Insulin

Lispro, Aspart	Regular	NPH	Glargine, Detemir, Degludec (basal)
O:<15 m	O:.5-1	O:2-4	O:2-4
P:1-2	P:2-3	P:4-10	P:N/A
D: 3-4	D:3-6	D:10-16	D:24

Tofacitinib

Janus kinas inhibitor PO	
2x/day reduced to 1x if	Potent CYP3A4 and CYP2c19 inhibitors (e.g. fluconazole)
	Severe renal impairment
	Mod liver impairment
Combined w/methotrexate or nonbio DMARD	
DO NOT combine w/bio DMARD	

Other DMARDs in Refractory RA

Azathioprine, Cyclophosphamide, Cyclosporine, Penicillamine

Last-line therapy in refractory disease

use is limited by higher rates of adverse effects

Anaesthetics SE

CNS effects
Reduction of vascular resistance
Increased intracranial pressure
Decrease BP
Entrorane and Halothane decrease CO
Decreased blood flow to liver and kidneys
Decrease respiratory rate
Malignant hyperthermia (uncontrolled Ca release)
Treated with dantrolene

Local Anesthetics

Intermediate chain linking amino to aromatic ring	
block Na+ channels in nerve	
sympathetic → sharp/dull → touch/temp → motor paralysis	
More effect on small C fibers and small A fibers	
Amino Esters	Surface: Benzocaine, cocaine
	Short: Procaine
	Long: Tetracaine
Amino Acids	Medium: Lidocaine
	Long: Bupivacaine, ropivacaine
Lidocaine Patch	12hr on/12 off
	3 patch max

Opioids

Act on Mu, Kappa, Delta receptors	
Phenanthrenes	(natural) Codeine, Morphine
Phenanthrenes	(semisynthetic) Hydrocodone, Hydromorphone, Oxycodone
Phenylpiperidines	Fentanyl, Meperidine (chills)
Phenylethylamines	Methadone, Propoxyphene
Extended	Oxycodone, Morphine, Fentanyl
Tramadol	Mu receptor agonist, inhibit serotonin and NE reuptake
	Mild to moderate pain
	SE: ↓resp depression than other opioids, sedation, constipation, dry mouth, nausea, serotonin tox
Morphine	Controlled or immediate
	SE: potential accumulation, itch

Opioids (cont)

	Not indicated in pts w/renal
Oxycodone	High oral bioavailability w/no food effect
	No significant metabolites
	minimally affected by age renal or liver
Methadone	alpha 8-12, beta 24-36
	NMDA receptor antagonist/ Serotonergic properties
	SE: Toxicity, QTc prolongation
Meperidine	Causes euphoria, most addictive, seizures
Agonists	Oxycodone, Codeine, Hydrocodone
Mixed	Buprenorphine
Antagonists	Naltrexone, Naloxone
SE: CNS/resp depression (5-7 days), N/V (codeine), constipation, itch/rash	

Lipid Lowering Drugs

HMG-CoA reductase inhibitors	E.g. Atorvastatin, Rosuvastatin, red rice yeast
	Primary agents
	↓ LDL and TG, ↑ HDL, ↓ morbidity/mortality
	antithrombotic effects, ↓endothelial inflammation
	SE: myopathy and hepatotox, elevated LFTs, CPK (muscle/jt pain, rhabdo), proximal muscle weakness
	CYP450 (grapefruit, Cimetidine)

Lipid Lowering Drugs (cont)

	Memory loss, diabetes
Bile acid sequestrants (resins)	E.g. Cholestyramine; ↓ LDL, ↑HDL and TG; Unpleasant taste, GI effects, intxns; Other meds 1 hr before or 4 hr after
Fibrates	E.g. Gemfibrozil, fenofibrate
	↓ LDL and TG, ↑ HDL
	Toxicity additive w/statins
	Rhabdo, myopathy, LDL increase
Nicotinic Acid	↓ LDL and TG, ↑ HDL
	Flushing, itching, HA, Hyperuricemia in gout, Hyperglycemia, Hepatotox
Chol absorption inhibit	E.g. Ezetimibe
	Decrease LDL, increase HDL
	HA Diarrhea Upper resp infection
	hepatotox + rhabdo with statins

Acetaminophen

central COX inhibitor

Analgesic & Antipyretic

NOT anti-inflammatory or antithrombotic

SE: Hepatotoxicity

1st line for OA

Avoid alcohol

No Raye's syndrome

Acetaminophen (cont)

Similar to NSAIDs, better tolerated

2 wks before considering treatment failure

GLP-1 Agonist

E.g. Exenatide, Liraglutide

↑ insulin release

↓A1C ~0.7

SE: GI upset, weight loss

Maybe pancreatitis, gallbladder disease, thyroid cancer

Caution in renal disease

CV benefit

Anti-Factor Xa Inhibitors

Fondaparinux	SC treat/prevent DVT/PE
	Avoid use in Crcl <30 ml/min
	Monitor: Anti-Xa, sx of bleeding
Apixaban	Inhibit factor X
	adjust in Afib if ⅔ >80 yo, Scr >1.5, weight <60kg
	Intxns: phenytoin, carbamazepine, fluconazole, rifampin
	bleeding, compliance
Rivaroxaban	inhibit factor X
	Take w/evening meal
	Intxns: phenytoin, carbamazepine, fluconazole, rifampin

Thiazolidinediones

E.g. Pioglitazone, Rosiglitazone (not used, ↑CVD)

↓HDL, triglycerides; neutral LDL

Decrease fasting plasma glucose 35-40

Reduce A1C ~0.5-1%

6 weeks for max effect

SE: weight ↑, edema, hypoglycemia

Thiazolidinediones (cont)

Contraindicated liver problems or CHF

Reversal of anticoagulation

Warfarin	Vitamin K
Keparin	Protamine
Enoxaparin	Protamine (less reliable)
Dabigatran	Idarucizumab
Apixaban	zhzo Xa
Rivaroxaban	zhzo Xa

Statin Monitoring

CK	Baseline: only in pts at increased risk for musc injury
	Routine: only in pts w/musc pain/weakness
ALT	Routine: only if symptoms of hepatotox occur
FLP	Routine: 4-12 wks after initiation, then Q3-12 months as indicated
Hgb A1c	Baseline: only if diabetes status unknown

Anticoagulants

Heparin	Unfractionated heparin (UFH); IV/SC
	monitor aPTT, platelets, hgb, hct, HIT
Low-molecular-weight heparin	Enoxaparin, SC
	Renal adjust Crcl <30
	monitor less frqnt, Anti-Xa levels not aPTT
Anti-Factor Xa inhibitor	Fondaparinux, SC
	Apixaban, PO
	Rivaroxaban, PO
Direct Thrombin Inhibitors	Argatroban, IV
	Dabigatran, PO

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Published 21st June, 2018.
Last updated 22nd June, 2018.

Anticoagulants (cont)

Vitamin K antag	Warfarin, PO
	Onset: slow, anticoagulation occurs 48-72 h after the first dose once factors are depleted
	Monitor INR (goal 2-3), Hgb/hct, bleeding
	Intxn: Food: green leafy vegetables Meds: cipro, bactrim, flagyl, fluconazole, rifampin
	Preferred in renal dysfunction

Local Anesthetics Additives

Vasodilation prevented by vasoconstrictor (e.g. epinephrine); prolong effect/decrease dose -- do not use in fingers/toes

Bicarbonate Decrease burning sensation during admin

Direct Thrombin Inhibitors

Do not require antithrombin

Monitor aPTT, platelets, hgb, het, bleeding

Continuous infusions

Used in HIT mgmt

Short duration

Argatroban	Falsely elevate INR
	No monitoring or reversal agent
	ADE: upset stomach, bleed
	Intxns: avoid rifampin
	Store in original container and use within 30 days of opening

IV Anesthetics

Etomidate	Hypnotic
	Rapid onset gen anesthesia
	Min cardiopulm SE
	Good for CV and pulm comorbid
Propofol	Short acting hypnotic
	Very rapid recovery
Thiopental sodium	Respiratory depressant, no analgesia
	Rapid safe induction
	Barbiturate
Midazolam	Benzodiazepine
	Amnesia
	Potentially long halflife
Ketamine	Dissociative analgesia

Anticoagulant Dosing

DVT ppx: enoxparin 40mg q24 or 30mg q12 or heparin 5k units bid-tid.
PE/DVT tx: Enoxaparin 1.5mg/kg q24 hrs and 1mg/kg q12 hrs; heparin drip 18 units/-kg/hr

Non-Bio DMARDs

RA w/in 3 mo, max 6-12 mo

LF, HCQ, MTX need blood count, liver, Cr every 2-4wk/3mo then every 8-12 wks

Methotrexate	1st line, 2-8 wk onset PO/IM immunosuppressant
	SE: GI, liver tox, bone marrow, stomatitis, hair loss, pulm tox
	Folic acid decrease sx
Leflunomide	Immunosuppressant effective as MTX
	SE: GI, rash, hair loss, liver tox
	Work w/in 1 mo, weaker

Non-Bio DMARDs (cont)

Hydroxychloroquine	Low tox, 2-6 mo onset, min monitor
	SE: GI, retinal, derm, HA
Sulfasalazine	2-3x/day PO anti-inflam
	SE: GI, leukopenia, anemia, photosensitive, skin, hepatitis, pneumonitis, agranulocytosis, hypersensitivity
	>HCQ, <DMARDs
	poor tolerate, lots of monitoring
	Potentiate anticoagulants

Non-Opioid Analgesics

NSAIDs, ASA, salicylates	Prostaglandin inhibitors
	Inhibit COX-1 and COX-2
	GI side effects
	ASA = antiplatelet primarily used to prevent heart disease and stroke
	Thromboxanes involved in platelet aggregation and thrombus formation
Selective COX-2 inhibitor	e.g. Celecoxib
	↑ MI and stroke
	Rofecoxib and Valdecoxib taken off market
	Celecoxib ↓GI SE in pt not on ASA

Do not cause tolerance, not addictive

All have ceiling effect to analgesia

Biguanides

e.g. metformin

↓ glucose product, ↑ glucose uptake

↓ A1C 1-1.5

Low risk hypoglycemia

SE: Diarrhea/GI, ↓B12, l. acidosis, weight ↓

Contraindicated GFR<30

Meglitinides

e.g. Repaglinide, Nateglinide

Stimulate insulin secretion

Shorter acting, best taken after eating

↓A1C ~1

SE: Hypoglycemia, weight ↑

Safe w/greater renal insufficiency than SU

SGLT2 Inhibitors

E.g. Canagliflozin, Empagliflozin

↑glucose excretion

↓A1C 0.7-1

Empagliflozin: avoid if GFR <45

SE: Genital fungal infxn, UTI, AKI, dizzy, hypotension, hyperkalemia, hypoglycemia, fractures, ↓BMD, CV benefits

Opioid Withdrawal

Body aches, weakness, fatigue
Diarrhea, stomach cramping
Insomnia
Irritability
Loss of appetite
Nausea/vomiting
Increased BP/HR
Runny nose, sneezing, yawning
Chilliness and “goose bumps”

Patient Controlled Analgesia

e.g. Morphine, hydromorphone

Monitor HR, BP, RR, Pain, usage, O2

Capsaicin Cream

Inhibits release of substance P in peripheral

Max effect takes 2-4 wks application 4x/day

More role in OA than RA

Viscosupplimentation

E.g. hyaluronic acid

lubricant during low-stress mvmt, anti inflam

Has more role in OA than RA, esp knee

3-5 wkly injections = 1 cycle

Max effect 8-12 wks, lasts 6-12 mo

Bio DMARDs

Non-TNF	Abatacept SE: Pulmonary infection, allergic rxn, HA/dizzy
	Anakinra SE: inj site rxn, infection, allergic rxn
	Rituximab SE: rash, infection, neuro, infusion rxn, Tumor Lysis, multifocal leukoencephalopathy
TNF inhibit	Adalimumab: SC every 2 wk, mild-mod inject rxn
	Etanercept: SC 1-2/wk, mild-mod inject rxn
	Infliximab: IV at 0,2,6,8 wk; infusion rxn
	Increased malignancy risk
	SE: hypersensitivity, Lupus-like, hepatotox, pancytopenia, aplastic anemia, heart failure
	MTX combo or solo
	Mod-severe RA

Possibly reactivates TB, no live vaccine

Sulfonylurea

e.g. Glyburide, Glimepiride, Glipizide

↑endogenous insulin secretion

↓A1C 1-2

SE: hypoglycemia, ↑weight, photosensitive

Least expensive

Caution in renal, elderly

Often discontinued once insulin started

ADP Receptor Inhibitors

Clopid-ogrel	Indications: ASA + Clopidogrel in pts receiving stents
Prasugrel	More potent, less variable platelet response than Clopid-ogrel
	reduction of thrombotic CV events (including stent thromb-osis) in pts w/ACS who are to be managed w/PCI
	Risks may exceed benefits in pts w/ >75 yo Previous history of TIA or stroke <60kg
	Likely to undergo CABG = bleed risk
	Hold for 7 days before surgery
Ticagrelor	SE: bleeding, dyspnea, bradycardia
	2x/day
	Avoid in pts w/hx of hemorr-hagic stroke
	Avoid aspirin >100 mg CYP 3a4 inducers (rifampin, carbamazepine, phenytoin) CYP 3A4 inhibitors (ketocona-zole, ritonavir) Monitor digoxin levels

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Published 21st June, 2018.
Last updated 22nd June, 2018.

Glucosamine/Chondroitin

Glucosamine	cartilage building block
Chondroitin	Increase protein synthesis

OTC, not 1st line, may improve OA knee pain

Weeks to months for effect

SE: GI upset

DPP-4 inhibitors

e.g. Sitagliptin, Saxagliptin

↑ incretin, insulin release

↓A1C ~0.7

Well tolerated, no weight gain, no hypoglycemia

Maybe pancreatitis, jt pain, heart failure

Dose modification in renal impairment

CYP3a4 interactions

Heparin Induced Thrombocytopenia

Type 1	10-20%
	Onset: 2-3 d
	Platelet <50% decrease, nadir >100k
Type 2	1-3%
	Onset: 5-10 d
	Platelet >50% decrease, nadir 10-20k
	Antibody mediated
	Thromboembolic sequelae 30-80%
	D/c all heparin products, initiate direct thrombin inhibitor/coumadin

Thrombolytics

Alteplase (IV)

Dissolve clots acutely/clear IV line

Relative contraindication: HTN

Absolute contraindication: recent head trauma

ADR: bleeding, hemorrhage

C

Antiplatelets

Aspirin

ADP receptor inhibitors e.g. Clopidogrel Prasugrel Ticagrelor

PO

monoclonal antibodies/PCSK9 inhibit

SC

Reduce LDL by additional 60% with statin

E.g. evolocumab, alirocumab

Advantages: injected once or twice/month

SE: common cold, itching, flu, injxn site rxns, allergic rxns

Other Antidiabetics

Alpha-glucosidase inhibitors	e.g. Acarbose
	block enzymes that digest starches in small intestine
	GI upset, flatulence, bloating
Amylin analogs	e.g. Pramlintide
	Injectable
Bile acid sequestrants	e.g. Colesevelam
	GI side effects

Corticosteroids

E.g. Dexamethasone, Hydrocortisone, Methylprednisolone

Intraarticular	1-6 wk relief for OA/RA knee
	3-4/yr limit
	Lidocaine sometimes added
Systemic	RA, not OA

Acute SE: Hyperglycemia, HTN, euphoria/-psychosis, weight↑/edema, GI bleed

Corticosteroids (cont)

Chronic SE: Cushing's appearance, cataracts, hyperlipidemia, muscle/tendon, OP/fractures, infection, HPA suppression

NSAIDs

1st line in RA, 2nd in OA

Aspirin	Most widely used, analgesic, antinflammatory, antipyretic, antiplatelet
Diclofenac	more potent than other NSAIDs, ADRs occur in 20%
Ibuprofen	fever, GI side effects ~5-15%
Indomethacin	Dose related side effects (i.e. confusion); 35-50% pts
Ketorolac	Orally or IM, IV doses provide postoperative analgesia equivalent to opioids
	not used >5 days due to ADR
Naproxen	Similar to ibuprofen, less frequent dosing 2x/day

SE: GI, acute renal failure, BP, hypersensitivity

GI SE: Celecoxib < Diclofenac < Ibuprofen & Naproxen < ketorolac

Take ibuprofen at least 2 hours after ASA -- makes aspirin ineffective

GI ulcers/bleed prophylaxis: Misoprostol, Proton pump inhibitors (pantoprazole), H2RAs (ranitidine)

Use with caution on pt on anticoagulants

Need to take continuously for antiinflam

2-4 wk trial needed

Lidocaine Patch

12 hr on/12 hr off

3 at at time max

Anaesthetics Pharmacokinetics
highly lipid soluble
When discontinued, drugs will continue to enter systemic circulation
Lethargy, confusion

NM Blocking Agents	
Non-Depol-arizing	Competitive Ach antag
	Pancuronium O: 4-6 min D: 120-180 min
	Rocuronium O: 1-2 min D: 30-60 min
Depola-rizing	Overstimulate receptor
	Succinylcholine O: 1-1.5 min D: 5-8 min

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Published 21st June, 2018.
Last updated 22nd June, 2018.