Common Toxicities of Cytotoxic Chemotherapeutic Drugs
A. Myelosuppression: leukopenia → infections thrombocytopenia → bleeding immunosupression → infections & cancer
B. Other adverse consequences: mucositis, cancer, genetic diseases, teratogenesis, infertility
C. Acute-subacute symptoms of chemo: hair loss, NV, loss of appetite

Covalent Modifiers DNA		electrophilic; mono (react with one DNA base) or bifunction (react with two to produce crosslink); N7 guanine Nu	
Alkylating Agents	CCNS		
busulfan		sulfonate; N-7 of guanosine, interfers DNA repl/RNA transcr;	seizures (must use prophylaxis AED) sinusoidal obstruction syndrome: life-threatening liver toxicity, prevent using ursodiol
cyclophosphamide	NM	prodrug requires activation aldophosphamide then phosphoramide mustard (ifosfamide slower)	hemorrhagic cystitis (doses >1000mg/m2 require mesna); SIADH, cardiac toxicity high doses
ifosfamide	NM	toxic acrolein (hem cyst), use mesna; chloroacetaldehyde (neuro/nephotox)	hemorrhagic cystitis (always require mesna); neurological toxicity
mechlorethamine	NM	nitrogen mustard: 1. crosslinking 2. destruction of purine ring 3. depurination 4. abnormal base pairing	
melphalan	NM	--strained aziridinium ring then Cl leaving group, then again for second Nu	mucositis
bendamustine	NM		rash, requires antiviral and PJP prophylaxis
carmustine		nitrosourea; use: BMT conditioning, brain tumors, HL	neurotox (seizures), pulm fibrosis, myelosupp (delayed/prolong), infus rxns give over >2hrs
dacarbazine		triazene; methyl diazonium ion	flu-like syndrome
procarbazine		diazene; methyl diazonium ion	Antabuse-like reaction, MAOI intx
carboplatin			thrombocytopenia, Calvert equation (dose mg = target AUC*(GFR+25)
cisplatin	no myelosupp	water kicks off Cl twice forms adduct, reacts N7 G/A bifunctional adducts	nephrotoxicity, electrolyte hypoMg/K, NV, ototoxicities; sodium thiosulfate soln protect kidney
oxaliplatin			cold-induced neuropathy (via Ca chelation of oxalate)
Antitumor Antibiotics			
bleomycin	G2-M	DNA strand scission; antitumor activity based on DNA single and double strand breaks --inactivated by bleomycin hydrolase (amine protonated higher pKa); Fe(III)-BLM mediated C4' radical	no myelosupp pulmonary fibrosis (test pulm function prior); hypersensitivity, fever/chills, mucositis, skinrash
Anthracyclines	CCNS	1. DNA damage (reactive O2 species) 2. Topoisomerase II inhib 3. DNA intercalation (unwinds helix) - helix deformed, interfere with DNApol/repair binding; crosslinking amino N2 via formaldehyde	cardiotox (acute/subacute/chronic), myelosupp (highest with daunorubicin), NV, vesicant, alopecia, radiation recall, mucositis, diarrhea
daunorubicin		redox cycling generated superoxide (quinone→semiquinone form via P450 or NADPH reductase)	- stain tears/contact lenses/urine orange-red for 1-2 days
doxorubicin		- ROS formation causes cardiotox; heart tissue low catalase, anthraquinone chelates cations	- stain tears/contact lenses/urine orange-red for 1-2 days (cardiotox prevent with dexrazoxane)
mitoxantrone		- alc metabs accum heart tissue, disrupt metab of Ca and other ions; dexrazoxane antidote for anthracyc extravasation	- less cardiomyopathy, less NV, less alopecia; more mucositis; blue-green secretions
idarubicin		mitoxantrone has cationic side chain; lower cardiotox	
Topoisomerase Inhib		Topo1 makes transient 3'-phosphotyrosyl linkage	
irinotecan	G2-M	inhibits Topoisomerase I, Camptothecins; prodrug (solubility) to active via carboxylesterase; 3A4 UGT ddi	diarrhea: early <24hrs treat with anticholinergics, late >24hrs treat with antidiarrheals
topotecan	G2-M	inhibits Topoisomerase I, Camptothecins	
etoposide	G1-S	inhibits Topoisomerase II; semisynth; does NOT require activation	myelosuppression, mucositits, alopecia
Microtubule Inhibitors		epothilones/taxanes microtubule stabilizers at high conc; disrupt microtubule dynamics at low conc vinca/eribulin inhibit tubulin polymerization at high conc	
Taxanes	M		
docetaxel	M	3A4 Pgp substrate	fluid retention (dexa), hypersensitivity reaction, peripheral neuropathy, alopecia, myelosuppression
paclitaxel	M	binding of taxanes to β-tubulin within microtubules; stabilize against depolymerization	hypersensitivity rxns (can use abraxane), peripheral neuropathy, alopecia, myelosuppression
Vinca alkaloids	M	IV only; 3A5; vinca domain, enhanced depolymerization; microtuble dynamics suppressed at low conc left side of molecule catharanthine, right side vindoline	
vinblastine	M		myelosuppression, HTN, less neuropathy than other vinca alkaloids
vincristine	M		peripheral neuropathy, constipation, paralytic ileus, minimal myelosuppression
vinorelbine	M	semisynth	myelosuppression, neuropathy
Microtubule inhibitors	M		
ixabepilone	M	epothilones	
eribulin	M	binds +end of β-tublin and free heterodimer	
Antimetabolites	S		
Folic acid analogs	S		
methotrexate	S	inhibit dihydrofolate reductase (DHFR); blocks TMP/purine synthesis; FA required for one-carbon transfers which affect DNA/RNA/PS synth; For DNA/RNA, MTX inh TMP syn from dUMP and purine synthesis resistance: 1. ↓MTX uptake (folate transporter) 2. ↓ polyglutamylation of MTTX and retention in cells 3. ↑synthesis of DHFR target (incr gene copy/exp <24h) 4. altered DHFR target enzyme with lower MTX affinity	nephrotoxicity, mucositis, hepatotoxicity; high dose MTX requires leucovorin rescue and urinary alkalization (pH>7 to promote renal elim) - avoid aspirin, penicillin, Bactrim, probenecid, NSAIDs, PPIs with HD MTX
pemetrexed	S	inhibit thymidylate synthase and purine biosynthesis	myelosuppression, erythematous and pruritic rash; requires premed with folic acid and B12
Purine analogs			
6-mercaptopurine	S	after activation, metabs inhibit purine/DNA/RNA/PS synth; dose red if allopurinol use, inh xanthine oxidase/decr uric acid inhibit DNA synthesis via inhib purine ring synthesis and nucleotide interconversions; HGPRT resistance: decreased HGPRT level in cancer cells (hypoxanthine-guanine phosphoribosyl transferase)	myelosuppression
fludarabine	S	dephos rephos to triphos: inhibits DNA pol, DNA ligase, ribnucleotide reductase; incorp DNA blocking polyme inhibit DNA synthesis; arabinose	myelosuppression/immunosuppression (requires viral and PCP prophylaxis); mild NV, flu-like sx; neurotox in older/renal (flud) [all with cladribine]
pentostatin	S	inhibit adenosine deaminase, ↑adenosine ↑deoxyA, inhibits ribo reductase, ↓deoxynucleotide levels, ↓DNA synth ribose	
Pyrimidine analogs	S		
5-fluorouracil	S	- phosphorylation of fdU by thymidine kinase, or add ribose to 5FU by PRPP transferase or uridine phosphorylase results in 5-fluorodeoxyuridine monophosphate (5dUMP); phosphoribosyl transferase/uridine phosphorylase base analog inhibit thymidylate synthase, ↓TMP; ↓DNA synth; incorp metabolites into RNA, inhibit RNA synthesis	Bolus: mucositits/diarrhea, dermatitis, nail changes, hyperpig, myelosupp Continuous infusion: hand-foot syndrome, EKG changes/MI
capecitabine	S	5-FU prodrug (via hepatic esterase, cytidine deaminase, thymidine phosphorylase)	dose-limiting hand-foot syndrome, diarrhea, NV
cytarabine	S	phosphorylated to ara-CTP, inhibits DNA polymerase; incorp DNA inhib chain elong; arabinose	myelosuppression, rash, HA, fever; high dose (>1g/m2): conjunctivitis, cerebellar toxicity
gemcitabine	S	phosphorylated to difluorodeoxycytidine triphos, competes dCTP, incorp DNA, inhib chain elong; ribose	myelosuppression, rash, flu-like syndrome

5-azacytidine	S	inhibits pyrimidine synthesis; tri incorp DNA/RNA/PS inhib, inactivates DNA methyltransferase, reducing DNA	myelosuppression, NV	
decitabine (deoxy-aza)	S	methylation, promotes differentiation of leukemia cells in marrow; ribose	myelosuppression, NV	
Miscellaneous				
hydroxyurea	S	inhibit ribonucleotide reductase	myelosuppression, diarrhea, NV, rash, mucositits, hyperpigmentation	
pegasparagase		inhibit protein synthesis via L-asparaginase deamination of asparagine	hypersens rxn, thrombosis, pancreatitis, ↑LFTs, hyperbili, hypofibrinogenemia, ↑INR/PT	
olaparib		inhibit PARP		
dactinomycin		inhibit RNA synthesis		
PALA		inhibit pyrimidine synthesis (PALA=phosphoacetyl aspartate)		
venetoclax		binds BCL2, prevents intx with BAX, blocks prosurvial effect of antag BAX; restores apop to cancer cells	myelosuppression	
ATRA		inducer of differentiation	differentiation syndrome, pseudotumor cerebri, LEFT elevations	
arsenic trioxide		inducer of differentiation	myelosupp, QTc, monitor Mg/K	
bortezomib				
Targeted				
trastuzumab (Herceptin) pertuzumab		anti-HER2		
idelalisib (Zydelig)		inhibits PI3Kδ		
dabrafenib (Tafinlar)		anti-BRAF		
trametinib (Mekinist)		anti-MEK		
palbociclib (Ibrance)		CDK4/6 inhibitor		
everolimus (Afinitor)		mTOR inhibitor		
sorafenib (Nexavar)	T2	Raf Ser/Thr kinase inhibitor, and others (vegf, rafk)		
imatinib (Gleevec)	T2	BCR-ABL tyrosine kinase inhibitor and others (c-kit)		

cisplatin	NSCLC SCLC	**nephrotoxicity**, electrolyte hypoMg/K, NV, ototoxicity		
carboplatin	NSCLC SCLC BC	**thrombocytopenia**, less nephrotox, Calvert (dose mg = target AUC*(GFR+25)		
oxaliplatin	CC	**cold-induced neuropathy** (acute-cold; long-last can be perm); myelosupp (thrombocytopenia>neutropenia), NV	renal, no dose adj	
docetaxel		**fluid retention** (dexameth), hypersensitivity reaction, peripheral neuropathy, alopecia, myelosuppression		
paclitaxel		**peripheral neuropathy**, hypersensitivity rxns (can use abraxane), alopecia, myelosuppression		
vinorelbine	NSCLC	myelosuppression, neuropathy		
vincristine		**peripheral and autonomic neuropathy**, constipation; minimal myelosuppression		
doxorubicin	BC	cardiotox (use dextrazoxane), red fluids, NV, vesicant, alopecia, radiation recall, mucositis, diarrhea		
etoposide	NSCLC SCLC	myelosuppression, mucositits, alopecia		
irinotecan	CC	**diarrhea** (<24h antichol; >24h loperamide); myleosupp (neutropenia>thrombocytopenia); NV	hepatic dose adj 3A4/UGT	
fluorouracil	BC CC	neutropenia (bolus), diarrhea, mucositis, HFS (cape>fu), cardiotox (EKG/MI with CI); capecitabine is oral form	hepatic dose adj	
gemcitabine	BC LC	myelosuppression (worse with slower inf rate), rash, flu-like syndrome		
methotrexate		**mucositis**, diarrhea, nephrotoxicity, myelosuppression; HDMTX requires leucovorin rescue; urinary alkalization (pH>7 renal elim)	CNS prophylaxis/Tx	
bevacizumab		HTN, proteinuria, wound healing (hold 28d before sx), VTE/ATE, HA, voice hoarseness, hemorrhage		
cetuximab		skin rash, hypersens rx, electrolyte abnormalities		
panitumumab		skin rash, hypersens rx, electrolyte abnormalities		
nivolumab	melanoma	Immune-related adverse events: Dermatitis (rash), Transaminitis (↑ liver enzymes), Colitis (diarrhea), Hypophysitis (severe fatigue, headaches), Pneumonitis (cough, SOB), Diabetes (↑ BG)		
pembrolizumab		Immune-related adverse events: Dermatitis (rash), Transaminitis (↑ liver enzymes), Colitis (diarrhea), Hypophysitis (severe fatigue, headaches), Pneumonitis (cough, SOB), Diabetes (↑ BG)		
dabrafenib	BRAF emtpystomach	Fevers, Vision changes, Derm toxicity: rash, dermatitis, HFS, acneiform rash, Cardio toxicity: cardiomyopathy (SOB, swelling feet/ankles),		
trametinib	MEK emtpystomach	QTc prolongation (abnormal beat, chest pain), Hyperglycemia, especially if DM, Cutaneous squamous cell carcinoma, VTE, Hemorrhage		
encorafenib	BRAF wowfood			
binimetinib	MEK wowfood			
encorafenib	BRAF wowfood			
binimetinib	MEK wowfood			

rituximab obinutuzumab ofatumumab	anti-CD20	CLL, HL, DLBCL	infusion reactions (cytokine release vs. hypersensitivity): obin > ofat > ritu onset delayed >1hr into infusion; typically with first inf, likelihood with subseq - arthralgia/myalgia, bronchospasm, cough, dizziness, fever, dyspnea, fatigue, HA, hypo/hypertension, nausea, vomiting, pruritus, rash, rigors, sweating, tachycardia, pain premed APAP, AH, dexa (obin ofat only); rescue AH, steroid, epi **HepB** react if HBsAg+ (active inf) or HBcAb+ (past infection)—entecavir/teno 6-12mo	slow rate/hold, administer H1/H2 antag (DPH+famot), CS (hydrocort or methylpred) restart infusion at 50% rate and titrate to tolerance; rechallenge discouraged with recurrent G3-G4 --rigors (meperidine, hydromorph), fevers (apap, CS), bronchospasm (albuterol, montelukast)
ibrutinib	BTKi/BCRi	CLL	**bleeding, Afib, HTN**, diarrhea, rash, GI, infection, fatigue; serious: cardiac arrythmias (QTc), invasive infections 3A4 ddi, **antiplatelets, anticoagulants** (warfarin is contraindicated); bleeding hold 3 days before after minor surgery, 7 days major	420mg qday, wowfood; caps/tabs
acalabrutinib	BTKi/BCRi	CLL	**HA** (resolves 1-2mo), myelosupp, infection, diarrhea, ms pain; rarer but serious: afib, bleeding 3A4, antiplatelets, anticoagulants, **gastric acid-reducing agents**	100mg bid wowfood; caps
venetoclax	BCL2i, **takewfood**	CLL	**myelosuppression** (WBC/neutrophil), diarrhea, N, infection, cough, ms pain, fatigue, edema; serious: **tumor lysis syndrome (TLS)**, febrile neutronpenia 3A4, oral chemo compliance; titrations 20, 50, 100, 200, 400 over 5 weeks **3A4 DDI** azoles dose red - TLS monitor/allopurinol	titrate to 400mg qday **with food**
idelalisb	PI3Ki (δ)	CLL, FL	**diarrhea**, cytopenias, **rash**, fatigue; BBW: **colitis**, **pneumonitis**, infections, intestinal perforation, fatal/serious hepatotox; warnings: myelosupp, skin tox 3A4; supportive: viral prophylaxis, PJP prophylaxis, monitor CMV	idelalisib 150mg bid wowfood + rituximab 375mg/m2 IV day 1,15; q28d
duvelisib	PI3Ki (δγ)	CLL, FL	**diarrhea**, neutropenia, **rash**, fatigue, pyrexia, cough, N, resp inf, myalgia, anemia; BBW: **diarrhea/colitis, pneumonitis**, cutan rxns; Warn: hepatox, fetaltox 3A4 (substrate, moderate inhibitor); supportive: viral prophylaxis, PJP prophylaxis, monitor CMV	duvelisib 25mg bid wowfood
copanlisib	PI3Ki	CLL, FL	**hyperglycemia**, cytopenias, **HTN**, diarrhea, fatigue, N, infection	60mg IV days 1 8 15 q28d
bendamustine	alkylating	FL	*requires antiviral and PJP prophylaxis; rash, **NV**, **myelosupp** (nadir 14-21d), alopecia; secondary malignancies	
imatinib	TKI BCR-ABL	CML	myelosupp (WBC Neutro RBC Plt), rash, fluid ret/edema, fatigue, NV, diarrhea/constipation, muscle cramps, bleeding/bruising, increase in LFTs	takewfood; higher incidence of GI	
dasatinib	TKI BCR-ABL SRC	CML		QTc, pleural effusions; PAH; myelosupp (thrombocytopenia, neutropenia, anemia, leukopenia)	3A4 substrate, watch antacids/PPIs
nilotinib	TKI BCR-ABL	CML		QTc, sudden deaths	3A4 substrate
bosutinib	TKI BCR-ABL SCR T315I	CML		takewfood; higher incidence of GI	
ponatinib	TKI BCR-ABL SCR T315I +	CML		(dirty drug) arterial thrombosis, hepatotoxicity, pancreatitis	
omacetaxine	PSinh T315I	CML C A	myelosupp, thrombocytopenia, anemia, neutropenia, lymphopenia; GI (diarrhea, N); fatigue, injection site rxn, pyrexia		
asparginase		ALL	ADEs worse in adults; thrombosis, pancreatitis, LFTs ele, hyperbili-fibrino;	
bortezomib	PI	MM VRd	acyclovir prophylaxis herpes; bortez give SC ↓neuropathy (bort>ixa>carf), thrombocytopenia, neutropenia, edema, diarrhea/constipat, NV low	
carfilzomib	PI	MM KRd	acyclovir prophylaxis herpes; neuropathy (bort>ixa>carf), thrombocytopenia, neutropenia, edema, diarrhea/constipat, NV low	
lenalidomide	IMiD	MM VRd	BBW: embryo-fetal toxicity; neutropenia and thrombocytopenia, VTE SE: fatigue, diarrhea/constipation, rash, muscle cramps REMS	
daratumumab	anti-CD38	MM DVRd	HepB HSV reactivation; 50% chance infusion rxn; fatigue, decreased WBC	
blinatumomab	anti-CD19	ALL	cytokine release syndrome (CRS, fever hypotension, tachy); neurotox, LFTs CI 24hr for 28 days	
brentuximab	anti-CD30	HL	BBW: PML SE: myelosupp (neutropenia), neuropathy, N, diarrhea, fatigue	
doxorubicin	anthracycline	HL, DBLCL	BBW: HF, secondary malignancy SE: NV myelosupp, red fluids, alopecia	
daunorubicin	7+3	AML	tumor lysis syndrome, NV, mucositis, alopecia, cardiotox (ECHO), red fluids, risk inf/neutropen fever/extravasation	
cytarabine	7+3	AML	myelosuppression, rash, HA, fever; HIDAC: high dose (>1g/m2): conjunctivitis, cerebellar toxicity; rash, infection/neutropen fever (GCSF)	
Vyxeos	lipo-cytara-dauno	AML	liposomal 7+3; similar side effects but better tolerated; prolonged cytopenias	
bleomycin	antitumor	HL	BBW: pulmon toxicity SE: rash, allergic rxn	
vinblastine	vinca	HL	BBW: ileus SE: myelosupp, HTN, const	
vincristine	vinca	ALL DBLCL	BBW: ileus SE: neuropathy, const	
dacarbazine	alkylating	HL	SE: NV myelosupp, flu-like sx	
cyclophos	alkylating	DBLCL	BBW: hemorrhagic cystitis NE: NV myelosupp	
decitabine	hypomethylating	AML	fewer SE than intensive: myelosupp, NV low; no renal/hepatic	
azacitadine	hypomethylating	AML	fewer SE than intensive: myelosupp, NV low; no renal/hepatic	
prednisone	steroid	ALL DBLCL	no difference in overall survival/relapse; fewer SE SE: hyperglycemia, insomnia, dyspepsia, jitteriness, HTN, osteoporosis	
dexameth	steroid		better CNS penetration, decreased risk of CNS relapse, improved event free survival; increased rate of myopathy, osteonecr, neuropsych SE	MM VRd diff syndrome (from IDH) 10mg q12h
midostaurin	TKI for FLT3+	AML	SE: NV mod, QTc, pulmonary rare	
ivosidenib	IDH1i	AML	QTc; SE: hyperleukocytosis, diff syndrome, hyperbili; wowfood; 3A4 decrease dose with strong 3A4 inhibitors	
enasidenib	IDH2i	AML	SE: hyperleukocytosis, diff syndrome, hyperbili; wowfood; no ddis	
gilteritinib	FLT3i	AML	QTc, myalgias/arthralgias, LFT elevations; 3A4/P-gp substrate sorafenib another FLT3i	
gemtuzumab	anti-CD33	AML	SE: hepatotox, veno-occlusive disease (**VOD**), myelosupp, prolonged thrombocytopenia, hypersens, QTc premed APAP DPH steroids	
ATRA		APL	all trans retinoic acid VitA; give asap; SE: diff syndrome, pseudotumor, LFT ele CI induction 2on2off	
arseneic		APL	SE myelosupp CI induction, 4on4off	
purines	mercapto/thioguan	ALL	dosing complicated, take empty stomach (2hrs milk/citrus)	

Lung Cancer

NSCLC Limited, Resectable

IA-B (<4cm): surveillance

IB (>4cm): adjuvant chemo, start 6-12wk after sx

- cisplatin + vinorelbine x4 cycles

NSCLC Limited, Unresectable

Concomitant chemoradiation

- cisplatin + etoposide → main durvalumab x1yr (IIIA-C)
- carboplatin + paclitaxel → main durvalumab x1yr (IIIA-C)

IIIA-C maintenance: main durvalumab x1yr

SCLC Limited (single hemithorax, in single radiation port)

Concomitant chemoradiation

- cisplatin + etoposide x4 cycles

SCLC Extensive

Chemo + anti-PD-L1 (no radiation)

- carboplatin + etoposide + atezolizumab x4 cycles → main atezolizumab alone

2nd-line and beyond: depends on duration of completion

>6mo repeat carboplatin + etoposide (without atezolizumab)

<6mo single agent (lurbinectedin, topo/irinotecan, paclitaxel, etc.)

Metastatic 1st-line

monotherapy anti-PD-1

- nivolumab
- pembrolizumab

combined anti-PD-1 + CLTA-4 inhibitor

- nivolumab + ipilimumab
- pembrolizumab + ipilimumab

combined BRAFi + MEKi (if BRAF+) +/- PD-L1i

- dabrafenib + trametinib
- vemurafenib + cobimetinib +/- atezolizumab
- encorafenib + binimetinib

Metastatic 2nd-line

Other Regimens

- ipilimumab
- high-dose IL-2

Certain Circumstances

- ipilimumab/intralesional T-VEC
- cytotoxic agents (decarb, temozo, paciltax, alb-pacl, carbo+pacl)
- imatinib if KIT+
- larotrectinib/entrectinib for NTRK+
- binimetinib for NRAS mutated

NSCLC Metastatic

EGFR+	•osimertinib [3A4 rash, diarrhea, cardiomyopathy/QTc, nail changes]
ALK+	•alectinib (lorlatinib 2nd) [muscle pain and ↑CK, bradycardia; with food] [3A4 hypercholes, hypertriglyc, cognitive and mood effects]
ROS-1	•entrectinib [3A4 cardiomyopathy, cognitive effects]
MET ex14	•capmatinib [3A4 peripheral edema, NV]
RET fusion	•selpercatinib OR pralsetinib [3A4 edema, HTN, QTc; avoid PPI (or take food)] [3A4 constipation, HTN, musculoskel pain; empty stomach]
BRAF V600E	•dabrafenib AND trametinib [3A4 fever, rash, secondary skin cancers; empty stomach] [fever, rash; store in fridge]

NSCLC Metastatic, No Mutation

PD-L1 ≥50%	nonsquam	•pembrolizumab alone → upon progression: carboplatin + pemetrexed	maintenance: pemetrexed
	squamous	•pembrolizumab alone → upon progression: carboplatin + paclitaxel	maintenance: none
PD-L1 <50%	nonsquam	•carboplatin + pemetrexed + pembrolizumab x4 cycles	maintenance: pemetrexed + pembrolizumab
	squamous	•carboplatin + paclitaxel + pembrolizumab x4 cycles	maintenance: pembrolizumab
Progression	tyrosine kinase agent if mutation; otherwise, single-agent nonplatinum IV chemo - pemetrexed (nonsquam), paclitaxel, docetaxel, gemcitabine, vinorelbine		

Melanoma

Treatment Overview

Node Negative	Stage 0	in situ disease	wide excision	common follow up
	Stage IA	<0.8mm, no ulceration	wide excision	common follow up
	Stage IB	<0.8-1mm or <0.8+ulc	wide excision +/- consider sentinel node biopsy	common follow up (sentinel node negative)
	Stage IB/II	>1mm thick	wide excision +/- offer sentinel node biopsy	common follow up (sentinel node negative)
Node Positive	Stage IIIA-D	sentinel node positive	nodal ultrasound or complete lymph node dissection → adjuvant therapy or observation	
	Stage III	clinically positive node	core biopsy or fine needle aspiration → wide excision and therapeutic lymph node dissection → consider radiation and/or adjuvant therapy or observation	
	Stage IV	metastas/progress on adjuv	resection, primary RT, systemic therapy, intralesional T-VEC, observation	

Adjuvant Stage III node(+)

- nivolumab
- pembrolizumab
- dabrafenib + trametinib (if BRAF+)

Duration 1 year

Breast Cancer

ESBC HR(+) HER2(+) *all adjuvant endocrine therapy

Node(+) or large >5cm
- AC-T doxorubicin + cyclophosphamide q2-3wk x4 cycles followed by paclitaxel q2wk x4 cycles/q1wk x12 doses
- TC docetaxel + cyclophosphamide q3wk x 4 cycles (anthracycline sparing d/t cardiotox or max dose)

Node(-) low score: no chemo, adjuvant endocrine therapy

Node(-) high score
- TC docetaxel + cyclophosphamide q3wk x 4 cycles (preferred)
- AC doxorubicin + cyclophosphamide q2-3wk x4 cycles

ESBC Triple Negative HR(-), HER2(-)

- AC-T doxorubicin + cyclophosphamide q2-3wk x4 cycles followed by paclitaxel q2wk x4 cycles/q1wk x12 doses

ESBC Adjuvant Endocrine Therapy

Pre-menopausal • tamoxifen x5-10yr

Pre "high risk" • AI/tam + ovarian suppression (oophorectomy/LHRH agonist)

Post-menopausal • anastrazole/letrozole x5-10yr
- tamoxifen x5-10yr (if OP/fract)
- tamoxifen x2-3yr then anastrazole/exemestane (if peri)
- tamoxifen x5yr then letrozole x5yr (if peri)

ESBC HER2(+)

HER2(+) regardless of size, node, ER/PR: add trastuzumab q3wk x1yr with taxane

HER2(+) >2cm or node(+), any ER/PR: add pertuzumab q3wk x4-6 cycles or x1yr with taxane

"High Risk" >2cm and/or node(+): PTP/PTD x4→AC x4→HER2 x1y or TCH-P x6→HER2 x1yr
- pertuzumab + trastuzumab + paclitaxel/docetaxel x4 cycles → doxorubicin + cyclophosphamide → trastuzumab +/- pertuzumab
- pertuzumab + trastuzumab + carboplatin + docetaxel q3wk x6 cycles → trastuzumab +/- pertuzumab

"Low Risk" <2cm and node(-)
- paclitaxel + trastuzumab x4 cycles → trastuzumab x1yr
- adjuvant TCH x6 cycles → trastuzumab x1yr

ESBC Favorable

>50yo (post-meno) nodes negative, small tumor (<1cm)
ER(+)/PR(+) (HR(+)), HER2(-), tumor grade 1 (well diff)
negative lymph, low Ki67 index

ESBC Unavorable

<50yo (pre-meno) nodes positive, large tumor (<3cm)
ER(-)/PR(-) (HR(-)), HER2(+), Triple Neg, tumor grade 2/3 (poorly diff)
positive lymph, high Ki67 index

MBC HER2(+)

1st-line • PTD pertuzumab + trastuzumab + docetaxel

2nd-line • ado-trastuzumab-emtansine or tucatinib+capecitabine+trastuzumab

3rd-line • lapatinib+capecitabine • lapatinib+trastuzumab • trastuzumab+salvage chemo

MBC HER2(-)

1st-line • paclitaxel weekly 3wk on 1wk off • liposomal doxorubicin (if anthra naïve) - capecitabine (after taxane and/or anthra)

Triple Negative (if PDL1+) • nab-paclitaxel + atezolizumab • pembrolizumab + chemo

3rd-line: eribulin or sacituzumab govitecan

Salvage regimen "dealers choice" (should have used taxanes, anthracyclines, eribulin, capecitabine by now)
- CTs, gemcitabine, carbo/cisplatin, ixabepilone, liposomal doxo, vinorelbine, olaparib/talazoparib (BRCA mut), paclitaxel alb-bound, rechall endocrine if ER+

MBC Adjuvant Endocrine Therapy

Pre-menopausal • ovarian suppression, then treat as postmeno

Post-menopausal (ER+)

1st-line • AI +/- CDK4/6 inhibitor

2nd-line • fulvestrant IM +/- CDK4/6 inhibitor

3rd-line • everolimus + exemestane

"ride the endocrine therapy train"; can use PI3K inhibitor (apelisib) with fulv if mutation

HER2+ receive 1 year of trastuzumab +/- pertuzumab

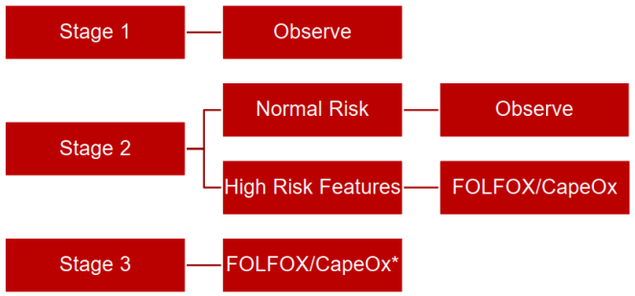
Colon Cancer

Treatments

FOLFOX (q2w) oxaliplatin IVPB + leucovorin IVPB + flurouracil IV PUSH + fluorouracil CIV over 46h
FOLFIRI (q2w) irinotecan IVPB + leucovorin IVPB + flurouracil IV PUSH + fluorouracil CIV over 46h
CapeOX (q3w) oxaliplatin IVBP on day 1, then capecitabine po days 1-14

Early Stage

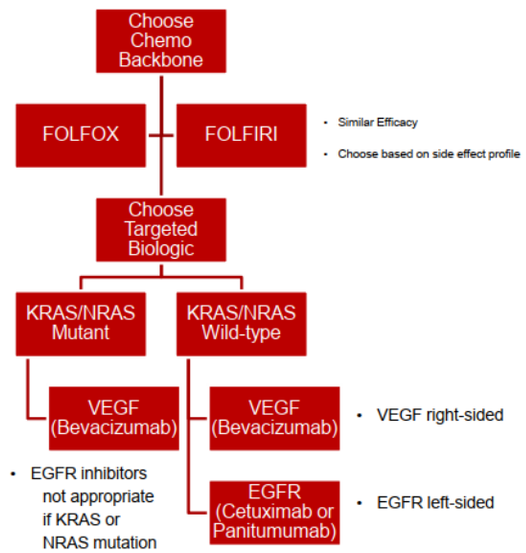
Stage I surgery + observation
Stage II surgery +
Stage II surgery + 5FU alone or no chemo
high-risk surgery + FOLFOX preferred or CapeOX (high-risk: T4 tumor, poorly different, lymph/vasc invasion, <12nodes exam, obstruct/perf/+margin)
Stage III: surgery + FOLFOX preferred or CapeOX (*consider 3mo for low-risk CapeOx —T1-3, N1)



Metastatic

1st-line • FOLFOX or FOLFIRI (similar efficacy, choose based on SE profile)

KRAS/NRAS mutant • FOLFOX or FOLFIRI + bevacizumab
KRAS/NRAS wt, right-sided • FOLFOX or FOLFIRI + bevacizumab (VEGFi)
KRAS/NRAS wt, left-sided • FOLFOX or FOLFIRI + cetuximab/panitumamab (EGFRi)



ADEs

FOLFOX: diarrhea, mucositis, myelosupp, NV, HFS cold-induced **neuropathy**
FOLFIRI: diarrhea, mucositis, myelosupp, NV, HFS ***diarrhea**
CapeOX: diarrhea, abd pain, myelosupp, NV, HFS, hyperbili cold-induced **neuropathy**
bevacizumab: HTN, proteinuria, wound healing (hold 28d before sx), VTE/ATE, HA, voice hoarseness, hemorrhage
cetuximab/panitumumab: skin rash, hypersens rx, electrolyte abnormalities

fluorouracil hepatic dose adj; neutropenia (bolus), diarrhea, mucositis, HFS (cape>fu), cardiotox (EKG/MI with CI)
oxaliplatin renal, no dose adj; neuropathy (acute-cold; long-last can be perm); myelosupp (thrombocytopenia>neutropenia), NV
irinotecan hepatic dose adj 3A4/UGT; diarrhea (<24h antichol; >24h loperamide); myleosupp (neutropenia>thrombocytopenia); NV

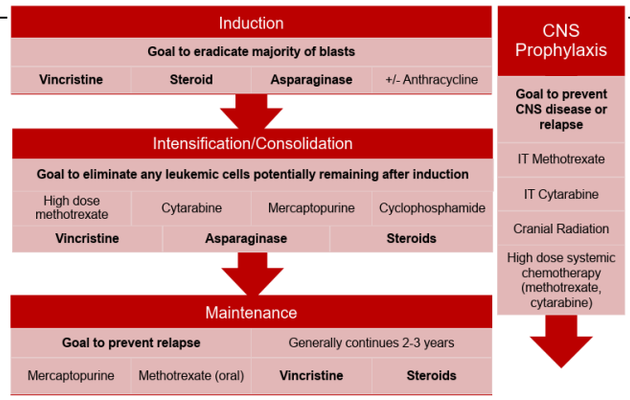
CML: hydroxyurea, busulfan, interferon alfa, imatinib, dasatinib, nilotinib, bosutinib, ponatinib, omacetaxine
CART: axicabtagene ciloleucel, tisagenlecleucel, brexucabtagene autoleucel; tocilizumab, siltuximab levetiracetam, dexamethasone, methylprednisolone
FL: rituximab, obinutuzumab, lenalidomide, bendamustine, cyclophosphamide, doxorubicin, vincristine, prednisone, idelalisib, copanlisib, duvelisib, tazemetostat
DLBCL: rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, polatuzumab, tafasitamab, bendamustine, lenalidomide, dexamethasone, cytarabine, gemcitabine, etoposide, cisplatin, carboplatin, oxaliplatin
HL: brentuximab, doxorubicin, bleomycin, vinblastine, dacarbazine, etoposide, cyclophosphamide, vincristine, procarbazine, prednisone, vinorelbine, gemcitabine, pembrolizumab, nivolumab
OL: acalabrutinib, zanubrutinib, belinostat, bexarotene, mogamulizumab, romidepsin, vorinostat, pralatrexate, romidepsin, siltuximab
CLL: ibrutinib, acalabrutinib, obinutuzumab, venetoclax, duvelisib, idelalisib, rituximab
ALL: vincristine, steroids (prednisone, dexamethasone), asparaginase, imatinib, dasatinib, nilotinib, bosutinib, ponatinib, mercaptopurine, thioguanine, hyperfractionated-cyclophosphamide, doxorubicin, cytarabine, methotrexate, blinatumomab, inotuzumab, nelarabine
AML: 7+3 (cytarabine, daunorubicin), midostaurin, liposomal cytarabine+daunorubicin (Vyxeos), decitabine, azacitadine, venetoclax, enasidenib, ivosidenib, sorafenib, gilteritinib, gemtuzumab; APL: all trans retinoic acid ATRA Vitamin A, arsenic
MM: bortezomib, ixazomib, carfilzomib, lenalidomide, pomalidomide, thalidomide, daratumumab, dexamethasone, cyclophosphamide

ALL—initial

induction: vincristine, steroid, asparaginase +/- anthracycline
1-2mo, goal eradicate blasts
consolidation: HyperCVAD, vincristine, steroid, asparaginase
6-12mo, goal eliminate leukemic cells remaining 28d cycle x8 A=induction, B=consol
A: hyperfract-cyclophosphamide + vincristine + doxorubicin + dexameth + IT chemo
B: HD-methotrexate + HD-cytarabine + IT chemo; add TKI on days 1-14 for Ph+
maintenance: vincristine, steroid, mercaptopurine, methotexate
2-3yr, goal prevent relapse
CNS prophylaxis: IT-methotrexate, IT-cytarabine, HD-sys MTX/Cytar

ALL—R/R

Ph+: TKI (imatinib dasa nilo bosu pona); mono or combo chemo
CD19+: blinatumomab
CD22+: inotuzumab
T-cell: nelarabine
<26yo: CAR-T tisagenlecleucel (Kymriah)
Others: clofarabine-regimen, liposomal vincristine, other combos
Note: transplant is only curative treatment



AML—induction

intensive induction:
- 7+3 (cytarabine + daunorubicin)
- 7+3 with midostaurin if FLT3+
- liposomal cytarabine + dauno (Vyxeos) if changes

less-intensive induction:
- hypomethylating agents (decitabine, azacitadine)
- venatoclax + hypomethylating or LD cytarabine if >75yo/comorbid
- IDH inhibitor (enasidenib, ivosidenib)

AML—consolidation

HIDAC: High Dose Ara-Cytarabine 3g/m2 q12h day 1 3 5
IDAC: Intermediate Dose Ara-Cytarabine 1g/m2 q12h day 1 3 5 if >60yo/renal

AML—R/R

Clinical Trial preferred
intensive:
- reinduction with initial if late response
- MEC (mitoxantrone, etoposide, cytarabine)
- FLAG +/- idarubicin (fludarabine, cytarabine, G-CSF)
- CLAG +/- idarubicin, mitoxantrone (cladribine, cytarabine, G-CSF)

less-intensive: hypomethylating agent if prev not received
targeted therapy
IDH1: ivosidenib IDH2: enasidenib CD33: gemtuzumab
FLT3: mitostaurin, gilteritinib, sorafenib

APL t(15;17)
ATRA (all trans retinoic acid, Vit A) give asap if APL suspected
arsenic; chemo not required unless high risk (add anthracycline)

CLL—initial

- ibrutinib
- acalabrutinib +/- obinutuzumab
- venetoclax + obinutuzumab

CLL—R/R

- acalabrutinib
- ibrutinib
- venetoclax +/- rituximab
- duvelisib
- idelalisb + rituximab

CML **Ph+**

hydroxyurea and busulfan (palliat); interferon alfa; all getting viral prophylaxis

CML: First-Line Therapies	^off-label	
Chronic Phase	**Accelerated Phase**	**Blastic Phase**
imatinib 400mg	imatinib 600mg	imatinib 600mg
dasatinib 100mg	dasatinib 100mg^	dasatinib 140mg^
nilotinib 300mg bid	nilotinib 300mg bid^	nilotinib 300mg bid^
		induction chemotherapy
	allogenic transplant	allogenic transplant
clinical trial	clinical trial	clinical trial
CML: 2nd, 3rd, 4th -Line Therapies	*T135I coverage	†must fail 2 TKIs
dasatinib 100mg	dasatinib 100mg	dasatinib 140mg
nilotinib 300mg bid	nilotinib 400mg bid	
bosutinib		bosutinib
ponatinib*	ponatinib*	ponatinib*
omacetaxine*† (3rd)	omacetaxine*† (3rd)	omacetaxine*† (3rd)
		induction chemo
allogenic transplant (3rd/4th)	allogenic transplant (3rd/4th)	allogenic transplant
clinical trial	clinical trial	clinical trial

Infection prophylaxis • Antibacterial: FQs • Antifungal: fluconazole • Antiviral: acyclovir/vala • PCP: Bactrim/dapson
Febrile Neutropenia • Education on what constitutes a fever • Antibiotics
Tumor Lysis Syndrome • Monitor labs • IV fluids • Allopurinol • Rasburicase PRN
Steroid Management • Hyperglycemia • Steroid psychosis • Stress ulcer prophylaxis • Insomnia • Bone health
Nausea/Vomiting • Antiemetic prophylaxis and PRN

Mucositis: topical anesthetics (lidocaine, magic mouthwash), opioids, Caphasol (prevention), palifermin (prevention)
Diarrhea: loperamide, diphenoxylate/atropine (Lomotil), octreotide, opium tincture
NV: aprepitant (prevention only), 5-HT3 antagonists (ondansetron), prochloperazine, metoclopramide, haloperidol, olanzapine, lorazepam, corticosteroids
Gastritis: PPI (esomeprazole), H2RA (famotidine) Pain: opioids Menorrhagia: leuprolide, oral contraceptives, progestins

Grade 1: levetiracetam prophylaxis
Grade 2: dexamethasone + levetirace: work up other causes and consider neuro consult
Grade 3: dexamethasone + levetirace: neuro consult, consider ICU if pt worsens; for non-responders, may to treat according to grade 4
Grade 4: methylprednisolone + levetirace; ICU, may need respiratory hemodynamic support; may consider refractory management

FL—early NHL

Stage I/II nonbulky: radiation, observation
Stage I/II bulky: anti-CD20 +/- chemo +/- radiation

FL—advanced stage (III/IV) tx not required until symptomatic

- rituximab/obinutuzumab + bendamustine/CHOP/CVP

Others: rituximab/obinutuzumab + lenalidomide
[CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone]
[CVP: cyclophosphamide, vincristine, prednisone]

For elderly/infirm:
- rituximab weekly x4doses (pref elderly/infirm)
- alkylating agent (cyclophos/chlorambucil) +/- rituximab
- radioimmunotherapy

FL—maintenance/consolidation

- rituximab 375mg/m2 day 1 every 2mo x 2yr
- obinutuzumab 1000mg day 1 every 2mo x 2yr

FL—R/R

- rituximab/obinutuzumab + bendamustine/CHOP/CVP
- rituximab + lenalidomide
- lenalidomide +/- obinutuzumab
- rituximab or obinutuzumab monotherapy

Relapsed/Refractory to 2+ prior therapies:
- idelalisib, copanlisib, duvelisib (PI3Ki)
- tazemetostat (oral EZH2 inhibitor)

For elderly/infirm:
- rituximab weekly x4 doses
- alkylating agent (cyclophos/chlorambucil) +/- rituximab
- radioimmunotherapy

For elderly/infirm 2nd-line maintenance/consolidation:
- rituximab 375mg/m2 day 1 every 2mo x 2yr
- obinutuzumab 1000mg day 1 every 2mo x 2yr
- high dose therapy with autologous stem cell rescue
- allogenic cell transplant for highly selected patients

Nausea/Vomiting

HEC	cisplatin+etop anthra+cyclophos	NK1-RA + 5HT3-RA + dexameth +/- olanzapine
MEC	FOLFOX	dexamethasone + 5HT3-RA

Antiemetic efficacy - PO and IV have similar efficacy
Aprepitant drug interactions (inhibits CYP 3A4, induces 2C9)
QTc warnings with IV ondansetron and IV dolasetron

5HT3 Antagonists: ondansetron, granisetron, dolasetron, palonosetron
NK-1 Antagonists aprepitant/fos, netupitant-palonosetron, rolapitant
Dopamine Antagonists: metoclopramide, haloperidol
Phenothiazines: prochlorperazine, promethazine

DLBCL—initial NHL

Stage I/II
nonbulky (<7.5cm): RCHOP x3 + radiation or RCHOP x6 +/- radiation
bulky (LN≥7.5cm): RCHOP x6 +/- radiation
Stage III/IV:
- RCHOP x6

CNS prophylaxis: high risk score 4-6 (>60yo, LDL>, performance >1, SIII-IV, nodal sites)
- IT chemo x4 doses (1 per cycle)
- HD-methotrexate x3 doses (1 per cycle)

DLBCL—R/R

Transplant eligible:
- salvage chemo RDHAP, RGDP, RICE, etc

after ≥2 therapies: bendamustine + rituximab + polatuzumab (CD79b)
- complete response: autologous stem cell transplant
- partial response: CAR-T therapy (axicabtagene/tisagenlecleucel)
- no response: alternate regimen/hospice

Transplant ineligible:
- palliative chemo RGemOX, RGDP, lenal+ritux/tafasitmab (CD19), bend+ritux

RDHAP: ritux, dex, cytara, cisplatin RGDP: ritux, dex, gemcita, cisplatin
RICE: ritux, ifosfamide, carboplatin, etoposide RGemOx: ritux, gemcita, oxaliplatin

HL—initial

Stage I-II fav *ABVD no growth factor
- ABVD x2-4 cycles +/- radiation

doxorubicin, bleomycin, vinblastine, dacarbazine

Stage I-II unfav (B sx, ESR≥50, >3 sites of disease)
- ABVD x4-6 cycles +/- radiation

BEACOPP considered if bad response on PET after 2 cycles
bleomyc, etoposide, doxorubicin, cyclophos, vincristine, procarbazine, prednisone

Stage III-IV
- ABVD x 2 cycles → PET

CR: remove bleomycin, complete 6 cycles
PR: change to escalated BEACOPP x 3 cycles, repeat PET
CR: continue BEACOPP, complete 6 cycles
PR: refractory disease, 2nd-line therapy

- brentuximab + AVD x6 cycles (for pt w/ no neuropathy, IPS≥4, or bleo Cl'd)
  - growth factor required*
- escalated BEACOPP x4-6 cycles (for pt IPS≥4, <60yo)

HL—R/R

Transplant eligible:
- salvage chemo GVD, ICE, DHAP, gemcit+bend+vinorelb+bretunx

CR/PR: auto stem cell → brentuximab maintenance (high risk)
NR: alternate regimen/hospice

consider pembrolizumab or nivolumab in progress post-transplant

Transplant ineligible:
- palliative chemo consider pembrolizumab or nivolumab

MM—induction NHL

Transplant Eligible (induction x3-4 cycles→transplant→maintenance)
VRd gold: bortezomib + lenalidomide + dexameth
CyBord: cyclophosphamide + bortezomib + dexameth (pref ESRD/renal)
KRd: carfilzomib + lenalidomide + dexameth (pref high-risk MM)
DVRd: daratumumab + bortezomib + lenalidomide + dexameth (pref high-risk MM)

Transplant Ineligible (induction x8-12 cycles→maintenance)
VRd gold: bortezomib + lenalidomide + dexameth
CyBord: cyclophosphamide + bortezomib + dexameth (pref ESRD/renal)
Vd: bortezomib + dexameth (renal/intolerable)
Rd: lenalidomide + dexameth (older/unfit)
DRd: daratumumab + lenalidomide + dexameth (nontransplant candidate)

MM—maintenance

Post-Transplant Eligible
standard: ixazomib or lenalidomide until progression
high-risk: bortezomib until progression (del17p or other)

Transplant Ineligible
standard: lenalidomide +/- dexameth until progression
high-risk: bortezomib-based therapy until progression

MM—R/R

lots of regimens; salvage therapy, aim to get myeloma under control, minimize toxicities, improve QoL
Determine: what pt has tried, when relapse (maintenance or not), transplant, comorbid, tolerable SE, QoL
e.g., bortezomib/carfilzomib/ixazomib + lenalidomide + dexameth darat + bort/carf + dex darat + lenal + dex

**bisphosphonates*, PJP quinolone/Bactrim, HSV acyclovir

Other Lymphomas

mantle cell lymphoma: acalabrutinib, zanubrutinib
cutaneous T-cell lymphomas: belinostat, bexarotene, mogamulizumab, romidepsin, vorinostat
T-cell lymphomas: pralatrexate, romidepsin
Burkitt's lymphoma: treated similar to ALL
Castleman's disease: siltuximab

	ALL	**AML**
Age	younger (15yo)	older (68yo)
Morph	lymphoid (B cells, T cells) ↑lymphoblast ↑B/T lymphocytes; ↓WBC RBC Plt ALLeukemia blasts >20%; ALLymphoma blasts <20%	myeloid (Auer rods present) ↑myeloblast, ↓WBC RBC Plt
Sx	low counts more coagulopathies possible lymphadenopathy, night sweats/fever	low counts APL: highest risk of coagulopathies
CNS	common; must use prophylaxis	uncommon (except M5 subtype)
Tx	backbone: vincristine, steroids, pegaspargase, anthracyclines (cyclophosphamide, mercaptopurine, methotrexate)	intensive: 7+3 +/- midostaurin, Vyxeos less-intensive: hypomethylating agents, IDH inhibitors
Targeted	Ph+: imatinib dasa nilo bosu pona CD19: blinatumomab CD20: rituximab CD22: inotuzumab T-cell: nelarabine CAR-T (CD19): tisagenlecleucel	FLT3: midostaurin, gilteritinib IDH1: ivosidenib IDH2: enasidenib CD33: gemtuzumab APL: ATRA/arsenic

Neutropenia—
fever: ≥38.3 or ≥38-1hr period
neutropenia: ANC <500 or ANC <1000 predicted to <500 over next 48hrs
ANC <100 (profound) for 7 days (prolonged)
Low risk (outpatient): **MASCC ≥21**, solid tumor, anticipated neutropenia <7 days, no hemodynamic instability
High risk (inpatient): **MASCC <21**, hematologic malignancy or HCT, anticipated neutropenia ≥7 days

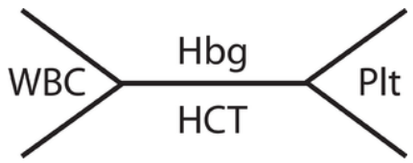
Empiric antimicrobials Low risk (outpatient): MASCC ≥21, solid tumor, anticipated neutropenia <7 days, no hemodynamic instability
amox-clav MSSA, CoNS, S. pneum, E. coli, S. pyog
levoflox MSSA, CoNS, S. pneum, E. coli, Pseudomonas
moxiflox MSSA, CoNS, S. pneum, E. coli
ciproflox CoNS, E. coli, Pseudomonas (good for renal failure) amox-clav + cipro combo covers gram negatives

Empiric antimicrobials High risk (inpatient): MASCC <21, hematologic malignancy or HCT, anticipated neutropenia ≥7 days
cefepime gram positive, gram negative, Pseudomonas (no anaerobic coverage, could add metronidazole; no CoNS)
pip-tazo gram positive, gram negative, Pseudomonas + ANAEROBIC COVERAGE (for anaerobic coverage, needed if a GI component-severe mucositis, abdom pain)
meropenem gram positive, gram negative, Pseudomonas + ANAEROBIC COVERAGE (reserved if history ESBL or MDR gram negative organisms)
vancomycin added if:
- CVC infection at site
- hemodynamically unstable (hypotensive, tachycardia, poor capillary refill time = peripheral vasoconstriction = septic shock)
- MRSA suspected bacteremia/pneumonia or fulminant severe pneumonia
- gram positive blood culture while waiting for susceptibility test
- cellulitis

Empiric antifungal agent when neutropenic and febrile **≥4 days** from first fever

Hb	F12-15 M13-17	↑Polycythemia ↓Anemia	
Plt	150-400k	↑Thrombocytosis ↓Thrombocytopenia	
WBC	4-10k w/ bands	↑Leukocytosis ↓Leukopenia (ANC <1000 ↓Neutropenia) ↑Leukocytosis with left shift	ANC = [(%neutrophils) + (%bands)] x WBC
MCV	80-100	↑Macrocytic ↓Microcytic	

Hct [35-50] Haptoglobin [36-195] Ferritin [15-300] Serum iron [50-170] TIBC [250-370] Cobalamin [200-900] Folate [5-16]			
Hemolysis	↓Hb ↓Hct **↓haptoglobin**		
Anemia of iron deficiency	↓Hb ↓Hct **↓MCV** **↓ferritin** **↑TIBC** ↓serum iron		if normal ferritin = anemia of chronic disease
Anemia of chronic disease	↓Hb ↓Hct —MCV —/↑ferritin ↓TIBC ↓serum iron		ferritin normal/high
Anemia of chronic kidney CKD	↓Hb ↓Hct —MCV —/↑ferritin ↓TIBC ↓serum iron; Burr cells		ferritin normal/high; normal MCV+haptoglobin
Anemia of cobalamin defic	↓Hb ↓Hct **↑MCV** ↓Cobalamin		
Anemia of folate deficiency	↓Hb ↓Hct **↑MCV** ↓Folate		



Innate, Non-Specific Immunity (Myeloid Cell Line)	**Acquired, Specific Immunity (Lymphoid Cell Line)**
Granulocytes - Basophils - Neutrophils - Eosinophils - Mast cells	T Lymphocytes - Helper T cells - Cytotoxic T cells - Regulatory T cells - Memory T cells
Monocytes/Macrophages	B Cells - Plasma cells - Memory B cells
Erythrocytes	Natural Killer Cells
Thrombocytes	

Vasopressors			- hypertension tissue necrosis, acute renal failure - ischemia: cardiac, mesenteric, decreased peripheral perfusion	
epinephrine	[β1 = β2 > α1* = α2*]	*At high plasma concentrations, α = β selectivity	tachycardia, hyperglycemia	
norepinephrine	[β1 = α1 > β2 = α2]		tachycardia, hyperglycemia	
phenylephrine				
dopamine	[β1 = β2 > α1*]	beta-agonist effect is gonna be maximized before the alpha-agonist effect can take place	tachycardia, hyperglycemia; decreased peristalsis arrhythmias (DA >> E/NE > PE/VP)	
vasopressin				
angiotensin II			hypernatremia, hypokalemia, thrombosis	
Inotropes	If you fix SV with inotropes, the HR will come down			
dobutamine	β1 β2 α1 agonist [β1 > β2 > α1] Onset <10min *HL 2-3min* 2-10 mcg/kg/min (max 20) metab: plasma clearance	HR ↑ MAP - PCWP↓ CO↑ SVR -/↓ Net effect is cardiac stimulation with modest vasodilation	tachyarrhythmia, hypotension, eosinophilia (rare)	consider: concomitant BB may limit effect
milrinone	$PDE_{3/4}$ inhibitor Onset 5-15min *HL 1-3hrs* 0.2-0.5 mcg/kg/min (max 0.75) metab: renal clearance	HR -/↑ MAP -/↓ PCWP↓ CO↑ SVR ↓	tachyarrhythmia, hypotension, thrombocytopenia (rare)	consider: delayed onset, prolonged HL in renal dysf
IV Vasodilators				
nitroglycerin	venous: ↓preload=↓pulm congestion HL 2-3min Use: acute relief of symptoms (dyspnea)	CVP↓↓ SVR -/↓ CO -/↑ PCWP↓ higher for SVR fx 5-10 mcg/min, titrated 5-10 q5-10min to effect (range: 10-200)	HA, hypotension	consider: tolerance (need for dose escalation); niche use in patients with concern for ischemia
nitroprusside	mixed: ↓preload=↓pulm cong; ↓afterload=↑CO HL 1-3min Use: optimization of CO/CI, relief of sx; eval of pulmonary HTN	CVP↓ SVR ↓↓ CO ↑ PCWP↓ 0.3-3mcg/kg/min	cyanide/thiocyanate toxicity may limit duration of use (esp hepatic/renal impairment), hypotension	consider: cost
NMBA	RASS -4 to -5 prior to initiation	sugammadex reversal roc/vec		
succinylcholine	depolarizing Onset 15-30s Dur 5-10min 1 mg/kg IV (one time dose for intubation)		Malignant Hyperthermia: rare genetic, rigidity, fever, ischemia, v-arrhy Muscle weakness, fasciculation, ↑IOP/ICP, hyperkalemia	CI: hyperkal, burn, crash, denervating injury (SC) Malignant Hyperthermia tx: dantrolene
pancuronium vecuronium rocuronium atracurium cisatracurium				Long Term ADEs: most common with panc/vecur Prolonged Neuromuscular Blockade Critical Illness Myopathy/ICU Acquired Weakness
Misc				
propofol	sedation no amnesia/analgesia; onset 1-2min, quick offset		resp depression, decreased BP/CO, hyperTGs, pancreatitis, infect	**PRIS** brady, hypo, dyslip, rhabd, met acid, fatal
dexmedetomidine	α2 agonist, onset 5-30min, use <24h in ICU		HTN, bradycardia, NV, heart block, no resp depress	
ketamine	hyponotic+analgesic		halluc, HTN, tachy, emergence rxns, ICP	
etomidate	hyponotic, for procedures; onset 10-20sec, duration 4-10min		myoclonus, tachy but no BP/CO, seizure threshold, cortisol dec	
Classes				
PCC	Kcentra 4-factor, dose INR <4 25u/kg <6 35u/kg >6 50u/kg	use factor IX units when dosing; dose factor Xa 25-50u/kg		
DOAC reversals	andexanet alfa; idarucizumab (dabig), ciraparantag (all, trials)			
P2Y12 inhibitors				
GIIb/IIIa inhibitors				

	Dosing	**Elimination**	**HL min**	**Metab**	**Adverse Effects**	**Cost**	**Avoid Use In**
pancuronium	LD 1, 1-2 mcg/kg/min	renal hepatic	100-300	Yes	Histamine release, Vagolytic, Tachycardia, HTN	$	CAD, liver/renal dysfunction
vecuronium	LD 1, 1-2 mcg/kg/min	renal hepatic	80-300	Yes	Bradycardia, Prolonged blockade on discontinue	$$	liver/renal dysfunction
rocuronium	LD 6-12, 10-15 mcg/kg/min	renal hepatic bile	80-130	Yes	Some histamine release but less CV effects	$$	liver/renal dysfunction
atracurium	LD 3, 5-15 mcg/kg/min	Hofmann/ester hydrolysis	20-25	No	Histamine release	$$$	possibly hypotension?
cisatracurium	LD 1, 3-5 mcg/kg/min	Hofmann/ester hydrolysis	20-30	No	No significant histamine release or CV effects	$$$$$	none

α1	↑SVR ↑MAP	blood vessels	vasoconstriction glycogenolysis, gluconeogen
α2	α2a ↓SVR ↓HR α2b ↑SVR ↓HR	presyn neuron smooth muscle	negative feedback constriction inhibits insulin release, induce glucagon
β1	↑CO ↑HR	heart blood vessels	chronotropy/inotropy vasodilation
β2	↓SVR	lungs blood vessels	bronchodilation vasodilation
D1 D2	↓SVR	kidney blood vessels	↑UOP vasodilation
vasopressin	↑SVR	blood vessels	vasoconstrict, Na-H2O retention, ↑cortisol
angiotensin II	↑SVR	blood vessels	vasoconstrict, aldosterone release

epinephrine 0.005-0.02 mcg/kg/min >0.05 mcg/kg/min	mixed α β more β1 β2 more α1 α2	 ↑chronotropy/inotropy vasoconstriction
norepinephrine	α1 α2 primarily (some β1 β2)	vasoconstriction ↑chronotropy/inotropy
phenylephrine	α1 α2	vasoconstriction
vasopressin	vasopressin	vasoconstriction
dopamine 1-5 mcg/kg/min 5-10 mcg/kg/min 10-20 mcg/kg/min	 D1 D2 β1 β2 α1 α2	 ↑UOP ↑chrono/ino ↓SVR vasoconstriction
angiotensin II	angiotensin II	vasoconstriction ↑Na ↓K, thrombosis

Vasopressors						
	DA	**α1**	**β1**	**β2**	**Other**	
dopamine*	+++++	+++	++++	++		2.5-20 mcg/kg/min
epinephrine*		++++	++++	+++		0.02-1 mcg/kg/min
norepinephrine*		+++++	+++	++		0.02-3.3 mcg/kg/min
phenylephrine		+++++				0.5-9 mcg/kg/min
vasopressin					V1 V2 agonism	0.01-0.04 units/min
angiotensin II					ATII agonism	5-30 ng/kg/min^
Inotropes						
dobutamine		+	++++	++		2.5-20 mcg/kg/min
milrinone					$PDE_{3/4}$ inhibitor	0.25-0.75 mcg/kg/min

*higher doses more α1 activity ^dose (up to 80 for 3h); lower if ACEi, won't work ARB

DA vasodilation (renal) **α1** vasoconstriction **β1** chronotropy/inotropy **β2** vasodilation

Epipinephrine [$\beta_1 = \beta_2 > \alpha_1^* = \alpha_2^*$] anaphylactic shock, cardiogenic shock, cardiac arrest; Low doses produce cardiac stimulation and vasodilation, which turns to vasoconstriction at high doses. *At high plasma concentrations, α = β selectivity.

Norepinephrine [$\beta_1 = \alpha_1 > \beta_2 = \alpha_2$] severe hypotension, septic shock; Reflex bradycardia masks direct stimulatory effects on sinoatrial node.

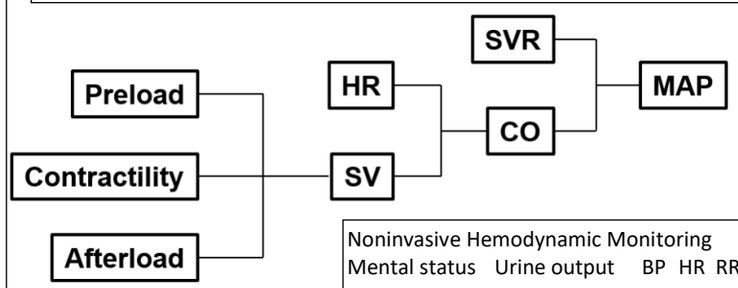
Dopamine [$\beta_1 = \beta_2 > \alpha_1^*$] acute heart failure, cardiogenic shock, acute renal failure; At low doses, it stimulates the heart and decreases SVR; at high doses, vasodilation becomes vasoconstriction as lower affinity α-receptors bind to the DA; also binds to D1 receptors in kidney, producing vasodilation.

Dobutamine [$\beta_1 > \beta_2 > \alpha_1$] acute/refractory heart failure, cardiogenic shock; Net effect is cardiac stimulation with modest vasodilation.

Low SVR can be seen with Sepsis, Anaphylaxis, Spinal shock, Adrenal Insufficiency, Hyperthermia, AV fistula, Vasodilator use
High SVR can be seen with Hypovolemia, Cardiogenic Shock, Hypothermia, Vasopressor use
Increased PVR can be seen with hypoxia, hypercapnea, increased sympathetic tone, polycythemia, precapillary pulmonary edema, pulmonary emboli, or lung compression (pleural effusion) and in ventilated patients.
Decreased PVR can be seen with oxygen, adenosine, isoproterenol, alpha-antagonists, inhaled nitric oxide, prostacyclin infusions, and high dose calcium channel blockers.

MAP	Mean Arterial Pressure (mean BP) MAP = (1/3 SBP) + (2/3 DBP)	70-10 mmHg
SV	Stroke Volume (from LV per beat) SV = CO/HR (mL/beat)	60-130
SI	Stroke Volume Index (mL/m^2/beat)	30-65
CO	Cardiac Output CO = SV*HR	4-8 L/min
CI	Cardiac Index CI = CO/BSA	2.8-4.2 $L/min/m^2$
CVP	Central Venous Pressure (Preload R)	2-8 mmHg
PCWP	Pulmonary Capillary Wedge Pressure (Preload L)	6-12 mmHg
RAP	Right Arterial Pressure	2-6 mmHg
RVP	Right Ventricle Pressure	15-25 mmHg
PAP	Pulmonary Artery Pressure	10-22 mmHg
SVR	Systemic Vascular Resistance (Afterload L, pressure LV has to pump against) SVR = 80*(MAP-CVP)/CO SVR ≅ MAP/CO	900-1400 $dyn*s/cm^5$
PVR	Pulmonary Vascular Resistance (Afterload R, pressure RV has to pump against) PVR = 80*(mPAP-PCWP)/CO	150-250 $dyn*s/cm^5$
PaO_2	partial pressure O_2	90 mmHg
SaO_2	arterial oxygen saturation	98%
pCO_2	partial pressure CO_2	40 mmHg (arterial)
$ScVO_2$	mixed venous oxygen saturation	60%–80%
$ScvO_2$	central venous oxygen saturation	

MAP = CO*SVR product of cardiac output and systemic vascular resistance
SVR afterload L, pressure LV has to pump against
CO = HR*SV product of HR and volume ejected by the heart
HR (chronotropy)
SV is impacted by preload, contractility, afterload
Preload volume in ventricles at end of diastole prior to systole; an increase in preload = increase contractility (except HF)
CVP preload right side volume status; PCWP preload left side volume status
Contractility (inotropy) ↑inotropy via ↑sympathetic activation, ↑catecholamines, ↑parasymp (vagal) inhibition, ↑afterload, ↑HR
Afterload resistance LV has to overcome to eject blood volume into aorta; controlled by vasoconstriction/vasodilation



Noninvasive Hemodynamic Monitoring
Mental status Urine output BP HR RR Pulse oximetry Capillary refill Skin temperature Skin color Skin turgor Transthoracic echocardiogram (TTE)

Invasive Hemodynamic Monitoring
Serum lactate Transesophageal echocardiogram (TEE) Arterial line Central venous catheter Pulmonary artery (PA) catheter (Swanz-Ganz catheter)

Hypovolemic Shock
↓preload, invasive monitoring CVP/PCWP
Hemorrhagic: volume loss secondary to blood loss (trauma, GI, surgery, anticoag)
Nonhemorrhagic: intravascular volume depletion (burns, dehydration, pancreatitis)
Management: source, fluid crystalloids, PRBCs, vasopressors MAP ≥60

Distributive (Vasodilatory) Shock
↓afterload (SVR)
1. Septic:
goal UOP >0.5, MAP >65, CVP 8-12
fluid resuscitation 30ml/kg crystalloids; vasopressors MAP >65 (norepi, epi)
empiric antimicrobial +/- antifungal/viral
2. Anaphylactic
epi 0.3-0.5 IV/IM stat
fluid resuscitation; vasopressor/epi MAP >65
supportive care (DPH/famot, steroids, albuterol)
3. Neurogenic
fluid resuscitation; vasopressors if refractory MAP 85-90
atropines sx brady

Cardiogenic Shock
↓CO (HR/contractility); hypofusion d/t cardiac failure (cold, wet/dry)
Monitor invasive (PCWP CVP CO ScVO2), noninvasive (hypo, ECHO, fluid/edema)
Management: early definitive restoration of coronary blood flow
cold/wet: inotrope+diuretic cold/dry: inotrope
when inotropes fail: epi/norepi, mechanical

Obstructive Shock
extra-cardiac obstruction
PCWP↑impaired diastolic fill; PCWP↓impaired systolic contraction
Monitor: invasive not required
Management:
cardiac tamponade (pericardiocentesis, drainage)
tension pneumo (fine needle decomp)
PE (heparin +/- thrombolysis/embolectomy)

↓ Low Values	Hemodynamic Parameter	↑High Values
volume expansion	CVP/PCWP—preload	diuresis or venodilators
vasopressors	SVR/PVR—afterload	arteriovasodilators
positive inotropes	CO/CI—inotropy/contractility	negative inotropes
positive chronotropes	HR—chronotropy	negative chronotropes

	MAP	CVP	PCWP	CO	SVR
Hypovolemic	↓	↓	↓	↓	↑
Distributive	↓	↓	↓	↑↓	↓
Cardiogenic	↓	↑	↑	↓	↑
Obstructive	↓	↑	#	↓	↑

Distributive=Vasodilatory; preload = CVP PCWP, afterload = SVR

FASTHUG – **F**eeding, **A**nalgesia, **S**edation, **T**hromboembolic Prevention, **H**ead of Bed Elevation, Stress **U**lcer Prophylaxis, **G**lucose Control

Sepsis
Fluid Resuscitation
IV fluid resuscitation is initiated to stabilize sepsis-induced tissue hypoperfusion
- at least 30ml/kg IV crystalloid fluid in first 3 hours
- target MAP 65
- resuscitated with goal of normalizing lactate
- avoid hydroxyethyl starches

Consider the 5 D's of fluids (drug, dose, duration, de-escalation, drug)
and ROSE 4 phases of therapy: ROSE (sine wave):
1. resuscitation (minutes) [net-positive]: 1st hit: shock; early goal-directed fluid management; early administration of fluid boluses
2. optimization (hours) [net-neutral]: 2nd hit: ischemia + reperfusion; organ rescue, guided fluid boluses
3. stabilization (days) [net negative-neutral]: 2nd hit: cont'd; organ support, late conservative fluid management
4. evacuation (weeks) [net negative]: 3rd hit: global increased permeability syndrome; late goal-directed fluid removal

	MAP	CVP	PCWP	CO	SVR	
Hypovolemic	↓	↓	↓	↓	↑	Preload, Contractility, Afterload → SV → HR → CO → SVR → MAP
Distributive	↓	↓	↓	↑↓	↓	Preload, Contractility, Afterload → SV → HR → CO → SVR → MAP
Cardiogenic	↓	↑	↑	↓	↑	Preload, Contractility, Afterload → SV → HR → CO → SVR → MAP
Obstructive	↓	↑	#	↓	↑	OR Preload, Contractility, Afterload → SV → HR → CO → SVR → MAP

Sepsis
qSOFA Criteria (≥2 criteria greater risk of poor outcomes, only valid ED/floor, not ICU): **SBP** <100 mmHg, **RR** >22, **AMS** mental status
SIRS Criteria (≥2 criteria for SIRS dx): **Temp** >38°C or <36°C, **HR** >90 bpm, **RR** >20, **WBC** >12k or <4K or >10% immature bands
sepsis: life-threatening organ dysfunction caused by a dysregulated host response to infection
[known/suspected infection + qSOFA ≥2 or change in SOFA ≥2]
septic shock: a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality
[sepsis + hypotension requiring vasopressors or lactate >2]

Tx:
fluid resuscitation: 30ml/kg IV bolus crystalloid fluid (NS, Lactated Ringers, plasmalyte) in first 6hrs
antimicrobials after culture (but don't delay)
vasopressors if hypotension refractory to IV fluids—norepi first-line, phenylephrine if tachy; can add another like epi, vasopressin if tachy
steroids: hydrocortisone 50mg IV q6h

Pain
causes: endotracheal tube, vascular access, procedures, underlying illness/injury, rolling/moving patient, immobile
consequences: suffering, increased stress response, chronic pain, PTSD< impaired wound healing

Numerical Pain Scale gold std Behavioral Pain Scale (**BPS**): goal 0 to 3 **CPOT**, in ICU: goal 0 to 2
Tx: opioids mainstay therapy: SE resp depression, decreased gastric motility, sedation, hypotension, GI upset
multimodal agents: APAP, epidurals, gabapentin, lidocaine, NSAIDs, ketamine
analgosedation: analgesia-based sedation regimen (pain treated first)
- allows intermittent dosing (preferred over CI to allow for drug clearance, prevention of accumu/over sedation)

oxycodone 3-6 hrs	continuous: n/a intermittent: 5-15 mg PO q4-6h	IR tablets can be crushed and put down NGT good enteral option
fentanyl 15-30 min	continuous: 50-200 mcg/hr intermittent: 25-100 mcg IVP q15-60min	accumulation in hepatic impairment, chest wall rigidity can use in true morphine allergy; tachyphylaxis occurs 200
hydromorphone 2-3 hrs	continuous: 0.2-2 mg/hr intermittent: 0.2-1 mg IVP q1-2h; 2-4mg PO q4-6h	accumulation in renal and hepatic impairment therapeutic option in morphine/fentanyl tolerance
morphine 3-5 hrs	continuous: 2-10 mg/hr intermittent: 2-4 mg IVP q1-2h; 10-20 mg PO q4-6h	accumulation renal impairment (typically not used in ICU) **histamine** release results in incr **hypotension**, itchiness, rash

APAP	PO: 325-1000 mg q4-6h IV: 650-1000 mg q4-6h	max 4000 mg/day reduce dose in hepatic impairment and elderly ≥65yo
gabapentin	PO: 100-300 mg TID, then 300-1200 mg TID	renal dose adjust SE drowsiness, dizziness, altered mental status
ketamine	bolus: 0.1-0.5 mg/kg infusion: 0.05-0.4 mg/kg/hr	hallucinations, hypertension analgesic + sedative
NSAIDs	ibuprofen: 200-800 mg PO q3-6h (2400 mg/d) ketorolac: 15-30 mg IV q6h (max 5 days)	avoid renal impairment and GI bleed contraindicated post-CABG

Agitation
causes: pain, lines/tubes, delirium, hypoxemia, sleep disturbances, withdrawal
consequences: increased cost, anxiety/PTSD, ventilator dyssynchrony, delirium, dislodging lines, harm

light sedation = RASS -2 to +1 critically ill, mechanically ventilated patients (+4 combative -5 unarousable)
deep sedation = RASS -4 to -5 ventilator dyssynchrony, NMBA paralytics, status epilepticus, intracranial pressure

Benzos Risks: ↑risk of delirium, ↑duration of mechanical ventilation, ↑ICU/hospital length of stay - not first-line sedation
Place: status epilepticus, alcohol withdrawal, deeper sedation (paralytics, vent dyssync), chronic med, hemodynamic instab

midazolam* 1-2 hrs	continuous: 1-10 mg/hr intermittent: 1-2 mg IVP q2h	accumulation in renal and hepatic impairment
lorazepam 6-8 hrs	continuous: 0.5-6 mg/hr intermittent: 1-2 mg IVP/PO q2h	propylene glycol toxicity (with CI and higher doses)
diazepam 2-8 hrs	continuous: n/a intermittent: 5-10 mg IVP/PO q6-8h	accumulation in renal and hepatic impairment quick onset, long acting (active metabolite)

dexmedetomidine	continuous: 0.2-1.5 mcg/kg/hr	bradycardia, hypotension, heart block light sedation/*no resp depression (no ventilation needed); *no delirium
ketamine	continuous: 0.5-2 mg/kg/hr	hallucinations, hypertension analgesic + sedative
propofol* quick onset short dur	continuous: 5-80 mcg/kg/min	hypotension, hyperTGs, resp depress, PRIS (prop-rel infusion syndrome) quick onset, short duration; lipid emulsion; must be ventilated

Implement non-pharmacologic interventions (bed positioning, day-night cycles, etc.)
Identify and correct underlying cause (pain, sleep disturbances, delirium, etc.)
- Treating pain first is most important when addressing agitation (analgosedation)
Target light sedation with lowest effective dosages & minimal benzodiazepines

Delirium
causes: pain, lines/tubes, immobility, ICU environment, sleep/wake disturbances, withdrawal, medications, procedures
medications associated with delirium: benzos, anticholinergics, corticosteroids
complications: incr length of stay/costs, incr agitation + longterm cognitive, incr mortality/duration mechanical ventilation

hyperactive: irritable, angry, restless, combative/violent, uncooperative, nightmares, inappropriate behavioral response (i.e. laughter)
hypoactive: lethargic, apathetic , depressed, anorexia, sleep pattern disturbances, altered speech/mental status, decr alertness/awareness

CAM-ICU (+ or -): Confusion Assessment Method-ICU
1. acute changes/fluctuating mental status 2. inattention (letters) 3. altered level of consciousness (RASS level) 4. disorganized thinking (questions)

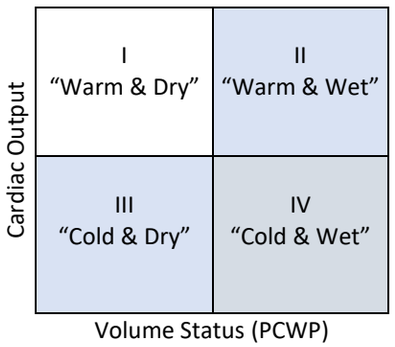
Nonpharm - treat underlying cause or disease - daily spontaneous awakening, breathing trials
- early mobilization -optimize senses (glasses, hearing aids, etc.)
- sleep hygiene - optimization of analgesic and sedative agents

	Dosing	QTc	Sedation	Antichol
haloperidol	2-5 mg IV q4h prn	moder	low	low
olanzapine	2.5-10 mg PO QD	low	moderate	moderate
quetiapine	12-5-100 mg PO BID	low	moderate	moderate
risperidone	0.25-1 mg PO/ODT BID	low	low	low

haloperidol ("There is no evidence that treatment with haloperidol reduces duration of delirum.")
Pharm no role in preventing/treating/reducing duration of delirium in patients with ***hypoactive*** delirium.
Prevention is key: nonpharmacologic interventions are first line
None have shown to reduce duration or prevent delirium; may be beneficial in **hyperactive** delirium to prevent harm

"Dry" Euvolemic

"Wet" (Congestion, ↑PCWP, volume overload)
- SOB, dyspnea on exertion, orthopnea, PND
- edema (peripheral/pulmonary), weight gain
- JVD, S3 gallop, pulmonary rales, pleural effusions
- elevated BNP/NT-ProBNP, congestive hepatopathy (↑INR LFTs)



"Warm" Adequate Perfusion

"Cold" (↓CO, low output, Hypoperfusion)
- fatigue, sx hypotension, cool extremities
- tachycardia, narrow pulse pressure
- early satiety, nausea, anorexia
- altered mental status, hyponatremia

Subset I "Warm & Dry"

goal: provide sx relief

maintain or increase: ACE/ARB, βBlocker, MRA

Subset II "Warm & Wet"

goal: remove fluids, net neg 1-2L/day, relieve dyspnea

IV furosemide (20mg IV = 40mg PO = T20PO = B1PO); 2-2.5x home dose

increase dose, increase frequency, change to continuous CI

add metolazone to overcome resistance

IV vasodilator nitroglycerin to relieve acute dyspnea

maintain: ACE/ARB, βBlocker, MRA

Subset III "Cold & Dry"

goal: ↑CO

IV inotrope if sx hypo or SBP <90 or end organ dysfunction

if above absent, consider IV vasodilator and change to inotrope

reduce or withdraw: ACE/ARB, βBlocker, MRA

Subset IV "Cold & Wet"

goal: ↑CO, remove fluid; "warm them up to dry them out"

IV inotrope + IV diuretics if sx hypo or SBP <90 or end organ dysfunction

if above absent: IV diuretics +/- IV vasodilator

withdraw: ACE/ARB, βBlocker, MRA

ßblocker: signs cardiogenic shock (low CO, end organ dysf); sx hypo/brady (SBP<90 HR<50); dose reduce before dc

ACE/ARB: cardiogenic shock, sx hypo (SBP<90), AKI, hyperkal

MRA: renal dysfunction, hyperkalemia

SGLT2: CrCl <25, DKA risk (inf, NPO, surgery)

ivabradine: cardiogenic shock, sx hypo/brady; new afib

F – Failure to comply with fluid/sodium restriction
A – Arrhythmia (atrial fibrillation), Apnea (sleep)
I – Ischemia (MI), infection
L – Levothyroxine – hyper/hypothyroidism
U – Uncontrolled HTN
R – Renal Failure
E – Embolus (pulmonary), Electrolyte disturbance
D – Drugs: associated with worsening HF

– NSAIDs – Corticosteroids – Thiazolidinediones – NonDHP CCBs
– Probenecid, Bile Acid Sequestrants – New initiation/titration of BB
– Anti-arrhythmics that are negative inotropes, decrease CO further (Class I - quinidine, propafenone; Class III - dronedarone)

Neurohormonal Model of HFrEF

underlying cardiomyopathy manifests as decreased cardiac output:

1. ↑activation of the sympathetic nervous system (baroreceptors) leading to downstream to ↑HR ↑contractility, ↑vasoconstriction
2. ↓renal perfusion in kidneys, ↑activation renin-angiotensin RAAS system further ↑vasoconstriction and ↑circulating blood volume (fluid retention)

Short term GOOD: maintain BP, ↑SV/CO

Long term BAD: congestive sx, ↑afterload, ventricular remodeling

Management of STEMI/NSTEMI/UA – MONAB

STEMI

Primary PCI within <120 min

1. UFH/LMWH/bival as adjunct to PCI
2. ASA325mg x1
3. LD ticag/prasugrel/clop
4. Stent (BMS/DES)
5. +/- GP IIb/IIIa inhibitor (inadequate LD antiplatelet)

→ continued CP? rescue PCI

Fibrinolytics if no PCI in 120 min, sx <12h of medical contact, STEMI

1. Fibrinolytic therapy started
2. ASA325mg x1
3. clopidogrel 75-300mg
4. UFH/LMWH/fondaparinux for 48hrs

UFH: bolus 60 u/kg (max 4000u), continuous 12 u/kg/hr for 48h or end of PCI

LMWH: 1 mg/kg sc q12h; (0.3 mg/kg IV given if <2 sc doses or last dose 8-12h before PCI) continue for 24-48h or end of PCI

ticagrelor 30min to 50% (max 88%); pre-cath (CI hx intracranial hemorrhage)

prasugrel 60min to 50% (max 79%); after stent (CI hx intracranial hemorrhage, hx TIA/stroke)

clopidogrel 2-6h to 50% (max 35%); d/c 5d prior to CABG

300mg: fibrinolytics <75yo; LD <24h from fibrinolytic; medically managed/non-stent

NSTEMI/UA

LD antiplatelet (use clopidogrel if TIA, hx stroke, intracranial hemorrhage)

ticagrelor before cath (prasugrel only after stent)

+/- GP IIb/IIIa inhibitor high risk

Fibrinolytics

Indication: sx ACS <12h medical contact

Contraindications

Hx hemorrhagic stroke; or other strokes within <1yr

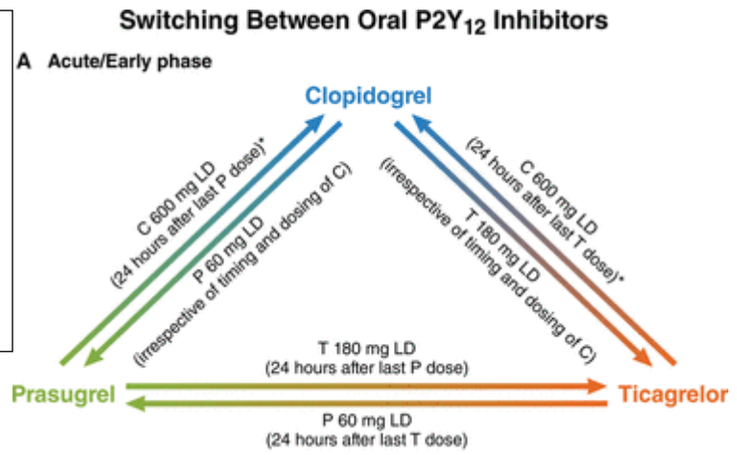
Hx intracranial hemorrhage

Active internal bleeding

Suspected aortic dissection

Precautions: Severe uncontrolled HTN (BP>180/100), Current use of anticoagulants in therapeutic dose (INR 2-3), Recent trauma (2-4 wk), head trauma prolonged CPR, major surgery(<3 wk), Noncompressible vascular punctures, Recent internal bleeding (2-4 wk), Active PUD, DOAC

Monitor: EKG, BP/HR, CBC (H/H Plts), bleed, mental



tPA Stroke alteplase 0.9 mg/kg IV (max 90mg); 10% IV bolus over 1min, infuse rest over 60min

Indication: sx onset <3h, BP <185/110

Contraindications

evidence of ICH
within last 3 months: ischemic stroke, severe head trauma, intracranial/intraspinal surgery
high clinical suspicion of SAH
GI malignancy or GIB within 21 days
coagulopathy (bleeding diathesis): platelet <100k, INR >1.7, aPTT >40s, or PT >15s
LMWH within 24hrs
NOAC within 48hrs with normal renal function [chart explaining half-life in renal impairment]
GPIIb/IIIa inhibitors (eptifibatide, tirofiban)

Monitor: STOP and obtain a CT if patient develops severe headache, acute hypertension, nausea, vomiting, neurologic

No Bleed: continue tPA Bleed: cryoprecipitate 10 units and TXA 1g or AMICAR 4-5g (to reverse tPA effect on plasminogen)

Monitor BP, neurologic function, bleeding: q15min during and after infusion x2hrs; q30min x6hrs, q60min x16hrs

Follow-up CT or MRI 24hrs after tPA administered

Stroke Computed Tomography (CT)**

Ischemic Stroke Secondary Prevention

Main: BP <140/90, statin, exercise, DM control, diet (Na 2.4g/day), sleep apnea, alcohol, smoking, OAC with Afib

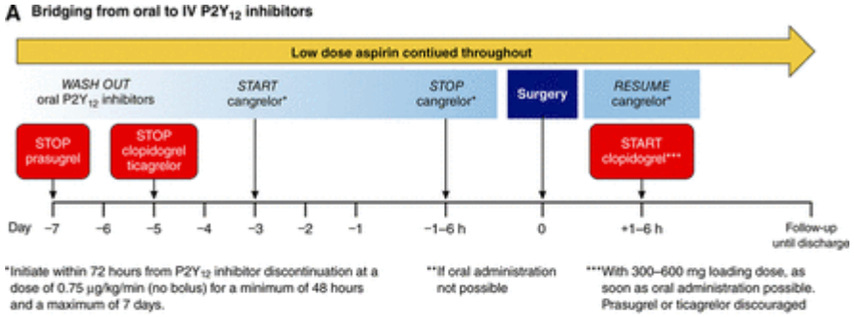
Statins: Secondary Prevention; Clinical ASCVD (post-stroke goal LDL <70)

Antiplatelets

TIA: no prev therapy = ASA + clopidogrel x21d (better than ASA alone); prev on ASA = add clopidogrel (lacks evidence)

AIS: ASA 50-325mg monotherapy; ASA 25mg + dipyridamole 200mg bid; clopidogrel 75mg qday (alternative to ASA/ASA-dipyridamole)

A Bridging from oral to IV $P2Y_{12}$ inhibitors

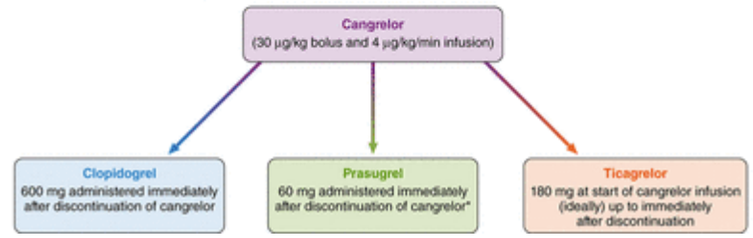


*Initiate within 72 hours from $P2Y_{12}$ inhibitor discontinuation at a dose of 0.75 µg/kg/min (no bolus) for a minimum of 48 hours and a maximum of 7 days.

**If oral administration not possible

***With 300–600 mg loading dose, as soon as oral administration possible. Prasugrel or ticagrelor discouraged

B Transition from IV to oral $P2Y_{12}$ inhibitors



*AIS: Risk Factors

NonModifiable: Age* (risk doubles each decade after 55yo); race (black 2x>white), FH stroke, hx stroke/TIA, gender (men>women)

Modifiable: HTN* (7x risk; BP <120/80 have half lifetime risk); DM (2x risk), CAD/CHF (2x risk), smoking (2x risk), others (estrogen, hypercoag, HA, diet, OSA, MHA, PFO)

Afib: 2019 AHA: For patients with AF and an elevated CHA_2DS_2-VASc of ≥2 in men and >3 in women, oral anticoagulants are recommended

AIS: BP goals received tPA <180/<105 no tPA no thrombectomy: <220/<120 no tPA + thrombectomy: SBP <160 hemorrhagic conversion: SBP <160

AIS: BP treatment labetalol 10-20mg **IVP** (double dose if repeated, max 300mg at once) hydralazine 10-20mg **IVP** nicardipine initial 5mg/hr **IV gtt**, titrated up by 2.5mg/hr q5min (max 15mg/hr) clevidipine initiate 4mg/hr **IV gtt**, titrate by doubling dose q2-5min (max 32mg/hr or 1L/24hrs--risk of TGs)

Other therapies O2 >94%, Temp <38C, euvolemia, Na 135-145, BG 140-180 ASA81 within 24-48h

BP control (reduce 15% during first 24h; <140/90 once neuro stable) VTE prophylaxis after 24h

	Dose	Onset	Duration	ADE
Continuous Infusion				
clevidipine	4-32 mg/hr	2-4 min	5-15 min	HA, N, Afib, insomnia (max 1000ml/24h)
nicardipine	5-15mg/hr	5-10	15-30->240	Tachycardia, HA, flushing, local phlebitis
nitroglycerin	5-100mcg/min	2-5	5-10	HA, V, methemoglobinemia, tolerance
labetalol	0.5-2mg/min	5-10	180-360	V, scalp tingle, bronchoconstrict, OH dizzy, heart block
Intravenous Bolus				
hydralazine	10-20mg	10-20	60-240	Tachycardia, HA, N, flushing, aggravation of angina
labetalol	10-20mg	5-10	180-360	V, scalp tingle, bronchoconstrict, OH dizzy, heart block

ICH Risk factors ***SBP goal <160 mmHg for most ICH**

Nonmodifiable: >55yo, Male, AA/Japanese, cerebral amyloid angiopathy (CAA)

Modifiable: HTN, alcohol, smoking, sympathomimetic use, anticoag use

*Severity scale – ICH Score 0-6 points

GCS (3-4 = 2 5-12 = 1 13-15: 0)
Age (≥80=1)
Bleed (infratentorial=1): pons, cerebellum
ICH vol (≥30cc=1)
intraventricular blood (yes=1)

30-day mortality: 0-0%, 1-13%, 2-26%, 3-72%, 4-97%, 5-100%, 6-100%

SAH BP Prior to securing aneurysm goal is SBP <140; utilize same agents as you would for ICH

After securing aneurysm goal is SBP <220 (after no more bleeding risk, let BP ride up due to risk of vasospasm; let BP rise so adequate distal perfusion)

SAH Vasospasm management

Complication: Vasospasm is consistent vasoconstriction of the artery secondary to blood surrounding the vessel

• Most likely to occur 4-21 days after ictus • Vasospasm leads to delayed cerebral ischemia (DCI)

***nimodipine** (Nimotop, Nymalize); lipid-soluble CCB; does not reduce vasospasm incidence; however, it significantly reduced DCI by 34% (improves morbidity)

Dose: 60mg PO q4h x21 days BBW: enteral administration only

ADE: hypotension; may reduce to 30mg PO q2h

***Vitamin K** (phytonadione) 1st target

Dose: 10mg IV at 1mg/min (**know this dose)

MoA: normalizes INR by providing necessary substrate to synthesize factors II VII IX X

Limitations: slower reversal; reduction of INR to <1.4 may take up to 24hrs

Advantage: vitamin K provides sustained and durable reversal of warfarin activity and is recommended to give in conjunction with other reversal agents

***Kcentra** (prothrombin complex concentrate **PCC**; 4-factor, unactivated) 2nd target

Dose: INR <4: 25 units/kg INR 4-6: 35 units/kg INR >6: 50 units/kg (max weight 100kg)

MoA: replaces factors II IX X and unactivated VII

Limitation: the most serious adverse reaction is the risk of thrombotic events including stroke, DVT, PE

Advantage: fast reconstitution and administration, low volume compared to FFP, **rapid** INR reversal

Expected compensation

Disorder	**Compensation**	
Metabolic Acidosis	Winter's formula: PaCO2 = 1.5(HCO3) + 8 ± 2	
	For each change in PaCO2 (relative to 40 mmHg)	**Change in HCO3**
Respiratory Acidosis		
Acute	↑10 mmHg	↑1 mEq/L
Chronic	↑10 mmHg	↑4 mEq/L
Respiratory Alkalosis		
Acute	↓10 mmHg	↓2 mEq/L
Chronic	↓10 mmHg	↓5 mEq/L

ROME – metabolic = equal direction

ROME – respiratory = opposite direction

	pH	PaCO2	HCO3
Respiratory Acidosis	↓	↑	↑
Respiratory Alkalosis	↑	↓	↓
Metabolic Acidosis	↓	↓	↓
Metabolic Alkalosis	↑	↑	↑

Respiratory Acidosis Etiologies

*COPD, central resp depress (sedation), airway obstruction, ARDS, pneumothorax, thoracic cage injury, rate too low on ventil

Metabolic Acidosis Etiologies normal anion gap <12

Anion gap MA [Na – (Cl + HCO3)] MUDPLIES: Methanol, Uremia, Diabetic ketoacidosis, Propylene glycol, Isoniazid/Iron, Lactic acid, Ethylene glycol, Salicylates

Nonanion gap MA (ACCRUED): Aldosterone inh, Compensation, Carbonic anhydr inh, Renal tubular acidosis, Ureteral diversion, Extra alimentation TPN, Diarrhea

Metabolic Alkalosis Etiologies

Chloride responsive (U_{Cl} <10): vomiting, nasogastric suctioning, previous diuretic use

*overall depletion of chloride

Chloride unresponsive (U_{Cl} >20): current use of diuretics, refeeding syndrome (hypokalemia), excess mineralocorticoid

*overall focused on hypokalemia that causes reabsorption of bicarb in proximal tubule

Compensation

Respiratory: Response observed within minutes of acid-base derangement; Full compensation seen within hours

Renal (metabolic): Initial response occurs within 6-12 hours after derangement; Full compensation may take 3-5 days

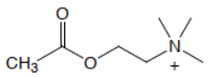
Acid-Base

pH <7.35 ↑CO2 Respiratory Acidosis
pH <7.35 ↓HCO3 Metabolic Acidosis
pH 7.35-7.45 Normal, Compensated, or Mixed
pH >7.45 ↓CO2 Respiratory Alkalosis
pH >7.45 ↑HCO3 Metabolic Alkalosis

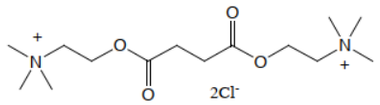
Physiological Values

Parameter	**Normal**	**Where can be found?**
pH	7.35-7.45	arterial blood gas
PaCO2	35-45 mmHg	arterial blood gas
HCO3	22-26 mEq/L	chemistry/arterial blood gas
Na	135-145 mEq/L	chemistry
Cl	96-106 mEq/L	chemistry
lactate	<2 mEq/L	chemistry

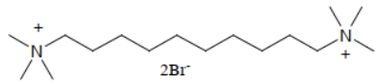
d-Tubo**cur**arine chloride: neuromuscular blocking effect has containing 2 positively charged ammonium ions separated by 10 – 12 carbons post-synaptic side of neuron
Each Acetylcholine receptor has 2 receptive sites and activation of the receptor requires binding to both of them.
Each receptor site is located at one of the two α subunits of the receptor.



Acetylcholine



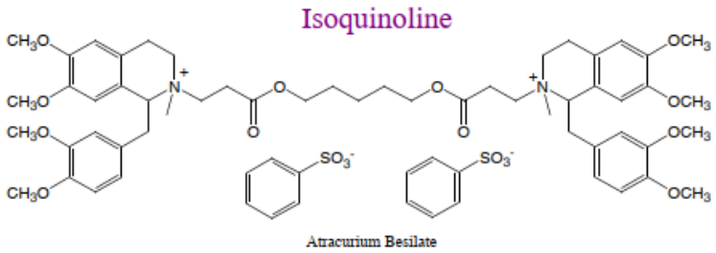
Succinylcholine



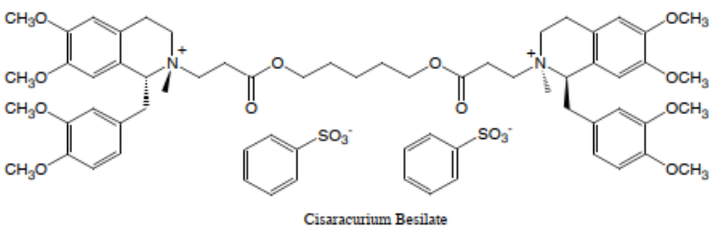
Decamethonium bromide

Depolarizing NMBA (Succinylcholine)
Depolarizing work by depolarizing plasma membrane of muscle fiber, similar to acetylcholine
Bind to acetylcholine binding site and open sodium channel
More resistant to degradation by acetylcholinesterase, thus more persistently depolarize muscle fibers
Constant depolarization and triggering of receptors keeps endplate resistant to activation by ACh (**densensitization**)
Phase I: depolarizing phase: membrane depolarizes, resulting in intiatl discharge that produces transient fasciulations followed by flaccid paralysis
Phase II: desensitizing phase: membrane repolarizes, but receptor densensitized to effect of ACh

Nondepolarizing NMBA
MoA: competitive antagonists by competitively block the binding of ACh to its nicotinic receptors and block muscle contraction
- neuromuscular blockade can occur even if only one alpha subunit blocked; since both subunits need to be occupied by ACh for receptor to work

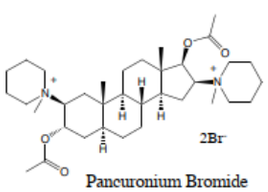


Atracurium Besilate

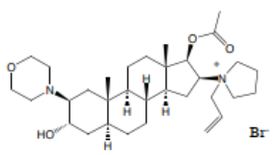


Cisaracurium Besilate

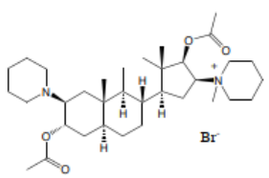
isoquinoline scaffold (atracurium, cisatracurium): quarternary nitrogen, permanently positively charged
atracurium (isoquinoline): ester hydrolysis x2, Hoffman elimination (nonenzymatic)
once you hydrolyze the first one, metabolite no longer active
steroidal (pancuronium, rocuronium, vecuronium): quarternary and tertiary amines
longer half-life, due to metabolism and metabolite still active



Pancuronium Bromide



Rocuronium Bromide



Vecuronium Bromide

Suggaamadex: selective relaxant binding agent (SRBA)
for reversal of neuromuscular blockade for rocuronium, vecuronium (not pancuronium due to both being quarternary charged amines)
γ-cyclodextrin with lipophilic core and hydrophilic periphery; negatively charged; bind to NMBA ionic intx
rocuronium bound within sugammadex's lipophilic core, is rendered unavailable to bind to ACh receptor at NMJ

Reversible Causes
- Hypoxia
- Hypovolemia
- Hydrogen ion
- Hypo/Hyperkalemia
- Hypothermia
- Toxin
- Tamponade (cardiac)
- Tension Pneumothorax
- Thrombosis (pulmonary)
- Thrombosis (cardiac)

ACLS: Asystole/PEA
- Non-shockable rhythm
- Pulse and rhythm check every 2 minutes
- Medications
  - Epinephrine 1mg every 3-5 minutes
  - Vasopressin 40 units (alternative to second epinephrine dose)
- Treat underlying cause!!

ACLS: VT/VF
- Shockable rhythm
- Pulse and rhythm check every 2 minutes
- Medications
  - Epinephrine 1mg every 3-5 minutes
  - Vasopressin 40 units (alternative to second epinephrine dose)
  - Amiodarone: First dose: 300mg, Second dose: 150mg
  - Lidocaine: First dose 1-1.5mg/kg, Second dose 0.5-0.75mg/kg
- Treat underlying cause!!

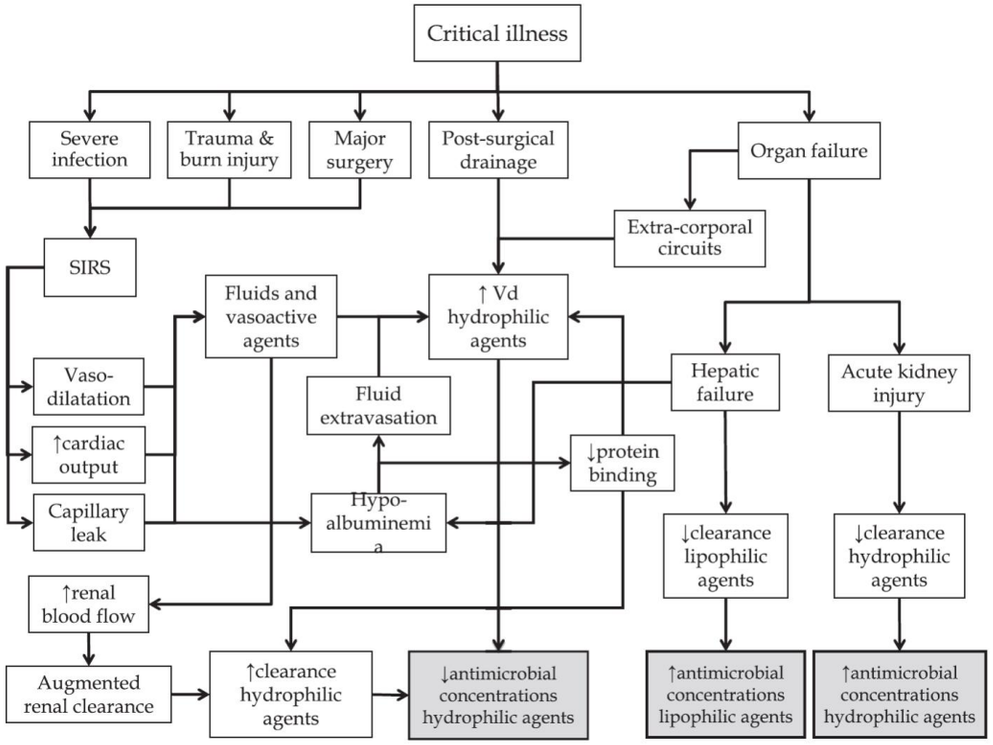
Hyperkalemia		
calcium gluconate	3g IV	stabilizes myocardium
regular insulin	10u IV	shifts K intracellular
albuterol	10-20mg inh	shifts K intracellular
sodium bicarbonate	50mEq IV	shifts K intracellular
furosemide	20mg IV	inhibits Na-K-Cl transporter; **removes K**
sodium polystyrene sulfonate	30-45g PO	Na-K exchanger; **removes K** (4-6h)

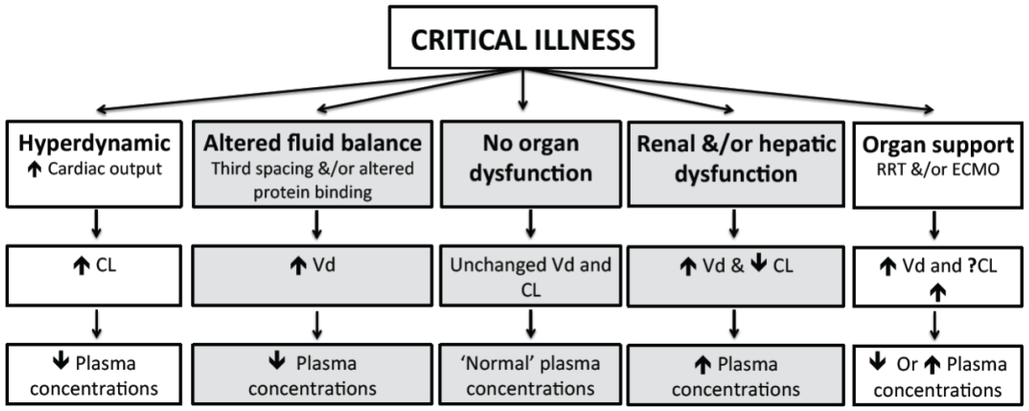
Rapid Sequence Intubation (RSI)
- Utilized to facilitate intubation in patients with respiratory compromise
- Utilization of pre-specified sequential steps including sedation followed by paralyzing agent
  - **SEDATION ALWAYS GOES FIRST!**
- Used to prevent aspiration and reduce sympathetic effects
- Optimal medication selection is imperative to reduce side effects

RIS Medications

	Onset	Duration	ADEs
Sedatives			
etomidate (GABA-A)	10-20 sec	4-10 min	myoclonus, adrenal suppression
ketamine (NMDA antag)	1-2 min	5-10 min	emergence phenomena, increased sympathetic response
propofol (GABA-A)	1-2 min	5-10 min	hypotension
midazolam (GABA-A)	3-5 min	1-2 hr	hypotension (less than propofol)
Paralytics			
succinylcholine (depolarizing)	15-30 sec	5-10 min	hyperkalemia
rocuronium (nondepol)	1-2 min	30-45 min	prolonged paralysis in hepatic failure
vecuronium (nondepol)	2-3 min	45-60 min	prolonged paralysis in hepatic/renal failure

*ASA81 Takeaway: ASA no role in primary prevention
USPS Task Force: men no reduction in stroke (reduces MIs); women 55-79yo recommended for stroke prevention
AHA 2014: ASA for CV prevention reasonable with 10yr risk >10%
ASCEND: controlled DM (A1c <8) ASA reduces serious vascular events but increased major bleeding
ASPREE: >70yo ASA did not reduce disability-free survival but associated with higher major hemorrhage and all-cause mortality
ARRIVE: moderate-risk (10yr CV risk 10-20%), ASA did not reduce CV events but doubled GI bleeding





PK Changes to Critical Illness

↑CO Cardiac Output = ↑CL = ↓Cp
Leaky capillaries or altered PPB = ↑Vd = ↓Cp
Normal organ function = unchanged Vd = normal Cp
End organ dysfunction (renal/hepatic) = ↓CL = ↑Cp

Absorption Highlights

- When changing medications from IV to PO it is important to look up the IV to PO conversion
- Enteral feeds can interact with medications administered via the enteral route:
  - Enteral feeds can increase the pH of the stomach reducing the absorption of drugs that need an acidic environment for absorption
  - Tube feed ingredients can directly bind to some drugs causing decreased absorption (i.e., phenytoin, ciprofloxacin)
- To overcome drug and nutrient interactions enteral feeds can be held 1 hour before and 2 hours after drug administration
  - To avoid underfeeding, tube feed rates should be adjusted so patients can receive the total daily caloric goal

Context Sensitive Half Life
Accumulation of lipophilic drugs in the deep adipose compartment causes longer duration of action than can be explained by the medications half lives; (context = infusion duration)

Distribution Highlights

- In critically ill patients with hypoalbuminemia, drugs like phenytoin, valproic acid, and ceftriaxone that are highly protein bound will have a greater free fraction of free drug, leading to increased pharmacologic effects even if the total drug level remains unchanged
- When possible, in the critically ill, drugs that are highly protein bound should be monitored by free levels instead of total levels • Consider increased dosing

Transformation of parent compounds into metabolites: Liver (primary site), GI tract, Kidneys, Lungs, Brain
Several alterations in critical illness: Hepatic enzyme activity, Protein binding, Hepatic blood flow
Metabolism: Hepatic Blood Flow
Increased hepatic blood flow and metabolism: Early sepsis (increased cardiac output), Vasodilator use (i.e., nitroprusside), Inotropes
Decreased hepatic blood flow and metabolism: Late sepsis (decreased cardiac output), Hypovolemic shock, Myocardial infarction and acute heart failure, Vasopressor use
Metabolism: Hepatic Enzyme Activity
Many critically ill states will results in an increased hepatic metabolism: Traumatic brain injury, Burn patients
Decreased activity of CYP450 enzymes occur during stress response: Prolonged effects of parent compounds, Reduced effects of prodrugs, Increase in toxic metabolites
Medications eliminated renally most impacted: Proportional to glomerular filtration rate or CrCl
Consider true CrCl collection/measurement: Challenging to assess due to fluctuations and fluid shifts; Consider true CrCl as opposed to calculations in some populations
Altered elimination in critically ill patients: Reduced clearance (kidney injury or failure); Augmented clearance
Augmented Renal Clearance
Hyperdynamic = ↑CO = ↑renal blood flow = ↑GFR
CrCl >130 ml/min (20-65% of critically ill); physiological mechanism poorly delineated; Associated with subtherapeutic concentrations of renally-eliminated drugs
Effects of PK Alterations of Cp
PK/PD Alterations: CRRT
Vd should be primary PK consideration for initial dosing: Critical illness, sepsis, AKI, CHF/reduced EF all potential factors
Remaining CLR and CLNR dictate maintenance dosing
CRRT clearance affected by protein binding, absorption, and CRRT settings
CRRT clearance will vary based on mode: CVVH – convective removal; CVVHD – diffusion of solute across filter membrane down a conc gradient; CVVHDF – combines both properties
Decreased CRRT clearance if: Large molecule, Highly protein bound, Vd > 1.5 L/kg
Factors Affecting Elimination
Clinical Implications
Antimicrobial success dependent on early initiation, appropriate selection, and dosing to attain PK/PD target
Negative impact on therapeutic level attainment
Affects renally cleared drugs, including B-lactams, vancomycin, & AG
Enhanced drug clearance will lead to shorter half-life, lower Cmax, and smaller AUC
May compromise drug efficacy and promote drug resistance

Elimination Highlights

- Commonly critically ill patients combat multi-organ failure as a complication of their critical illness
- Patients should be monitored closely for increased or decreased renal function
- Consider therapeutic drug monitoring via drug levels or therapeutic effect for renally-eliminated medications
- Medications that are cleared primarily by the kidneys should be evaluated for following: Dose, Interval, Therapeutic drug monitoring (drug levels or associated labs i.e. anti-Xa)

Intro

PN indications: inaccessible GI tract, short bowel syndrome (<200cm), intestinal obstruction/ileus, high output fistulas or ileostomies (>500 ml/day)
25-30 kcal/kg of nutrition per day maintenance **IV fluid 30-40ml/kg/day**
Total body water (TBW) is calculated based on **60% of ABW**.
Gastric electrolyte loss: **Na and Cl**.
ADH is released in response to **decreased** circulating volumes.
Hyperkalemia: calcium gluconate 1g IV over 3-5min stabilize myocardium
Correct electrolytes before PN

Nutritional Support

nutrition screening 24hrs; evaluate GI tract to determine type of nutrition
Dx: (2 of) energy intake, weight loss, body fat loss, muscle mass wasting, fluid/edema, handgrip strength
Spectrum: total enteral tube feedings = shortterm (NG, ND, NJ); longterm (PEG, PEJ) > peripheral PN > total PN

Malnutrition

Starvation-related: without inflammation; anorexia, homeless
Chronic disease-related: inflammation chronic mild-mod; RA/Crohns
Acute disease/injury-related: inflammation acute severe; sepsis, trauma

Enteral Products

"If the gut works, use it!" **20-30 kcal/kg day** start at 20ml/hr titrate q2-4h; glucose infusion rate should be <4-5 mg/kg/min
initiated when inadequate oral intake is expected for **7-14 days**.
- liquid preferred; enteral contain 70-84% water; hypertonic if fluid restrict
Hydrolyzed EN indicated **impaired GI digestion or absorption**.
Renal: lower protein K Mg P Hepatic: more BCAA less AAA DM: complex less CHO COPD: less CHO, more fat ARDS: mod lipid

Parenteral Products

overarching indication for PN is a **non-accessible GI tract**; once PN is started, at least **7 days** for nutritional benefit
Indications for PN support: • Inaccessible GI • Short bowel syndrome • Intestinal obstruction • High output fistulas (>500 ml/day) • Ileus

Calories = 20-30 kcal/kg/d (~28 kcal/kg/d) **Fluid** = 30-40 ml/kg/d
ILE = 1 g/kg/d (~20-30% of cals) = **[10 kcal/g]** **CHO** = 60-75% cals = **[3.4 kcal/g]** **Protein** = 1-1.5 g/kg/d (~10-15% of cals) = **[4 kcal/g]**

Na (tonicity, fluid balance) = 1-2 mEq/kg K (muscle cardiac function) = 1-2 mEq/kg Cl/acetate (extracell acid-base) = maintain acid-base balance
Phos (energy ATP) = 20-40 mmol Ca (bone, cardiac function) = 10-15 mEq Mg (cardiac, GI function) = 8-20 mEq

Hyperglycemia most common complication of PN (BG goal 100-180); dextrose max 100g

Hypoglycemia (<60)
- Avoid rebound hypoglycemia *Administer 10% dextrose at 50 ml/hr x 2 hr OR Taper PN at 50 ml/hr x 2 hr before discontinuing

Refeeding syndrome: a complication caused by rapid nutritional repletion in a malnourished patient which drives the following electrolytes intracellularly causing ↓K Ca Phos. If left untreated, refeeding syndrome could manifest in cardio-pulmonary collapse. within 2-3d, lasts 1-2wk
Early recognition is KEY; *Must limit sources of dextrose and reduce feeding rate – go "low and slow"
*Replace electrolytes aggressively *Increase nutrition to goal gradually

T. bili is > 7, hold **trace elements** (d/t Mn accum, neurotox)
*Thiamine deficiency (Vitamin B1): *At risk patients: Alcoholic, Post bariatric surgery, Refeeding syndrome
*Wet beriberi – lactic acidosis, cardiac failure, Wernicke's Korsacoff syndrome Dry beriberi – weakness, paresthesias
*additional Zn added in diarrheal conditions or high output fistula (5-10mg) d/t wound healing
*additional Se added for cardiomyopathy/woundheal (40-60mcg)

Efficacy of PN

progress towards goal: how long to achieve goal rate, tolerating well, any complications, signs of improvement/wound healing?
24h urine-Nitrogen Balance (NB): NB = intake (NI) – ((UUN x 1.2) + 1) ***goal = +1-4g/day** NI = g AA/d divided by 6.06 UUN = urine urea nitrogen
body composition: bioelectrical impedance (body fat, lean muscle, water); hand grip test; QoL

	ADH levels	Serum Na	Plasma Osmolarity
SIADH	HIGH	LOW	LOW
Diabetes Insipius	LOW	HIGH	HIGH

Na content	Water content	Serum Na (mEQ/L)
Normal	Normal	135-144
Normal	Increased	<135
Normal	Decreased	>145
Decreased	Normal	<135
Decreased	Decreased	<135, 135-144, >145
Decreased	Increased	<135 or severe at <130
Increased	Normal	>145
Increased	Increased	<135, 135-144, >145
Increased	Decreased	>145

	Starvation	Trauma/Disease
Metabolic rate	↓	↑↑
Body fuel	conserved	wasted
Body protein	conserved	wasted
Urinary nitrogen	↓	↑↑
Weight loss	slow	rapid

	Normal	Parenteral Req.	Serious: ↓	Serious: ↑
Na	135-145	1-2 mEq/kg	<130	>150
K	3.5-5.0	1-2 mEq/kg	<3	>5
Cl	98-108	maintain acid-base		
HCO3	23-30	maintain acid-base	<18 (CO2)	>30 (CO2)
Ca	9-10.5	8-20 mEq/day	<1.2	>2.5
Mg	1.7-2.4	10-15 mEq/day	<2	>5.5
P	2.5-4.5	20-40 mmol/day	<4.4 ionized	>10 total

(CO2): evaluate blood gas for actual serum pH < 7.2 severe acidemia; > 7.6 severe alkalemia

Monitoring PN	Initiation	Critically Ill	Stable
Electrolytes	daily x 3	daily	1-2x/wk
Glucose (serum) Glucose (POC)	daily x 3 q6h	daily q6h	1-2x/wk
Wt, I/O	daily	daily	daily
Serum TG	day 1	weekly	weekly
Liver enzymes	day 1	weekly	weekly
CBC w diff		weekly	weekly
Nitrogen balance		weekly	weekly

Macronutrients

Intravenous Lipid Emulsion (ILE) = Fat **[10 kcal/g]**
Dextrose = Carbohydrate (CHO) **[3.4 kcal/g]**
Amino Acid = Protein **[4 kcal/g]**

Glaucoma

Pathophys: disease caused by increase in intraocular pressure (IOP) from excess aqueous humor IOP >24mmHg considered IO-HTN, needs tx
↑aqueous humor = ↑IOP = leads to blindness via apoptosis of retinal ganglion cells, increased pressure of optic nerve, decreased signaling to thalamus

Risk factors: age >50yo, race (AA), FH, DM
Open-angle: *resistance* of trabecular meshwork, ↓drainage, ↑IOP (white, AA)
Closed-angle: *blockage* of trabecular meshwork, ↓drainage, ↑IOP (Asian)

Tx goals: ↓IOP, ↓production and ↑clearance of aqueous humor
Open-angle: prostaglandin → alt prostaglandin → add diff drops → surgical (laser trabeculopathy)
Closed-angle:
acute: carbonic anhydrase inhibitors +/- beta-blocker +/- alpha-2 agonist; adjunctive hyperosmotic (glycerin, mannitol); surgical
chronic: prostaglandin +/- beta-blocker +/- alpha-2 agonist; adjunctive carbonic anhydrase inhibitor; surgical

2) Gently grasp lower outer eyelid below lashes. Pull away from eye to create a pouch.
3) Place dropper over eye. Place ointment tube over eye.
4) Look up before applying. Place ¼ to ½ inch strip of ointment inside lower eyelid using sweeping motion. Avoid touching tip to tissue surface.
5) Release lid and gently close eye. Minimize blinking or squeezing of eyelid.

Macular Degeneration
nonexudative ("dry"); dry is 90% of cases; gradual, progressive vision loss > often starts with near vision issues
exudative ("wet"); majority of high severity cases; can be rapid or gradual vision loss

dry: Breakdown of the retinal pigment epithelium (RPE) > drusen deposits in macula;
Ultimate loss of function of the overlying photoreceptors; No cure or reversibility
wet: Neovascularization in the choroid resulting in serous/hemorrhagic leakage; Eventual elevation of the RPE or neurosensory retina leading to drusen deposits
Potential cessation with VEGF inhibitors (bevacizumab, ranbizumab, aflibercept)

Risk factors: age >65yo, female, White, genetic predisposition, smoking
AREDS recommended by AOA if Mild-moderate AMD in one or both eyes OR Advanced AMD in only one eye
- smoker use AREDS2 (beta-carotene increased risk of lung cancer)

Bacterial Conjunctivitis
Neisseria gonorr (STD), maternal-neonate (gonococ/chlamydial), S aureus, Haemo spp, Strep pneumo, Moraxella

Drug-Induced Dry Eye
anticholinergics, Postmeno HRT, benzos, SSRI SNRI TCA, antipsychotics (quetiapine), diuretics, beta-blockers, histamine antag (DPH, lorat, ranit), oral contraceptives, decongestants (pseudo, phenylephrine), levodopa

prostaglandins 25-35% latanoprost (fridge) bimatoprost (more effective)	MoA: Mimic endogenous prostaglandins; Improve uveoscleral pathway via stimulation of collagenases and matrix metalloproteinases Effect: ↑uveoscleral outflow and ↑removal of aq humor	ADEs: Better tolerated than other classes; Altered iris pigmentation (irreversible) Hypertrichosis (reversible) Hyperpigmentation of lids/lashes (reversible) Caution: Risk of uveitis in patients with ocular inflammatory conditions
beta-blockers 20-30% timolol levobun metopran carteo betaxolol (s)	MoA: Block β-adrenergic receptors in ciliary body Effect: ↓production of aqueous humor by ciliary body	ADEs: Local: dry eyes, blepharitis, blurred vision (temporary) Systemic: decreased heart rate, reduced blood pressure, negative inotropic effects, bronchospasm Caution: asthma, sinus bradycardia, CHF congestive heart failure, DM diabetes, and/or myasthenia gravis timolol gel qday, lower systemic betaxolol selective β1, less systemic, more stinging carteolol intrinsic sympathomimetic
alpha-2 agonists 18-27% apraclonidine brimonidine (1st-line)	MoA: Enhance α-2 adrenergic receptors in ciliary body Effect: ↓production of aqueous humor by ciliary body brimonidine also ↑ uveoscleral outflow	ADEs: Apraclonidine may cause an allergic-type reaction in roughly 30% of patients: Lip edema, eye discomfort, foreign-object sensation, itching, hyperemia Brimonidine may cause systemic effects: Dizziness, fatigue, somnolence, dry mouth Caution: CVD, cerebrovascular disease, renal insufficiency, DM Brimonidine CI in infants (hypotensive reactions, apneic spells)
carbonic anhydrase inh 15-26% dorzolamide brinzolamide	MoA: Inhibit secretion of Na and bicarb from ciliary body to the aq humor Effect: ↓production of aqueous humor by ciliary body	ADEs: Typically well tolerated, especially compared to systemic CAIs; SE are mild and transient: blurry vision, stinging dorzolamide (solution) brinzolamide (susp, more blurry vision, less stinging)
cholinergic agonist 20-30% pilocarpine carbachol	MoA: Enhance parasympathetic activity in ciliary body Effect: ↑outflow of aqueous humor via trabecular network	ADEs: mostly with pilocarpine: Miosis, Frontal headache, Brow ache, Periorbital pain, Eyelid twitching pilo (parasympathomimetic agent of choice, darker eyes higher doses) carbachol (longer duration, weak cholinesterase inh)

↑aqueous outflow (prostaglandins, alpha adrenergic agonists, cholinergic agonists, rho kinase inhibitor)
↓aqueous production (alpha adrenergic agonists, beta blockers, carbonic anhydrase inhibitors)

Table 2: Potentially Inappropriate Medication Use in Older Adults

Nitrofurantoin
Potential for pulmonary toxicity, hepatoxicity, and peripheral neuropathy, especially with long-term use; safer alternatives available
-Avoid in individuals with creatinine clearance <30 mL/min or for long-term suppression

Peripheral alpha-1 blockers for treatment of hypertension: Doxazosin, Prazosin, Terazosin
High risk of orthostatic hypotension and associated harms, especially in older adults; not recommended as routine treatment for hypertension; alternative agents have superior risk/benefit profile
-Avoid use as an antihypertensive

Central alpha-agonists: Clonidine for first-line treatment of hypertension; Other CNS alpha-agonists: Guanabenz, Guanfacine, Methyldopa, Reserpine (>0.1 mg)
High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension
-Avoid as first-line antihypertensive; Avoid other CNS alpha-agonists as listed

Digoxin for first-line treatment of atrial fibrillation or of heart failure
Use in atrial fibrillation: should not be used as a first-line agent in Afib, because there are safer and more effective alternatives for rate control supported by high-quality evidence.
Use in heart failure: evidence for benefits and harms of digoxin is conflicting and of lower quality; most but not all of the evidence concerns use in HFrEF. There is strong evidence for other agents as first-line therapy to reduce hospitalizations and mortality in adults with HFrEF. In heart failure, higher dosages are not associated with additional benefit and may increase risk of toxicity. Decreased renal clearance of digoxin may lead to increased risk of toxic effects; further dose reduction may be necessary in those with stage 4 or 5 chronic kidney disease.
-Avoid this rate control agent as first-line therapy for atrial fibrillation
-Avoid as first-line therapy for heart failure If used for atrial fibrillation or heart failure, avoid dosages >0.125 mg/day

Antidepressants, alone or in combination: Amitriptyline, Clomipramine, Desipramine, Doxepin >6 mg/day, Imipramine, Nortriptyline, Paroxetine, Trimipramine
Highly anticholinergic, sedating, and cause orthostatic hypotension; safety profile of low-dose doxepin (≤6 mg/day) comparable to that of placebo
-Avoid

Antipsychotics, first (conventional) and second (atypical) generation
Increased risk of cerebrovascular accident (stroke) and greater rate of cognitive decline and mortality in persons with dementia
Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (eg, behavioral interventions) have failed or are not possible and the older adult is threatening substantial harm to self or others
-Avoid, except in schizophrenia or bipolar disorder, or for short-term use as antiemetic during chemotherapy

Benzodiazepines, Short and intermediate acting: Alprazolam, Estazolam, Lorazepam, Oxazepam, Temazepam, Triazolam
Benzodiazepines, Long acting: Chlordiazepoxide (alone or in combo with amitriptyline), Clonazepam, Clorazepate, Diazepam, Flurazepam, Quazepam -Avoid
Older adults have increased sensitivity to benzos and decreased metabolism of long-acting agents; in general, all benoz increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults May be appropriate for seizure disorders, rapid eye movement sleep behavior disorder, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and periprocedural anesthesia

Meprobamate -Avoid
High rate of physical dependence; sedating

Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics (ie, "Z-drugs"): Eszopiclone, Zaleplon, Zolpidem - Avoid
Nonbenzodiazepine benzodiazepine receptor agonist hypnotics (ie, Z drugs) have adverse events similar to those of benzodiazepines in older adults (eg, delirium, falls, fractures); increased emergency room visits/hospitalizations; motor vehicle crashes; minimal improvement in sleep latency and duration

Sulfonylureas, long acting: Chlorpropamide, Glimepiride, Glyburide - Avoid
Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes SIADH
Glimepiride and Glyburide: higher risk of severe prolonged hypoglycemia in older adults

Metoclopramide -Avoid, unless for gastroparesis with duration of use not to exceed 12 weeks except in rare cases
Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults and with prolonged exposure

Mineral oil, given orally -Avoid
Potential for aspiration and adverse effects; safer alternatives available

Proton-pump inhibitors
Risk of Clostridium difficile infection and bone loss and fractures
-Avoid scheduled use for >8 weeks unless for high-risk patients (eg, oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (eg, because of failure of drug discontinuation trial or H2-receptor antagonists)

Skeletal muscle relaxants: Carisoprodol, Cyclobenzaprine, Methocarbamol, Chlorzoxazone, Metaxalone, Orphenadrine - Avoid
Most muscle relaxants poorly tolerated by older adults because some have anticholinergic adverse effects, sedation, increased risk of fractures; effectiveness at dosages tolerated by older adults questionable

Table 3: Drug–Disease or Drug–Syndrome Interactions That May Exacerbate the Disease or Syndrome

Syncope

AChEIs, Nonselective peripheral alpha-1 blockers (ie, doxazosin, prazosin, terazosin), Tertiary TCAs, Antipsychotics: Chlorpromazine, Thioridazine, Olanzapine -Avoid
AChEIs cause bradycardia and should be avoided in older adults whose syncope may be due to bradycardia.
Nonselective alpha-1 blockers cause orthostatic BP changes and should be avoided in older adults whose syncope may be due to orthostatic hypotension.
Tertiary TCAs and the antipsychotics listed increase the risk of orthostatic hypotension or bradycardia.

History of falls or fractures

Antiepileptics, Antipsychotics, Benzos, Z-hypnotics (Eszopiclone, Zaleplon, Zolpidem), Antidepressants (TCAs, SSRIs, SNRIs), Opioids
May cause ataxia, impaired psychomotor function, syncope, additional falls; shorter-acting benzodiazepines are not safer than long-acting ones. If one of the drugs must be used, consider reducing use of other CNS-active medications that increase risk of falls and fractures (ie, antiepileptics, opioid-receptor agonists, antipsychotics, antidepressants, z-hypnotics , other sedatives/hypnotics) and implement other strategies to reduce fall risk. Data for antidepressants are mixed but no compelling evidence that certain antidepressants confer less fall risk than others.
-Avoid unless safer alternatives are not available; avoid antiepileptics except for seizure and mood disorders Opioids: avoid except for pain management in the setting of severe acute pain (eg, recent fractures or joint replacement)

Table 4: PIMs: Drugs To Be Used With Caution in Older Adults

Aspirin for primary prevention of cardiovascular disease and colorectal cancer -Use with caution in adults ≥70 years
Risk of major bleeding from aspirin increases markedly in older age. Several studies suggest lack of net benefit when used for primary prevention in older adult with cardiovascular risk factors, but evidence is not conclusive. Aspirin is generally indicated for secondary prevention in older adults with established cardiovascular disease.

Dabigatran, Rivaroxaban -Use with caution for treatment of VTE or atrial fibrillation in adults ≥75 years
Increased risk of gastrointestinal bleeding compared with warfarin and reported rates with other direct oral anticoagulants when used for long-term treatment of VTE or atrial fibrillation in adults ≥75 years.
rivarox <50 15mg (avoid <15) apix: <1.5, ≥80yo, ≤60kg 2.5mg bid dabig: <30 75mg bid (avoid <15) edox: 15-50 30mg (avoid <15 >95)

Prasugrel -Use with caution in adults ≥75 years
Increased risk of bleeding in older adults; benefit in highest-risk older adults (eg, those with prior myocardial infarction or diabetes mellitus) may offset risk when used for its approved indication of acute coronary syndrome to be managed with percutaneous coronary intervention.

***Antipsychotics, Carbamazepine, Diuretics, Mirtazapine, Oxcarbazepine, SNRIs, SSRIs, TCAs, Tramadol** -Use with caution
May exacerbate or cause SIADH or hyponatremia; monitor sodium level closely when starting or changing dosages in older adults

Dextromethorphan/quinidine -Use with caution
Limited efficacy in patients with behavioral symptoms of dementia (does not apply to treatment of PBA). May increase risk of falls and concerns with clinically significant drug interactions. Does not apply to treatment of pseudobulbar affect.

Trimethoprim-sulfamethoxazole -Use with caution in patients on ACEI or ARB and decreased creatinine clearance
Increased risk of hyperkalemia when used concurrently with an ACEI or ARB in presence of decreased creatinine clearance

Table 5: PIMs: Drug-Drug Interactions that Should Be Avoided (Changes)

AED, AP, benzo, Z-hypnotic, TCA, SSRI, SNRI, opioid: avoid any combination of ≥3 of these CNS-active drugs
- reason for change is due to increased risk of falls; minimize number of CNS-active drugs shown to decrease risk of falls

opioids + benzos: increase risk of overdose
opioids + gabapentinoids: increased risk for severe sedation related adverse events

Table 7: Drugs with Anticholinergic Properties

Disopyramide, Amitriptyline, Amoxapin, Clomipramine, Desipramine, Doxepin (>6 mg), Imipramine, Nortriptyline, Paroxetine, Protriptyline, Trimipramine, Prochlorperazine, Promethazine, Brompheniramine, Carbinoxamine, Chlorpheniramine, Clemastine, Cyproheptadine, Dexbrompheniramine, Dexchlorpheniramine, Dimenhydrinate, Diphenhydramine (oral), Doxylamine, Hydroxyzine, Meclizine, Clidinium-chlordiazepoxide, Dicyclomin, Homatropin (excludes ophthalmic), Hyoscyamine, Methscopolamine, Propanthelin, Promethazine, Pyrilamine, Triprolidine, Darifenacin, Fesoterodine, Flavoxate, Oxybutynin, Solifenacin, Tolterodine, Trospium, Benztropine, Trihexyphenidyl, Chlorpromazine, Clozapine, Loxapine, Olanzapine, Perphenazine, Thioridazine, Trifluoperazine, Antispasmodics, Atropine (nonophthalmic), Belladonna alkaloids, Scopolamine (excludes ophthalmic), Cyclobenzaprine, Orphenadrine

deprescribing.org: PPIs, Antihyperglycemics, Benzodiazepines and "Z" Drugs, Antipsychotics, Cholinesterase Inhibitors and Memantine

Needs tapering: antidepressants, anticonvulsants, antipsychotics, benzos, beta-blockers, cholinesterase inhibitors, clonidine, steroids, memantine, PPIs, tizanidine, tramadol, Z-drug

5 Guiding Principles:
Patient Preferences
Interpreting the Evidence
Prognosis
Treatment Complexity and Feasibility
Optimizing Therapies and Care Plans

Patient Characteristics/Health Status	Rationale	A1c Goal	FPG	Bed BG	BP, Lipids
Healthy few coexisting chronic illnesses intact cognitive and functional status	Longer remaining life expectancy; can perform more complex tasks	<7.0-7.5%	80-130	80-180	<140/90, statin
Complex/intermediate multiple coexisting chronic illnesses or 2+ IADL impairments or mild-mod cognitive impairment	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90-150	100-180	<140/90, statin
Very complex/poor health LTC or end-stage chronic illnesses or mod-severe cognitive impairment or 2+ ADL dependencies	Limited remaining life expectancy makes benefit uncertain	^	100-180	110-200	<150/90, consider

^avoid reliance on A1c; prevent hypoglycemia and symptomatic hyperglycemia; goals above 8.5% are not recommended as they may expose patient to more frequent higher glucose values and the acute risk from glycosuria, dehydration, hyperglycemic hyperosmolar syndrome, and poor wound healing.

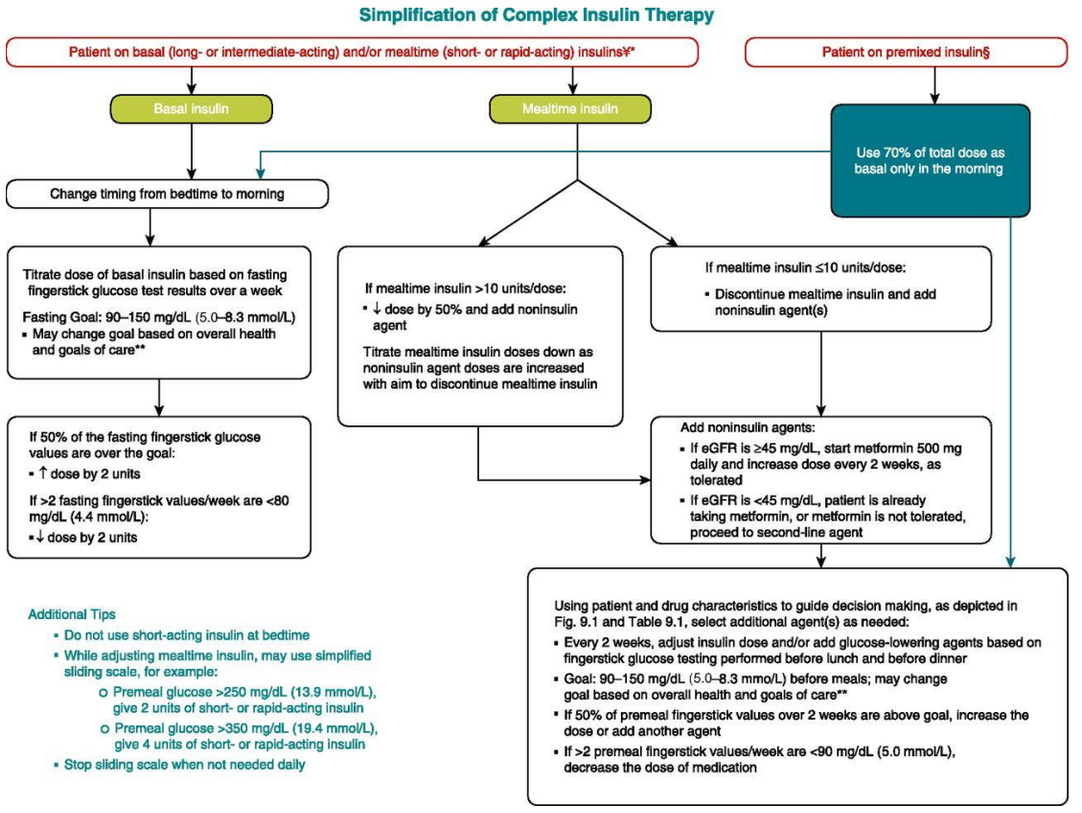
Metformin	preferred agent in older adults	caution renal (CI eGFR <30), hepatic, CHF
TZDs	not considered first-line	caution CHF, risk falls/fractures; avoid combo with insulin
SU, Meg	not considered first-line	caution hypoglycemia risk; if used, glipizide preferred
DPP-4i, GLP-1	adjunctive agents	DPP-4i expensive, GLP-1 NV potential, wt loss; CVD benefit
SGLT-2i	not considered first-line	long-term experience limited; ASCVD benefit
Insulin	reasonable qday basal	caution hypoglycemia, caution MDD

premixed → 70% as basal in morning
basal → change to morning (FPG 90-150)
- if 50% of FPG goal, ↑2u
- if >2 FPG below <80, ↓2u

mealtime
→ if bolus >10u, ↓dose 50%, add noninsulin
→ if bolus <10u, discontinue, add noninsulin

BP Goals: ACC/AHA <130/80, ACP/AAFP <150
Alzheimer's staging, MMSE/30: 24-20 mild, 10-19 moderate, <10 severe, 0 profound
Functional status: IADLs (shopping, cooking, housework, bills, laundry); ADLs (bathing, toileting, eating, climbing stairs, grooming, dressing)
The Clinical Fraility Scale (CFS): score 1-4 fit preserved function, score 5-6 loss of function, score 7-9 loss of function and altered ADL, score 9 terminally ill

- Low dose diuretics may be beneficial (watch for hyponatremia with Thiazides!)
- CCBs are quite useful because of their strong antihypertensive effects
- Combining 2 drugs at lower doses may be preferable to using a single drug at a high dose, because or the potential for adverse effects with the higher doses
- Beta-blockers may not be as effective as other first-line agents in patients aged 60 years or older, especially for stroke prevention; should probable be used when other indications are present, such as heart failure, previous MI/angina



Acne vulgaris
- Non-pharmacologic interventions
- Over-the-counter products
- Treatment
  – Severity guides treatment
  – Many options both topical and oral
- Patient education

***Mild**: topical retinoid or BPO, or topical retinoid + BPO if closer to moderate (1-2 agents)
***Moderate**: same but add oral antibiotic (might add 3rd agent)
***Severe**: oral isotretinoin

Psoriasis
- Genetic, immune-mediated, systemic, inflammatory, chronic disorder
- Severity guides treatment
  – Many treatment options
  – Topical vs systemic vs biologic
- Patient education

Atopic Dermatitis (Eczema)
- Hydration, hydration, hydration
- Treatment
  – First-line: topical corticosteroids
  – Second-line: topical calcineurin inhibitors, PDE-4i
- Patient education

Pediculosis/Scabies
- OTC vs RX treatment options
- Treatment resistance
- Non-pharmacologic treatment
- Patient counseling!

Anorexia Nervosa
Risk Factors:
- Obsessional traits in childhood
- Social pressures related to thinness/appearance
- Certain activities such as ballet, gymnastics, wrestling
- 1st deg relative with AN

Tx: Family Based Treatment (FBT)
- antipsychotics (olanzapine increase BMI) risk/benefit

Bulimia Nervosa
Risk factors:
- Low self-esteem, depression, or social anxiety disorder
- Childhood Obesity
- Certain activities such as ballet, gymnastics, wrestling
- Childhood trauma (physical or sexual)

Tx: Cognitive Behavioral Therapy (CBT) and fluoxetine (60-80mg)
- decrease in binging and purging to zero and almost none (x8wk)

Autism Spectrum Disorder
Risk factors:
- Shorter and longer time periods between births
- Advanced maternal or paternal Age
- Extremely premature birth
- Family member with autism

Tx: Applied Behavior Analysis (ABA)

Irritability: Antipsychotics (risperidone, aripiprazole)
- irritability in ASD = aggression, deliberate self-injurious behavior, temper tantrums, quickly changing moods; Two FDA approved APs

ADHD/Hyperactivity: Stimulants (methylphenidate)
- patients with ASD often struggle with hyperactivity/inattention; Most studied in ASD; Initiate with low dose IR product and titrate

Repetitive Behavior: Antidepressants (fluoxetine, clomipramine), Antipsychotics (haloperidol, rispderidone, aripiprazole)
- clomipramine (TCA, more ADEs); haloperidone shows benefit but not often used bc ADEs

Sleep Disturbances: Melatonin
- sleep hygiene education; Melatonin if needed: Reduces sleep latency, Increases length of nighttime sleep, No significant ADE