gen platinum derivative Can be used in cats; no emphysema
Non-chemotherapy tx for osteosarcoma		
Bisphosphonates **Pamidronate** **Zoledronic acid**	Inhibit osteoclasts ∴ ↓ bone resorption May be analgesic for chronic osteolytic bone pain in dogs Also used to tx hypercalcemia of malignancy (ex. adenocarcinomas secrete PTH-like protein)	Adjunctive therapy IV once per month Renal excretion, can cause nephropathy
Anti-metabolites (aka. Cell Enzyme Inhibitors): inhibit nucleic acid synthesis by inhibiting enzymes required for purine or pyrimidine synthesis (max in S phase)		
5-Fluorouracil (5-FU)	Inactivates thymidylate synthetase (blocks thymine synthesis) Systemic use limited dto nephrotoxicity Don't use in cats – nephrotoxic and hepatotoxic	Topical or IV Topical use for squamous cell carcinomas in horses
Methotrexate	Binds + inhibits dihydrofolate reductase needed for purine synthesis ADRs = anorexia, nausea, vomiting, myelosuppression	
Gemcitabine	Cytidine analogue → stops DNA replication ADRs = thrombocytopenia, pulmonary toxicity	Used in lymphoma
Cytarabine (Cytosar)	Inhibits DNA polymerase Very myelosuppressive → neutropenia	Used in lymphoma Nausea/vomiting
Rabacfosadine (Tanovea-CA1)	↑ permeability + accumulation of metabolites in mononuclear cells – inhibits DNA polymeraerases → S phase arrest + apoptosis Inhibits proliferation of mitogen-stimulated lymphocytes + lymphoma/leukemia cell lines ADEs = fatal pulmonary fibrosis (don't use in West Highland Terriers), other typical chemo ADEs	Conditionally approved in USA IV infusion over 30 mins Used for lymphoma in dogs (not solid tumors) Prodrug; converted to active forms
Enzyme Chemotherapy		
L-asparaginase (Kidrolase)	Breaks down asparagine → aspartic acid (asparagine not produced by some tumor cells, so they can't replace → interferes w/ protein synthesis → tumor cells die) Cell cycle specific for G1 ADEs = hypersensitivity reactions, minimal myelosuppression	High MW enzyme made by *E. coli* Expensive $$$ Used in some lymphoma protocols, melanoma + mast cell tumors
Toceranib (Palladia)	Not technically "chemotherapy"; doesn't kill tumor cells but is anti-tumor and anti-angiogenic Blocks tyrosine kinase → inhibits multiple growth factors → results in ↓ proliferation of endothelial cells Arrests cell cycle → causes apoptosis in tumor cell lines	Approved in CAN for cutaneous mast cell tumors Oral tablet ADEs = V/D, anorexia, lethargy, neutropenia, lameness, wt loss, melena. May cause vascular dysfunction → thromboembolism

Vinca Alkaloids (Microtubule Inhibitors)			
	Vincristine (Oncovin)	"spindle poisons"; bind tubulin → interferes w/ microtubules during mitosis chromosomal migration ∴ M phase specific ADEs = tissue necrosis if given perivascular, peripheral neuropathy, constipation, can rarely cause neutropenia	Used in lymphoma protocols, other tumors Therapy for immune-mediated thrombocytopenia; allows ↑ platelet survival w/i macrophages (platelet not destroyed by lysozymes)
	Vinblastine	No peripheral neuropathy, but associated with ↑ incidence of leukopenia than vincristine	Used for lymphosarcoma and disseminated mast cell neoplasia
Anthracine (anti-tumor) antibiotics			
	Doxorubicin (Adriamycin)	Kills throughout cell cycle, esp. S phase via intercalating b/w DNA bases → blocks transcription + protein synthesis. Also alters membrane ion transport and generated free radicals that are toxic to membranes ADEs = tissue necrosis if given perivascular, acute bone marrow suppression, cardiotoxicity dto Fe buildup in cardiomyocyte mitochondria → ECG changes & cardiac arrest. Also alopecia, GI toxicity, mast cell hypersensitivity	Aka. "red death" – is a red solution Used for lymphosarcoma, osteosarcoma, mammary carcinomas, other tumors Given slowly IV every 3 weeks Hepatic metabolism; ↓ dose if bilirubin increases
	Mitoxantrone	Minimal renal elimination: better for patients with renal insufficiency than doxorubicin Not cardiotoxic ADRs = bone marrow suppression, GI effects	Used for a wide variety of tumours, can be used for rescue therapy of lymphoma
Other categories:			
	Paclitaxel (Taxol)	Taxane drug; polymerizes the microtubular network → makes it useless → stops M phase ADEs = hypersensitivity to drug carrier → pruritis, anaphylaxis, hypotension, peripheral edema (so pretreat w/ steroids, cimetidine + antihistamine) Extremely myelosuppressive	Activity against many human tumor types Derived from bark of Pacific Yew tree P-gp substrate, so don't use in ABCB-1 mutants Very expensive $$$
	Glucocorticoids	Lyses lymphoid cells → active anti-lymphoma ↓ inflammation from cancer or other chemo ↓ ADEs of other drugs, stimulate appetite + attitude ↓ cachexia from TNF	May ↓ the amount of other chemotherapeutic you use Perks them up → they look better; good for palliative care to ↑ quality of life
	Piroxicam	NSAID COX expression is ↑ in some tumors, can be target for therapy	For transitional cell (bladder) carcinoma No evidence Meloxicam has any effect Some evidence for Deracoxib + piroxicam for osteosarcoma

Complications of chemotherapy:

- Neutropenia + sepsis: unlikely if neutrophils < $1x10^9$/L. If BAR → stay home. If febrile → IV fluids + antimicrobials. Lower subsequent done by 20%. Can use recombinant GSF (Neupogen) to stimulate neutrophil increase. Smaller dogs are at higher risk
- Vomiting: Immediate dto stumilation of CRTZ – can pretreat w/ ondansetron/maropitant. May be dto destruction of gastric mucosal cells → stop feeding or give bland diet, metoclopramide/maropitant
- Diarrhea: Destruction of intestinal mucosal cells – tx w/ loperamide
- Anaphylaxis: May pretreat w/ diphenhydramine, succinate/phosphase steroid formulations, or H2 blockers
- Extravasion: Doxorubicin + vincristine cause severe tissue damage that gets worse w/ time. What to do? Aspirate drug back out, infuse lots of saline/dexamethasone, surgical debridement

Immunomodulation Drugs

Drug	Method of Action	Notes
Immunosuppressive: to ↓ clinical signs of immune-mediated dzs		
Glucocorticoids **Prednisone, Prednisolone, Dexamethasone, Isoflupedrone, etc**	Non-specific anti-inflammatory/immunosuppressive effects depending on dose Altered leukocyte migration/function: ↓ macrophage phagocytosis, ↓ lymphocyte function (↓ antibody production)	Start parenteral, continue PO @ home For immunosuppression start aggressively and taper off slowly
Azathioprine (Imuran)	Blocks purine synthesis → interferes w/ DNA synthesis Variety of uses in dogs Lymphocytes must make own purines so are more susceptible ADRs = myelosuppression (esp cats), anemia, ↑ liver enzymes, pancreatitis, rebound hyperimmune response is stopped rapidly	Oral or injectable Individual variation in hepatic activation Don't use in cats
Chlorambucil (Leukaran)	Alkylating agent → crosslinks DNA Less potent and less toxic than cyclophosphamide which used to be used for immunosuppression ADRs = myelosuppression, vomiting, Fanconi's syndrome	Used in lymphocytic/plasmocytic infiltrative dzs, indolent ulcers, pemphigus, atopy Expensive – used in cats and small dogs Considered "steroid-sparing"
Cyclosporine (Atopica)	Inhibits calcineurin phosphatase; prevents induction of genes coding for cytokines & receptors → ↓ IL-2 production → ↓ T-cell activation/chemotaxis, antigen presenting cells, mast cell and eosinophil infiltration ADRs = V/D, gingival hyperplasia, P-gp/CYP drug interactions, 2^{o} infections (rare)	More targeted and subtle than generalized; safer than steroids and azathioprine Oral formulations licenced for dogs/cats Topical formulation (Optimmune) for keratoconjunctivitis, keratitis Used in cats for eosinophilic granulomas, plasmocytic stomatitis , IMHA dogs Variable oral bioavailability
Leflunomide (Arava)	2nd line systemic immunosuppressant Inhibits pyrimidine synthesis	Used in IMHA dogs
Mycophenolate mofetil	Purine synthesis inhibitor → inhibits B & T cell proliferation → ↓antibody production	Diarrhea in 40% of dogs; mild to severe
Tacrolimus (Protopic)	Similar to cyclosporine (calcineurin/T-cell inhibitor)	Topical for derm or ophthalmic conditions; expensive
Derm-specific Immunosuppressives		
Apoquel **(Oclacitinib)**	Janus kinase inhibitor → blocks IL-31 formation → anti-pruritogenic and anti-inflammatory Minimal effect on cytokines involved in hematopoiesis ADRs = immunosuppression (2^{o} infections, demodecosis), V/D	For control of pruritis associated w/ dermatitis, and for the control of atopic dermatitis in dogs at least 12 months of age Oral admin BID
Cytopoint **(LokivetMAB)**	A monoclonal antibody against IL-31 → same effect as Apoquel Can be used concurrently w/ other AD therapy	Reduces pruritis in dogs with atopic dermatitis Given as SC injection 1/month
Immunostimulants		
G-CSF Granulocyte-Colony Stimulating Factor (Neupogen, Neulasta)	↑ neutrophil counts + activate neutrophil function (↑phagocytosis)	Used for neutropenic chemo patients
IMRESTOR **(Pegbovigrastim)**	Recombinant pegylated bovine G-CSF - PEG (polyethylene glycol) will ↓ rate of protein clearance ↑ circulating neutrophils to counter neutropenia during periods of physiologic stress	Used for mastitis in 1st 30 lactation days SC injection at calving ADRs = rare, but occasionally fatal - idiosyncratic "hypersensitivity" reactions: vulvar swelling, dyspnea, edema

Antimicrobial Principles

Minimum inhibitory concentration (MIC) = lowest drug concentration that inhibits bacterial growth (dosing aims for plasma concentrations of 2-10x MIC)

Minimum bactericidal concentration (MBC) = lowest drug concentration to kill 99.9% of the bacteria

- No clinical difference between bactericidal and bacteriostatic

Post-antibiotic effect (PAE) = bacterial growth that remains supressed after the antimicrobial concentration has dropped below MIC

- May allow for longer dosing intervals, but is dependent on the bacteria and antimicrobial combination

Concentration dependent antimicrobials

- Want high concentration (AUC or Cmax) to MIC ratio
- With increasing dose, will get steeper kill curves
- More drug = better

Time dependent antimicrobials

- Want high time to MIC ratios
- With increasing dose, steepness of curve will not change. Need time
- More often = better (or long-acting formulations)

B-lactams (All members have a conserved beta-lactam ring)

Super family	Family	Drug names	Coverage/resistance	Mechanism of action	PK/PD/ADE/use
Penicillin	**Penicillinase-stable penicillin**	Oxacillin Methicillin Cloxacillin Flucloxacillin	No Gram -ve Anaerobic No enterococcal Many gram +ve **Anti-staphylococcal**	Resistant to staph aureus penicillinase No activity against MRSA or MRSP	
	Penicillin	Crystalline pen G (S) Procaine pen G (S, but L in oil) Benzathine pen G (L) Penicillin V	Gram +ve aerobes (lots of peptidoglycan, high affinity for PBPs) Wimpy gram -ve and -ve anaerobes (less peptidoglycan, low affinity for PBPs) Penicillinase or B-lactamase enzymes (almost all staph are resistant) Can't penetrate cell wall of some gram -ve	Disrupt synthesis of bacterial cell wall by inhibiting penicillin binding proteins, interferes with enzymes for peptidoglycan syn (Cell wall). Only works on actively growing bacteria	Poor oral absorption (stomach acid) except pen V) TIME DEPENDENT Can see type I, II, or III hypersensitivity reactions
	Aminopenicillin	Amoxicillin Ampicillin	Same as penicillin (maintains gram +ve activity) Improved Gram -ve coverage (like E. Coli) Anaerobes Resistance increasingly encountered (susceptible to B-lactamases), like staph	Amino group allows better penetration through outer layer of gram -ve bacteria	Oral absorption is okay (amox > amp) Can get SA and LA injectable amp TIME DEPENDENT and short T1/2 elim. BID-TID dosing
	Ureidopenicillin	Piperacillin	Decreased gram +ve activity Enhanced gram-ve spectrum - including most Enterobacteriaceae and susceptible		Expensive, only IV human forms are available

			Pseudomonas aeruginosa - Not against B-lactamase producers Antipseudomonal (can penetrate cell wall) Anaerobes		
Extended spectrum penicillins	**Carbapenems**	Imipenem Meropenem Ertapenem	Very broad spectrum Most Gram +ve, Gram-ve and anaerobes, resistant to B-lactamase Ertapenem has no activity against enterococci or *Pseudomonas* Not used in practice Save for very serious infections		Critical for human med, don't use! Usually IV Hydrolysed by dihydropeptidase enzymes in the kidney = toxic metabolites, formulated with dihydropeptidase inhibitor
B-lactamase inhibitors		Clavulanic acid	With amoxicillin: - Most gram +ve (including b-lactamase producing staph unless MRSA/P) - Many gram -ve - Anaerobes	Little activity by themselves but they irreversibly bind and inactivate B-lactamase enzymes, allowing B-lactam antimicrobial to bind w PBP	Oral tablets and suspensions Human forms have a different amox:clav ratio Good oral bioavailability Renal excretion T1/2 elim like amox Minimal ADE
Cephalosporin	**1st Gen**	Cefazolin Cephalexin Cefadroxil Cephapirin	Gram +ve and some activity against Gram -ve Treat pyoderma or dermatitis	Same MOA as penicillin: - Disrupt synthesis of bacterial cell wall - Inhibit PBPs - Interferes with peptidoglycan synthesis	Uses: gram +ve inc most staph, some gram -ve, anaerobes Oral absorption is better in the fed state
	2nd Gen	Cefuxime Cefaclor	Improved Gram-ve spectrum Somewhat less Gram +ve		

As Gen ↑: ↑ activity against Gram -ve ↑ resilience to B-lactamases			Can kill some E. Coli with narrower spectrum b-lactamases	Advantages: - Stable against some B-lactamase enzymes - Good affinity for PBPs - Good ability to penetrate bacterial cell wall (inc gram -ve) Resistance - B-lactamase enzymes (ESBLs, AmpC cephalosporinases, metallo-B-lactamase enzymes - Modify PBPs - Reduce cellular conc.	Parenteral absorption depends on formulation Glomerular filtration and tubular secretion for most ADE: hypersensitivity, GI upset, nephrotoxicity, coagulopathies
	3rd Gen	Cefovecin (Convenia) Ceftiofur (exceed/excenel) Ceftriaxone Cefpodoxime (simplicef) Ceftazidime	Very good activity against Gram -ve Some retain activity against Gram +ve No MWP for excenel (good for dairy)		
	4th Gen	Cefepime Cefquinome	Highly active against Gram -ve Good activity against Gram +ve Increasing resilience to b-lactamases		
	Cephamycins	Cefoxitin Cefotetan	Often classified with 2nd Gen, but not a good fit - Spectrum of activity and types of enzymes that are able to degrade these drugs are different Good Gram -ve and Gram +ve activity Great anaerobic coverage Commonly used to treat intra-abdominal infections after ruptured bowel		

Tetracyclines

Tetracycline	Broad spectrum agents Gram +ve activity more limited than Gram -ve Resistance is common - Methicilin will work - Susceptibility testing required Great for treating weirdo bacteria, intracellular parasites, *Brucella, Vibrio, Mycoplasma* Binds to 30S ribosomal subunit reversibility Bacteriostatic	
Doxycycline		
Minocycline		Reaches higher concentration in prostate, CNS, and intra-cellularly than others Activity against Stenotrophomonas (intrinsically resistant to many antibiotics)

<u>As you go down:</u>

↑ lipophilicity

Fluoroquinolones

	Drug names	**Coverage**	Inhibits DNA gyrase and topoisomerase IV

Quinolones	Nalidixic Acid	Only *Enterobacteriaceae (Escherichia)* Limited to E. Coli UTI	Prevents replication and organization (super-coiling) **Bactericidal**
1st Gen	Ofloxacin	Compounds are modified by fluoronating them Only Gram -ve bacteria Common ophthalmic tx *Pseudomonas*	
2nd Gen	Enroflaxin Ciproflaxin	Improved Gram -ve *Pseudomonas* Much more useful Some Gram +ve	
3rd Gen	Pradofloxacin	Broad spectrum Gram -ve Gram +ve Anaerobe *Mycoplasma* & *Pseudomonas*	

Aminoglycosides

	Coverage	
Streptomycin	Not widely used Mostly treated Plague, tularemia, etc. Bioterrorism	Binds to 30S ribosomal subunit - Causes incorrect tRNA translation - also affects electron transport chain, DNA metabolism, and cell membrane **Bactericidal** Protein synthesis inhibitors Only active against aerobic bacteria Will never kill anaerobe
Gentamicin	Gram -ve Anti-pseudomonas activity (some of the best) One of last lines of defense against Gram -ve	
Amikacin	Great Gram +ve and some Gram -ve Combined with b-lactam → great against Enterococcus - synergy! One of last line of defense against methicillin resistance	
Neomycin	Only active against Gram -ve rods May treat calf scours (E. Coli diarrhea)	
Spectinomycin	Gram -ve rods Some activity against *Mycoplasma* Not actually aminoglycoside, its an aminocyclotol	

MLS_BK

	Drug names	Coverage	
Macrolides	Erythromycin Tylosin Tildipirosin Tilmicosin, Tulathromycin	Primarily active against Gram +ve - Gram +ve anaerobes Some specific Gram -ve Staphs, Streps, BRD, anaerobes, clostridium, organisms causing upper resp tract (Bordetella), brachyspira	Reversible binding to 50S ribosomal subunit - different from tetracyclines! **Bacteriostatic** Generally good against Gram +ve and anaerobes
Lincosamides	Clindamycin, Lincomycin	Similar spectrum of activity Difference is in mechanism of resistance	
Ketolides	Clarithromycin	Improved activity against Clostridium Gram +ve (Staph and Streps) Rhodococcus (horses) – treat pneumonia in foals	
Azalides	Azithromycin Gamithromycin	Enhanced activity against Gram -ve Very lipid soluble Similar to macrolides + Enterobacteriaceae	
Streptogramins	Vinginiamycin	Treat Brachyspira Gram +ve cocci and bacilli Gram -ve cocci Anaerobes	

Phenicols

	Coverage	
Chloramphenicol	Banned in food animals Rare idiosyncratic aplastic anemia in people Irreversible and fatal Valuable for bacterial conjunctivitis – broad spectrum Good option for MRSP	Reversible binding to 50S ribosomal subunit Bacteriostatic Broad spectrum
Florfenicol	Not associated with aplastic anemia Primary utility in food animals Broad spectrum (Gram +ve, Gram -ve, anaerobes) Option for MSRP	

Misc

	Drug Name	Mechanism/Coverage
Folate synthesis inhibitors	Basic sulfa	Competitive inhibition to PABA - 1st step of pathway Sulfa can replace PABA and be incorporated which results in inactive metabolite
	Diaminopyrimidines	Do not competitively inhibit Indirectly inhibition
	Trimethoprim Sulfamethoxazole	Broad spectrum (Gram +ve and Gram -ve) except: - Enterococci - Pseudomonas - Group A Strep Methicillin – option for MRSP Parasites – Protozoans and Toxoplasma

Nitroimidazoles	Metronidazole	Disrupts DNA production by production of radical anions following intracellular metabolism Bactericidal Broad spectrum anaerobic coverage - no aerobe coverage Banned in food animals - carcinogen in people - over-used in vet med Most useful for Clostridium, Brachyspira (if non-food), parasites (Giardia)
Polymyxins	Polymyxin B Colistin	Only active against Gram -ve Disrupt out membranes surrounding Gram -ve bacteria Some are intrinsically resistant (mechanisms unknown) - Enterobacteriaceae Gram +ve and anaerobes are intrinsically resistant as they lack LPS-containing membrane