Drug Effects

Drug	Absorption After Oral Dose	Resistance to Penicillinase	Dose IV	Antimicrobial Spectrum	Side Effects
Penicillin G	Poor; about one third of dose; taken on empty stomach	No	1–10 MU q4–6h	*Streptococcus, Neisseria*	Increased K^+ (1.7 mEq K^+/1 × 10^6 units penicillin G); greater than 20 1 × 10^6 U/d can cause seizures; inhibits platelet aggregation
Penicillin V	Moderate; 2–5 times greater than penicillin G	No	0.5 g q6h PO	Like penicillin G	K^+ salt
Dicloxacillin	Good (30–80% of dose taken on empty stomach)	Yes	0.5–1 g PO q6h	*Staphylococcus aureus*	90–95% bound to albumin; not removed by dialysis
Ampicillin	Good; taken on empty stomach	No	1–2 g q6h (250–500 mg q6h PO)	Gram + cocci, gram negative, *H. influenza, Escherichia coli, P. mirabilis*	
Amoxicillin	Good (better absorption than ampicillin)	No	0.75–1.5 g PO q8h	Like ampicillin	Colitis when taken with clavulanate
Ticarcillin	Poor	No	50–75 mg/kg q6h	*Pseudomonas, Enterobacter, Proteus* (indole +) + ampicillin spectrum	CHF secondary to Na^+ overload; 5 mEq Na^+/g; low K^+ secondary to obligatory cation excretion with anion; decline in platelet aggregation
Piperacillin	Poor	No	2–6 g q8h	*P. aeruginosa, Enterobacter, some Klebsiella,* other gram negatives, gram + *cocci, Listeria monocytogenes,* ampicillin spectrum	Same as ticarcillin: 2 mEq Na^+/g

Key Reference: Petri WA: Penicillins, cephalosporins, and other β-lactam antibiotics. In Brunton LL, Chabner B, Knollman B, editors: *Goodman & Gilman's the pharmacological basis of therapeutics,* ed 12, New York, 2011, McGraw-Hill, pp 1477–1504; Bhattacharyya RP, Grad YH, Hung DT: Genomics and infectious disease. In Kasper D, Fauci A, Hauser S, et al, editors: *Harrison's principles of internal medicine,* ed 19, New York, 2015, McGraw-Hill, Chapter 146.

Perioperative Implications

Preoperative Concerns

- Is pt allergic to any penicillins? What exactly happens when the drug is taken (rash vs. anaphylaxis)?
- If pt is on large doses of penicillin G, ticarcillin, or piperacillin, are serum electrolytes normal?
- Hemostasis, especially platelet aggregation, may be inhibited by the antibiotics.
- If pt has renal insufficiency or failure, dose of antibiotic should be q12h or less frequently.

Induction/Maintenance/Postoperative Period

- Penicillins should have no effect on induction or maintenance unless allergic reaction occurs; no known interactions with any anesthetic agents.

Anticipated Problems/Concerns

- Relate to administration of large amounts of Na^+, K^+, and organic anions (acids). Possible bleeding problems due to platelet dysfunction.

Phencyclidine

Davide Cattano

Uses

- DEA Schedule I drug of abuse with no present medical indications; street terms for PCP include angel dust, supergrass, killer weed, embalming fluid, rocket fuel, wack, and ozone.
- Common routes of administration: Smoking (often laced in marijuana cigarettes), oral ingestion; less common is IV injection.
- Experimentally used for animal models of schizophrenia, neurodegenerative diseases and seizure disorders, ischemic neuroprotection, and anesthesia-induced neurotoxicity.

Risk

- Psychosis, seizures, anticholinergic-type syndrome.
- Experimentally, PCP causes irreversible brain damage through excitotoxicity, with the typical bull's eye neuronal cell and vacuolization.

Perioperative Risks

- Aggressive and/or psychotic behavior, hypertension, stroke, hyperthermia, rhabdomyolysis, aspiration

Worry About

- Kidney failure, aspiration, malignant Htn, prolonged action

Overview/Pharmacology

- Effects due to parent compound, highly lipid-soluble, pK_a of 8.6, peak effects in 15 min when smoked and 2 h by ingestion, distribution in 4 h, elimination takes up to 48 h. Metabolites are active and present for weeks in chronic users.
- Metabolized in the liver; urinary excretion of metabolites at low doses, excretion of free drug at high doses, only a small fraction of the drug is excreted unchanged.
- Produces an acute state of intoxication lasting 4–6 h but may produce a chronic state of psychosis that can last up to several days. With low to moderate doses, acute intoxication includes staggering gait, slurred speech, nystagmus, numbness of extremities, sweating, catatonic muscular rigidity, blank stare, changes in body image, disorganized thought, drowsiness, apathy, anterograde amnesia, and possibly aggressive behavior.
- With moderate to high doses, intoxication includes elevated HR and BP, hypersalivation, sweating, fever, repetitive movements, and muscle rigidity on stimulation.
- With high doses, anesthesia, stupor, coma, and convulsions can occur.

Drug Class/Mechanism of Action/Usual Dose

- Arylcyclohexylamine
- Acts at the *N*-methyl-D-aspartate receptor as a noncompetitive antagonist but a weak dopamine, serotonin, and noradrenergic agonist; there is also PCP-induced dephosphorylation of ERK ½ and Akt and dephosphorylation of GSK3-beta (activation) that is prevented by lithium.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tachycardia, Htn	Quantification, chronicity, acuity of drug exposure	Vital signs Diaphoresis	Blood, urine toxicology screens
RESP	Tachypnea vs. depression	Concurrent drug exposure (e.g., alcohol)	Respiratory rate Sat O_2%	
CNS	Psychosis, coma, convulsions, analgesia	Pupils, speech, reflexes		
ANS	Hypersalivation vs. dry mouth, hyperthermia		Observation, temp	

Key References: Lodge D, Mercier MS: Ketamine and phencyclidine: the good, the bad and the unexpected, *Br J Pharmacol* 172(17):4254–4276, 2015; Olney JW, Labruyere J, Price MT: Pathological changes induced in cerebrocortical neurons by phencyclidine and related drugs, *Science* 244(4910):1360–1362, 1989.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- No elective cases if pt has potentially taken PCP within 72 h.
- Steps to increase elimination of PCP from body; hydration and diuretics are supportive measures.
- Appropriate premedication (lorazepam, clonidine/dexmedetomidine).

Induction/Maintenance

- Ketamine is contraindicated (cross-tolerance) unless used cautiously to treat addiction and/or withdrawal symptoms (rare, deescalating doses); probably avoid nitrous oxide and isoflurane.
- Do not use selective beta-blockers with alpha effects (labetalol)
- Clonidine and dexmedetomidine

Postoperative Period

- Psychosis (acute vs. withdrawal), rhabdomyolysis, anticholinergic syndrome
- Precaution with muscle relaxant reversal

Anticipated Problems/Concerns

- Phenothiazines, anticholinergics, acidification of urine.
- There is no withdrawal, but addiction tolerance is common.

Phenothiazines

Eric Schnell

Uses

- Phenothiazine compounds are clinically useful antipsychotic and antiemetic medications.
- Phenothiazine antihistamines such as promethazine (phenergan) and prochlorperazine (compazine) are highly effective antiemetics.
- Phenothiazine neuroleptics such as chlorpromazine (thorazine) are used in the treatment of schizophrenia and psychosis.
- Chlorpromazine can also effectively treat uncontrollable hiccups and acute migraine headaches.

Perioperative Risks

- Common side effects of sedation and delirium may be particularly notable in the postop period and in susceptible pts.
- Severe extrapyramidal symptoms may arise from antidopaminergic activity.
- Tardive dyskinesia may result from long-term use and may be irreversible.
- Contraindicated in Parkinson disease; may worsen tremor and Parkinsonism.
- Autonomic dysfunction may result from sympatholytic and anticholinergic effects.
- Cardiac conduction defects and arrhythmias may occur with acute or chronic dosing, most commonly manifesting as a long QT interval.
- Accidental arterial injection or venous extravasation of promethazine can cause tissue necrosis.
- Neuroleptic malignant syndrome is a potentially fatal reaction to phenothiazines involving hyperthermia, rhabdomyolysis, tachycardia, and arrhythmias.

Pharmacokinetics/Pharmacodynamics

- Phenothiazines undergo hepatic metabolism; use caution in pts with hepatic dysfunction.
- Inactive metabolites excreted in bile/urine; pharmacokinetics rarely affected by renal failure.
- Phenothiazines are highly protein-bound (>90%).
- Prochlorperazine and promethazine have clinical half-lives of approximately 4–8 h after IV administration.

Drug Class/Mechanism of Action/Usual Dose

- Phenothiazines antagonize many receptors, primarily dopamine receptors (D_2-type) but also muscarinic receptors, serotonin receptors, alpha$_1$ adrenergic receptors and H_1 histamine receptors.
- Phenothiazine neuroleptics mediate their antipsychotic effects by blocking mesolimbic D_2 receptors, but D_2 blockade in striatum causes extrapyramidal side effects.
- Phenothiazine antiemetics are weak antipsychotics but potent H_1 histamine antagonists and antimuscarinic agents.
- Prochlorperazine is used at doses of 2.5–10 mg administered IV, IM, or PO q4–6h (max 40 mg/d) or 25 mg PR q12h.
- Promethazine is used at doses of 6.25–25 mg IV/IM q4–6h, IV doses given in diluted form slowly into a well-functioning large-vein IV line.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
ANS	Alpha$_1$ adrenoceptor blockade, antimuscarinic action		Orthostatic hypotension, tachycardia/bradycardia	Orthostatics
CNS	Extrapyramidal symptoms Neuroleptic malignant syndrome Sedation Decreased seizure threshold	Acute or chronic Muscle cramps, delirium	Akathisia, tardive dyskinesia Rigidity, tachycardia, hyperthermia, arrhythmias Lethargy, delirium	CK, K^+, uric acid EEG
CARDIO	Conduction defects: Long QT, ventricular and supraventricular arrhythmias	Can cause sudden death	Tachycardia, bradycardia, irregular rate	ECG
RESP	Respiratory depression	May potentiate opioids	Low respiratory rate	SpO_2, ABG, $ETCO_2$
VASC	Tissue necrosis (promethazine)	Arterial injection or tissue extravasation	Gangrene	
HEME	Leukopenia, agranulocytosis	Usually with chronic dosing only		CBC

Key References: Ohlow MJ, Moosman B: Phenothiazine: the seven lives of pharmacology's first lead structure, *Drug Discov Today* 16(3–4):119–131, 2011; Kwok J, Flood P: Drugs used for psychopharmacologic therapy. In Flood P, Rathmell JP, Shafer S, editors: *Stoelting's pharmacology & physiology in anesthetic practice*, ed 5, Philadelphia, 2015, Wolters Kluwer, pp 822–844.