## 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) |

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## 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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## 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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## 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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