Neurology Reference Handbook
Second Edition


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Neuro-Pharmaceuticals
## Anti-Epileptic Drugs

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**Carbamazepine:**
**Carnexiv:** an intravenous form of carbamazepine, got FDA approval in 2016. Used in patients where oral access is not possible (NPO due to illness, surgery or injury). Dose is 70% of the oral daily dose divided in 4 daily doses (Q6H). No data is available for intravenous loading or use in status epilepticus.

**HLA-B 15:02:** Patients with the HLA-B 15:02 (more prevalent in people of Asian descent) are more at risk of developing Steven Johnson Syndrome. Test for it before starting carbamazepine in people of Asian descent.

**PO loading:** 8mg/kg of oral suspension given in a single dose.

**Phenytoin:**
**PO Loading:** 20mg/kg in divided doses of maximum 400mg every 2 hours (if patient is 40kg: total dose is 800mg given as 400mg twice, 2 hours in-between)

**Dilantin Extended Cap:** start with TID dosing then once seizure is controlled, you can switch to the once daily dosing using Extended Capsules.

**Low albumin correction:** Corrected level = PHT level / [albumin x 0.2] +1

**Valproic acid & sodium divalproex:**
**Valproic acid (Depakene Cap & Syrup)**
More rapidly absorbed in the stomach, more irritant to GI tract (acid).
**Sodium divalproex (Depakote Tab, Syrup, Sprinkle):**
A combination of both valproic acid and sodium valproate. Sodium valproate is more slowly absorbed and less irritant to GI tract (salt).
**Sodium Valproate (Depacon IV injection):** less irritant to veins as compared with the more acidic valproic acid.

All the forms are pharmacologically equivalent (all convert to valproic acid in the GI tract), but they are not bioequivalent (differ in rate of absorption).

**Depakote tablets** (both the usual form which is DR ‘delayed release’ and the long-acting ER ‘extended release’) are prepared to dissolve slowly over 12h or 24h so they can’t be crushed. If you are using NG tube, use the syrup form Q8H instead.

**Conversion from Depakote to Depakote ER:**
Depakote ER = Depakote dose x 1.2 to achieve same therapeutic level.

**Valproate induced hyper-ammonemia:**
**Mechanism:** Valproate is a fatty acid that is undergoes beta-oxidation in hepatic mitochondria through the carnitine shuttle which depletes the hepatic carnitine and interferes with hepatic energy production.
**Treatment:** Stop Valproate or decrease the dose. Other way is to replete the hepatic levocarnitine “Carnitor”, IV (200mg/ml) or oral (solution 1gm/10ml) at a dose of 50mg/kg in divided doses (max 3gm/d).

**Lamotrigine:**
**Lamictal dosing frequency:** doses < 200mg can be given as once daily dose

**Lamictal patient titration kits:**
**Orange Kit** (patients not taking valproate): 25mg daily two weeks then 50mg daily 2 weeks then 100mg daily for 1 week.
**Blue Kit** (patients taking valproate): 25mg every other day for 2 weeks then 25mg daily for 2 weeks then 50mg daily for 1 week.
**Green Kit** (patients on liver enzyme inducers): 50mg daily for 2 weeks then 100mg daily for 14 days then 200mg daily for 7 days.

**Lacosamide:**
**Update:** Vimpat is now (11/2017) approved for children 4 years and older

**Schedule V:** Lacosamide is a controlled medication due to its nociceptive effect in animal studies & inducing euphoria, sedation, feeling high (psychological dependence) in human studies. However, it doesn’t cause physical dependence or withdrawal symptoms.
**Neuro-Pharmacology**

**Trough versus peak concentration:**
- **Trough** ($C_{\text{min}}$): is the lowest concentration in the blood, taken 30 minutes before next dose.
- **Peak** ($C_{\text{max}}$): is the maximum concentration in the blood, taken usually 1 hour after intravenous or 4h after subcutaneous (varies by drugs).
- **Random**: used only for drugs given by continuous IV infusions

**Trough** is used when you’re concerned about therapeutic levels (to make sure there is continuous therapeutic blood level) → **use trough for monitoring of all anti-epileptic drugs.**

**Peak** is used when you’re concerned about toxicity for drugs with narrow therapeutic index or when there is high risk from complications (aminoglycosides, enoxaparin in patients at risk of bleeding – 4h after S.C injection)

**Reloading**: if patient is already loaded or has been using the medication with sub-therapeutic serum level, use the following formula.

Reloading dose = Ideal body weight x Volume of distribution (VD) x delta Sr level

<table>
<thead>
<tr>
<th>Example</th>
<th>Drug</th>
<th>VD</th>
<th>Max Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>If current valproate level is 50 mcg/ml &amp; target level is 100.</td>
<td>Phenytoin</td>
<td>0.8 L/Kg</td>
<td>20 mcg/kg</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine</td>
<td>0.8 L/Kg</td>
<td>12 mcg/kg</td>
</tr>
<tr>
<td></td>
<td>Phenobarbital</td>
<td>0.6 L/Kg</td>
<td>40 mcg/kg</td>
</tr>
<tr>
<td>Reloading dose = 70kg x 0.2 L/kg x (100-50) = 700mcg</td>
<td>Valproate</td>
<td>0.2 L/Kg</td>
<td>100 mcg/kg</td>
</tr>
<tr>
<td></td>
<td>Levetiracetam</td>
<td>0.6 L/Kg</td>
<td>50 mcg/kg</td>
</tr>
<tr>
<td></td>
<td>Lacosamide</td>
<td>0.6 L/Kg</td>
<td>10 mcg/kg</td>
</tr>
</tbody>
</table>

**When compliance is an issue:**

1- **Long acting preparations:**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Formulation</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Tegretol XR 100 – 200 – 400mg</td>
<td>BID</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Dilantin Extended Cap 100mg</td>
<td>QD</td>
</tr>
<tr>
<td></td>
<td>Phenytine Cap 200, 300mg</td>
<td>QD</td>
</tr>
<tr>
<td>Divalproex</td>
<td>Depakote ER 250, 500mg</td>
<td>QD</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Trokendi XR 25, 50, 100, 200mg</td>
<td>QD</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Quedexy XR 25, 50, 100, 200mg</td>
<td>QD</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Lamictal XR 25, 50, 100, 200, 250mg</td>
<td>QD</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Keppra XR 500, 750mg</td>
<td>QD</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Oxtellar XR 150, 300, 600mg</td>
<td>QD</td>
</tr>
</tbody>
</table>

2- **Long acting medications:**

Clonazepam, Lamotrigine (doses < 200mg/day can be given as once a day), Zonisamide, Perampanel, Eslicarbazepine
<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Indications</th>
<th>Side effects</th>
<th>Black box warnings marked in Red</th>
<th>Metabolism / Excretion</th>
<th>Target Sr Level</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Na Channel blocker (SCN5A)</td>
<td>√ √</td>
<td>Neuro: Nystagmus, dizziness, blurred vision</td>
<td>Blood: BM suppression, aplastic anemia</td>
<td>Hepatic</td>
<td>4-12 total 1-3 free</td>
<td>D</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Blood: hyponatremia, decreased osmolality</td>
<td>Teratogenic: spina bifida</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>SJS/TEN specially in Asians with HLA-B 1502</td>
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</tr>
<tr>
<td>Ethosuximide</td>
<td>T-type Ca channel blocker</td>
<td>√</td>
<td>Neuro: drowsiness, headache</td>
<td>Gl: N,V, tongue swelling</td>
<td>Hepatic</td>
<td>40-100</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Blood: anemia, leukopenia</td>
<td></td>
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</tr>
<tr>
<td>Valproate</td>
<td>Na Channel blocker</td>
<td>√ √ √ √</td>
<td>Neuro: Tremors</td>
<td>Gl: anorexia, nausea, hyperammonemia, pancreatitis, Hepatotoxicity in kids &lt; 2 years, specially kids with Alpers syndrome</td>
<td>Hepatic</td>
<td>50-100 total 6-22 free</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Inhibits GABA-transaminase</td>
<td></td>
<td>Blood: Thrombocytopenia</td>
<td>Weight gain, PCOS, Reversible hair loss</td>
<td></td>
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<tr>
<td></td>
<td>NMDA antagonist</td>
<td></td>
<td>Teratogenic: spina bifida in 1%, women must use OCP</td>
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<tr>
<td></td>
<td>Histone deacetylase inhibitor</td>
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<tr>
<td>Phenytoin</td>
<td>Na Channel blocker</td>
<td>√ √ X</td>
<td>Neuro: Ataxia, nystagmus, vertigo, tremors</td>
<td>CVS: hypotension &amp; arrhythmia with IV infusion</td>
<td>Hepatic</td>
<td>Total: 10-20 Free: 1-2</td>
<td>D</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Gl: Gingival hyperplasia</td>
<td>Blood: aplastic anemia, Hemorrhagic disease in newborns</td>
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<tr>
<td></td>
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<td></td>
<td>Teratogenic: fetal hydantoin syndrome</td>
<td>SJS/TEN – hyperphosphatemia (fosphenytoin)</td>
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<tr>
<td>Phenobarbital</td>
<td>GABA agonist</td>
<td>√ √</td>
<td>Neuro: sedation, paradoxical hyperactivity in some children</td>
<td>Amelogenesis Imperfecta (abnormal teeth enamel)</td>
<td>Hepatic</td>
<td>10-40</td>
<td>D</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Blood: megaloblastic anemia, Vit K dependent coagulopathy</td>
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<tr>
<td>Gabapentin</td>
<td>Ca channel blocker CACNA2D1</td>
<td>√</td>
<td>DRESS – Sedation - Angioedema (as with other CCB)</td>
<td>In Kids: hostility – hyperactivity</td>
<td>Renal</td>
<td></td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>(Presynaptic Ca++ channels -&gt; ↓ transmitter release)</td>
<td></td>
<td>Elevated CPK, rhabdomyolysis (rare)</td>
<td></td>
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<tr>
<td>Neuro-Pharmacology</td>
<td>Anti-epileptic drugs (Mechanism &amp; Side effects)</td>
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<tr>
<td><strong>Lamotrigine</strong></td>
<td>VG Na Channel blocker √ √ ? SJS/TEN in 0.8% – DRESS – rare cases of NMS</td>
<td>Hepatic 2-15 D</td>
<td></td>
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<tr>
<td>Topiramate</td>
<td>VG Na Channel blocker ↑ GABA-A Rc activity ↓ AMPA Rc (glutamate Rc) Carbonic anhydrase inhibitor √ √ √ Naming &amp; cognitive problems Kidney stones (Ca phosphate stones, 1.5% annual risk) Paresthesia, weight loss, hyponatremia and hyperthermia in kids exercising in hot weather, metabolic acidosis.</td>
<td>Renal 5-20 D</td>
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<tr>
<td>Levetiracetam</td>
<td>Binds to SV2A presynaptic protein, ↓ transmitter release. Binds to CACNA1B. √ √ √ Aggression/irritability in kids Irritability in adults</td>
<td>Renal 10-50 C</td>
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<tr>
<td>Brivaracetam (Briviact)</td>
<td>20 times more affinity for SV2A than levetiracetam √ Sedation – Drowsiness</td>
<td>Renal C</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Na Channel blocker (SCN5A) √ Neuro: Nystagmus, dizziness, blurred vision Blood: BM suppression, aplastic anemia Endo: hyponatremia (due to SIADH), osteopenia Teratogenic: spina bifida SJS/TEN (not black box)</td>
<td>Hepatic 3-35 C</td>
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<tr>
<td>Zonisamide</td>
<td>Na Channel blocker T-type Ca channel blocker Carbonic anhydrase inhibitor √ √ √ Neuro: Sedation – Dizziness – Ataxia – Impaired Memory/ concentration Kidney stones (1.5% annual risk), hyponatremia/hyperthermia Acidosis (hyperchloremic non-anion gap) Sulfa allergy – SJS – DRESS</td>
<td>Renal 10-40 D</td>
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<tr>
<td>Lacosamide</td>
<td>Na Channel blocker (SCN9A, 3A, 10A) Inhibits neuronal growth in chronic epilepsy by Inhibitin CRMP-2 (the collapsin response mediator protein 2) √ Neuro: Ataxia/Dizziness Cardio: PR interval prolongation, In DM patients: syncope, atrial fibrillation DRESS</td>
<td>Renal 5-10 C</td>
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<tr>
<td>Clobazam (Onfi)</td>
<td>Potential GABA activity Adjunctive for LGS &gt; 2 years Neuro: Sedation (avoid opioids/CNS depressants) SJS/TEN</td>
<td>Hepatic 30-300 ng C</td>
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<tr>
<td>Perampanel (Fycompa)</td>
<td>AMPA antagonist √ √ Neuro: Aggression, Homicidal Ideation Dizziness, vertigo</td>
<td>Hepatic C</td>
<td></td>
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<tr>
<td>Neuro-Pharmacology</td>
<td>Anti-epileptic drugs (Mechanism &amp; Side effects)</td>
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<tr>
<td>Eslicarbazepine</td>
<td>Na Channel blocker √ Similar to oxcarbazepine</td>
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<tr>
<td>(Aptiom)</td>
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<td></td>
<td>Hepatic C</td>
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<tr>
<td>Ezogabine</td>
<td>Neuronal K channel opener √ (KCNQ)</td>
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<tr>
<td>(Potiga)</td>
<td>Neuro: Vision loss &amp; Retinal abnormalities (retinal pigment dystrophies) in 30% - Grey skin discoloration, QT prolongation</td>
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<td></td>
<td>Discontinued 06/2017</td>
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<td></td>
<td>Hepatic C</td>
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<tr>
<td>Tiagabine</td>
<td>GABA reuptake inhibitor</td>
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<tr>
<td>(Gabitril)</td>
<td>Adjunctive for patients &gt; 12 years</td>
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<tr>
<td></td>
<td>Seizures/Status epilepticus with over dosage</td>
<td></td>
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<tr>
<td></td>
<td>Cognitive symptoms with increased spike/wave discharges in EEG of 6% of patients (? NCSE)</td>
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<td></td>
<td>Hepatic C</td>
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<tr>
<td>Vigabatrin</td>
<td>Irreversible inhibition of GABA-transaminase</td>
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<tr>
<td>(Sabril)</td>
<td>Infantile Spasm</td>
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<tr>
<td></td>
<td>Neuro: Vision loss (concentric contraction of visual field)</td>
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<tr>
<td></td>
<td>Neuropathy in adults</td>
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<tr>
<td></td>
<td>Neurotoxicity: T2/DWI changes in BG in MRI of kids with IS, int myelinic edema (IME) with separation of myelin in animals.</td>
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<td></td>
<td>Renal &lt; 235 ng D</td>
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<tr>
<td>Felbamate</td>
<td>NMDA antagonist VG Na Channel blocker</td>
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<td></td>
<td>Adjunctive for refractory Sz</td>
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<tr>
<td></td>
<td>Hepatotoxicity</td>
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<tr>
<td></td>
<td>Aplastic anemia 1:5000</td>
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<td></td>
<td>Hepatic 30-60 mic C</td>
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<tr>
<td>Rufinamide</td>
<td>Prolongs inactivation of VG N Channel</td>
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<tr>
<td>(Banzel)</td>
<td>LGS</td>
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</tr>
<tr>
<td></td>
<td>Neuro: Ataxia/Dizziness</td>
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<tr>
<td></td>
<td>Shortens QTc interval (caution in familial short QT syndrome)</td>
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<td></td>
<td>Hepatic carboxylase C</td>
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<tr>
<td>Cannabidiol</td>
<td>Unknown (not related to CBD activity)</td>
<td></td>
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<tr>
<td>(Epidiolex)</td>
<td>LGS</td>
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<td></td>
<td>Hepatic</td>
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<tr>
<td></td>
<td>Dravet</td>
<td></td>
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<tr>
<td></td>
<td>Somnolence, sedation and weight loss (decreased appetite)</td>
<td></td>
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<tr>
<td></td>
<td>Metabolic acidosis symptoms: hyperventilation, fatigue, anorexia, kidney stones, cardiac arrhythmia, rickets, osteoporosis, seen with topiramate &amp; Zonisamide.</td>
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<tr>
<td>Stiripentol</td>
<td>Unknown (possibly GABA mediated)</td>
<td></td>
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<tr>
<td>(Diacomit)</td>
<td>Dravet</td>
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<tr>
<td></td>
<td>Neutropenia, thrombocytopenia (13% of patients)</td>
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<tr>
<td></td>
<td>Somnolence, sedation, decreased appetite</td>
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<tr>
<td></td>
<td>Hepatic</td>
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</tbody>
</table>

Common side effects to all AED: Suicidal ideation (Odds Ratio 1.8), sedation
DRESS: Drug reaction with eosinophilia and systemic symptoms (fever, rash, lymphadenopathy, +/- hepatitis/nephritis/myositis)
SJS/TEN: Steven Johnson syndrome / Toxic epidermal necrolysis
Metabolic acidosis symptoms: hyperventilation, fatigue, anorexia, kidney stones, cardiac arrhythmia, rickets, osteoporosis, seen with topiramate & Zonisamide.
Neuro-Pharmacology  Anti-epileptic drugs (Mechanism & Side effects)

When hepatic impairment is an issue:
Avoid: hepatotoxic AED as valproate, lamotrigine, carbamazepine, phenytoin, felbamate.
Preferred AED: no hepatic metabolism & no protein binding as levetiracetam, brivaracetam, gabapentin, topiramate, perampanel
Less preferred: safe on liver but sedating as clonazepam, clobazam, rufinamide, tiagabine
In mild-moderate hepatic impairment: no adjustment needed
In severe hepatic impairment: choose AED that can be traced by checking their level (levetiracetam, topiramate)

When renal impairment is an issue:
Use lipophilic drugs as: lamotrigine, Oxcarbazepine, carbamazepine, phenytoin, valproate, clonazepam
If using hydrophilic drugs: gabapentin, topiramate, ethosuximide, vigabatrin and levetiracetam, dose adjustment and post-dialysis dose will be necessary.

<table>
<thead>
<tr>
<th>AED</th>
<th>Daily dose changes</th>
<th>HD adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenytoin</td>
<td>Give Q8H</td>
<td>Not needed</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>No changes</td>
<td>Not needed</td>
</tr>
<tr>
<td>Valproate</td>
<td>No changes</td>
<td>Not needed</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>No changes</td>
<td>Not needed</td>
</tr>
<tr>
<td>Benzo diazepine</td>
<td>No changes</td>
<td>Not needed</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>No changes</td>
<td>May be needed (↓level by 20%)</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>↓Dose - ↑ Interval</td>
<td>Supplement after HD</td>
</tr>
<tr>
<td>Topiramate</td>
<td>↓Dose - ↑ Interval</td>
<td>Supplement after HD</td>
</tr>
</tbody>
</table>

Levetiracetam and topiramate: use half usual dose in ESRD with supplemental half dose after dialysis. (e.g: If the usual levetiracetam dose is 500mg bid, use 500mg daily in ESRD with 250mg after dialysis, if usual topiramate dose is 50mg bid, use 50mg daily in ESRD with 25mg after dialysis)

When pregnancy is an issue:
- There are no risk-free medications (Class A or B) to use during pregnancy.
- Medications with relatively less risk for teratogenicity: Levetiracetam, Brivaracetam, Lamotrigine, Oxcarbazepine & Lacosamide.
- Folic acid supplements (1 mg QD if not planning, 4mg QD if planning for pregnancy) are recommended for all women with epilepsy in child bearing period (regardless of what AED they use).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Teratogenicity</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Congenital malformations - Spina bifida</td>
<td>D</td>
</tr>
<tr>
<td>Valproate</td>
<td>Congenital malformations - Autism - Low IQ (average 8 points lower) Fetal Valproate Syndrome</td>
<td>D</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Fetal Hydantoin Syndrome (IUGR – microcephaly – hypoplastic nails and distal phalanges)</td>
<td>D</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Cleft lip, cleft palate, Low birth weight</td>
<td>D</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Cleft lip, cleft palate</td>
<td>C</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Minor skeletal abnormalities in animals</td>
<td>C</td>
</tr>
<tr>
<td>Brivaracetam</td>
<td>Minor anomalies in animals</td>
<td>C</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>IUGR, craniofacial and skeletal malformations</td>
<td>C</td>
</tr>
<tr>
<td>Lacosamide</td>
<td>IUGR and fetal mortality with high doses</td>
<td>C</td>
</tr>
<tr>
<td>Zonisamide</td>
<td>External and visceral anomalies seen in animals</td>
<td>C</td>
</tr>
<tr>
<td>Eslicarbazepine</td>
<td>Fetal mortality at all tested doses in rats</td>
<td>C</td>
</tr>
<tr>
<td>Neuro-Pharmacology</td>
<td>Immuno-modulatory Therapy</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
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<td></td>
</tr>
<tr>
<td><strong>MULTIPLE SCLEROSIS DISEASE MODIFYING THERAPY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Drug</strong></td>
<td><strong>Indic</strong></td>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td><strong>Self Injectables</strong></td>
<td></td>
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</tr>
<tr>
<td>IFB 1A Avonex 1996</td>
<td>RRMS</td>
<td>30mic IM weekly</td>
</tr>
<tr>
<td>IFB 1A Rebif 1998</td>
<td>RRMS</td>
<td>44mic SQ MWF</td>
</tr>
<tr>
<td>IFB 1A Plegridy 2014</td>
<td>RRMS</td>
<td>125mic SQ q2w</td>
</tr>
<tr>
<td>IFB 1B Betaseron, Extavia, 2009</td>
<td>RRMS</td>
<td>250mic SQ EOD</td>
</tr>
<tr>
<td>Glatiramer acetate Copaxone 1997 Glatopa 2015</td>
<td>RRMS</td>
<td>20mg SQ daily or 40mg SQ MWF</td>
</tr>
<tr>
<td>Daclizumab Zinbryta, 2016 Withdrawn in 2017</td>
<td>RRMS who failed 2 drugs</td>
<td>150mg SC monthly</td>
</tr>
<tr>
<td>Gatifloxacin Fingolimod Gilenya, 2010</td>
<td>RRMS</td>
<td>0.5 mg daily</td>
</tr>
<tr>
<td>Teriflunomide Aubagio, 2012</td>
<td>RRMS</td>
<td>14 mg daily</td>
</tr>
</tbody>
</table>

**Side effects:**
- Flu-like symptoms, headaches
- Leukopenia, anemia, depression, suicide
- Hepatotoxicity, Thyroid dysfunction
- Injection site necrosis with SQ inj
- Neutralizing antibodies, Pregnancy Class: C
- Risk for Depression

**Monitoring:**
- HGB, WBC, LFTs
- TSH/Free T4
- Risk for Depression
- Washout 1 month
- No Washout needed
- Pre-screen: ALT/AST, bilirubin, PPD (TB), HCV, HBV
- Avoid in chronic liver disease
- Then: ALT/AST/bili monthly.

**Effect:**
- ↓Relapses = 30%
- ↓CIS to CDMS = 50%
- ↓Relapses = 54%
- ↓EDSS = 30%
- ↓MRI = 74% (T2), 82% (Gd)
- ↓Relapses = 31%
- ↓EDSS = 30%
- ↓MRI = 67% (T2), 80% (Gd)

**Oral:**
- Bradyarrhythmia, AV block
- Varicella meningoencephalitis
- Macular edema
- Pulmonary function worsening
- Lymphopenia & PML - Transaminitis
- Malignancy risk
- Pregnancy Class: C
- Washout 2 month (t1/2 is one week)
- No Washout needed
- Pre-screen: CBC/LFT’s q6 months, fundus at 6m
- Beware of PML & malignancies
- Pregnancy test
- Pre-screen: LFT’s q6 months, HTN

**Pregnancy Class:**
- C
- X (Men = Women)
- Pregnancy Class: X (Men = Women)
- Washout needed till undetectable
- Oral cholestyramine or activated charcoal
<table>
<thead>
<tr>
<th>Neuro-Pharmacology</th>
<th>Immuno-modulatory Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dimethyl fumarate</strong>&lt;br<em>Tecfidera, 2013</em></td>
<td><strong>Flushing</strong> in 40% (give ASA) <strong>GI upset</strong> in 15% (give with Fatty foods) <strong>Lymphopenia</strong> (30% reduction), <strong>PML</strong> (if lymphocytic count &lt; 500) <strong>Relapses</strong> = 53%, <strong>EDSS</strong> = 38%, <strong>MRI</strong> = 85% (T2), 90% (Gd) <strong>Pregnancy Class:</strong> C - <strong>Washout 1 months</strong></td>
</tr>
<tr>
<td>120 mg BID x 7d then 240 mg BID</td>
<td><strong>Pre-screen:</strong> CBC (lymphs &gt; 1000) <strong>Then:</strong> CBC q6 months, beware PML more likely if lymph &lt; 500</td>
</tr>
<tr>
<td>Activates Nuclear factor-like 2 (Nrf2) pathways involved in cell response to oxid. stress. <strong>↓Relapses</strong> = 53%, <strong>↓EDSS</strong> = 38%, <strong>↓MRI</strong> = 85% (T2), 90% (Gd)</td>
<td><strong>IV infusions:</strong></td>
</tr>
<tr>
<td><strong>Mitoxantrone</strong>&lt;br<em>Novantrone, 2000</em></td>
<td><strong>Cardiotoxicity, Leukemia</strong> <strong>GI upset</strong>, Urine color changes, Bladder infections <strong>PML</strong>, Neutralizing Ab’s <strong>Infusion reactions:</strong> (headache 38%, fatigue 27%, erythema, nausea, dizziness) Hypersensitivity, fatigue, UTI’s, pharyngitis <strong>Washout 6 months</strong></td>
</tr>
<tr>
<td>SPMS (off label)</td>
<td><strong>Pre-screen:</strong> CBC, Echo <strong>Before infusion:</strong> CBC, Echo <strong>Post-dose:</strong> Echo annually for life</td>
</tr>
<tr>
<td>12 mg/m2 IV q3 months x2 yrs Max dose: 140 mg/m2</td>
<td><strong>Natalizumab</strong>&lt;br<em>Tysabri, 2006</em> <strong>Integrin Rc antagonist</strong> Prevents CNS lymphocyte migration through the blood brain barrier (Inhibits binging of ICAM to VCAM) <strong>↓Relapses</strong> = 68%, <strong>↓EDSS</strong> = 42% <strong>↓MRI</strong> = 83% (T2), 92% (Gd) <strong>Increase number of circulating lymphocytes</strong> <strong>Washout 3 months</strong></td>
</tr>
<tr>
<td>300 mg infusion q4w over 1 hour Max dose: 3 yrs</td>
<td><strong>Pre-screen:</strong> Serum JCV Ab w/Index <strong>On-dose:</strong> PML screening, serum JCV Ab every 6m</td>
</tr>
<tr>
<td><strong>Alemtuzumab</strong>&lt;br<em>Lemtrada, 2014</em> <strong>Available only through Lemtrada REMS Program</strong></td>
<td><strong>Infusion reactions:</strong> (headache, flushing) <strong>Autoimmune disorders:</strong> (↓ Platelets in 2%, thyroid dysfunction 3%, anti-glomerular basement membrane disease 0.3%, hemolysis) <strong>Cancer:</strong> Thyroid, melanoma 0.3%, lymphoma <strong>Infection:</strong> HSV/VZV 16% <strong>Washout 6 months</strong></td>
</tr>
<tr>
<td>RRMS who failed 2 drugs</td>
<td><strong>Acyclovir</strong> ppx (for 2 months or till CD4+ count &gt; 200 whichever longer) <strong>Labs:</strong> CBC, CK, UA q1m TSH q3m (up to 2 years after last infusion) <strong>Skin exam yearly</strong></td>
</tr>
<tr>
<td>12 mg IV over 4h daily for 5 days then for 3 days 1 year later. Give steroids with 1st 3 infusions</td>
<td><strong>On dose:</strong> Skin exam yearly for life</td>
</tr>
<tr>
<td><strong>Ocrelizumab</strong>&lt;br<em>Ocrevus, 2017</em> <strong>CD20 blocker</strong> (similar to Rituximab) Depletes B cells via antibody-dependent cell-mediated toxicity and complement-dependent cytotoxicity. Compared to rituximab, induces more ADCC and less CDC, which could reduce infusion-related toxicity <strong>Infusion reactions</strong> (in 34%, serious reactions in 0.3%) <strong>Pregnancy Class:</strong> C - <strong>Washout 3 months</strong></td>
<td></td>
</tr>
<tr>
<td>RRMS PPMS 300mg IV x2 – 2 weeks apart then 600mg IV q6m <strong>Pre-medicate:</strong> steroids and antihistamines</td>
<td><strong>Pre-Screen:</strong> HBV <strong>On dose:</strong> Skin exam yearly for life</td>
</tr>
<tr>
<td>2013 RRMS 120 mg BID x 7d then 240 mg BID</td>
<td></td>
</tr>
</tbody>
</table>
# Neuro-Pharmacology

## How to choose DMT:

1. **According to type of MS:**
   - **RRMS / SPMS**
     - **First line:** Interferons, glatiramer, fingolimod, teriflunomide, dimethyl fumarate, natalizumab, ocrelizumab
     - **Second line:** Daclizumab, alemtuzumab
   - **PPMS**
     - Ocrelizumab

2. **According to pregnancy category:**
   - **Class B**
     - Glatiramer acetate
   - **Class C**
     - Interferons, fingolimod, dimethyl fumarate, natalizumab, alemtuzumab
   - **Class D**
     - Mitoxantrone
   - **Class X**
     - Teriflunomide
   - **Not categorized**
     - Ocrelizumab – Daclizumab

3. **According to form of administration:**
   - **Oral**
     - fingolimod, teriflunomide, dimethyl fumarate
   - **IM**
     - Interferon B1a
   - **SC**
     - Interferon, glatiramer, daclizumab
   - **Infusion**
     - Alemtuzumab, ocrelizumab, natalizumab

## Immuno-modulatory Therapy

### 4- According to side effect profile:

<table>
<thead>
<tr>
<th>DMT</th>
<th>Limiting side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferons</td>
<td>Depression, hepatotoxicity, injection reaction</td>
</tr>
<tr>
<td>Fingolimod</td>
<td>Bradycardia, AV block, macular edema, ↓ WBCs</td>
</tr>
<tr>
<td>Teriflunomide</td>
<td>Alopecia, hepatotoxicity, teratogenicity</td>
</tr>
<tr>
<td>Dimethyl fumar</td>
<td>GI upset, flushing</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>PML risk</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Immune disorders, cancer, HSV/VZV infection</td>
</tr>
<tr>
<td>Ocrelizumab</td>
<td>Infusion related reaction</td>
</tr>
<tr>
<td>Daclizumab</td>
<td>Hepatotoxicity</td>
</tr>
</tbody>
</table>

### 5- According to screening measures needed:

<table>
<thead>
<tr>
<th>DMT</th>
<th>Pre-screening</th>
<th>Follow up labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferons</td>
<td>CBC, LFTs, TSH</td>
<td>CBC, LFTs, TSH Q6 months</td>
</tr>
<tr>
<td>Glatiramer</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Fingolimod</td>
<td>ECG, CBC, VZV, LFT</td>
<td>CBC &amp; LFT Q6 months</td>
</tr>
<tr>
<td>Teriflunomide</td>
<td>HCG, LFT</td>
<td>LFT, BP Q6 months</td>
</tr>
<tr>
<td>Dimethyl fumar</td>
<td>CBC</td>
<td>CBC Q6 months</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>JC Ab titer</td>
<td>JC titer Q6 months</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>CBC, CK, TSH</td>
<td>CBC, CK, UA q1m, TSH q3m</td>
</tr>
<tr>
<td>Ocrelizumab</td>
<td>CBC, HCG, HBV</td>
<td>HCG, HBV, CD19 Q6 months</td>
</tr>
</tbody>
</table>
Tysabri:
Factors that increase risk of PML with natalizumab (Tysabri)

1. **Treatment duration**, if duration > 2 years and:
   a. JCV Ab negative → risk is < 1/1000
   b. JCV Ab positive:
      i. 1-24 months → risk is <1/1000
      ii. 25-48 months → risk is 3/1000
      iii. 49-72 months → risk is 6/1000
   c. Seroconversion rate is 3-6% annually

2. **Prior treatment with immunosuppressants (MTX, cyclophosphamide)**

3. **JCV antibody index**:

<table>
<thead>
<tr>
<th>Antibody Index</th>
<th>1-24 months</th>
<th>25-48 months</th>
<th>49-72 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 0.9</td>
<td>1/10,000</td>
<td>3/10,000</td>
<td>4/10,000</td>
</tr>
<tr>
<td>&lt;= 1.1</td>
<td>1/10,000</td>
<td>7/10,000</td>
<td>7/10,000</td>
</tr>
<tr>
<td>&lt;= 1.3</td>
<td>1/10,000</td>
<td>1/1,000</td>
<td>1.2/1,000</td>
</tr>
<tr>
<td>&lt;= 1.5</td>
<td>1/10,000</td>
<td>1.2/1,000</td>
<td>1.3/1,000</td>
</tr>
<tr>
<td>&gt; 1.5</td>
<td>1/1,000</td>
<td>8.1/1,000</td>
<td>8.5/1,000</td>
</tr>
</tbody>
</table>

Fingolimod:
Modulates sphingosine-1 phosphate subtypes 1 & 3. Subtype 1 reduces lymphocyte recirculation from the lymph nodes. Subtype 3 reduces heart rate and prolongs the PR interval. Cardiac effects of fingolimod are maximal after the first dose but persist for about 14 days after initiation of treatment. *Ozanimod*, *Siponimod* and *Ponesimod* are SP-1p specific subtype 1 modulator that lack the cardiac side effects (still in phase II trials).
### Neuro-Pharmacology

#### Immuno-modulatory Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Rout</th>
<th>MOA</th>
<th>Adverse React.</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cladribine (Mavenclad)</td>
<td>RRMS</td>
<td>Oral (yearly dosing)</td>
<td>Purine nucleoside analogue, incorporated into DNA causing DNA breakage and shutting down DNA synthesis.</td>
<td>Nausea, anorexia, neutropenia (reverse in few weeks), infections.</td>
<td>Approved for RRMS in Europe CLARITY: showed 50% reduction in relapses with no reported malignancy risk.</td>
</tr>
<tr>
<td><strong>Ozanimod</strong></td>
<td>RRMS</td>
<td>Oral</td>
<td>Selective sphingosine-1 Rc agonist modulator (similar to fingolimod but specific to S-1P1 &amp; S-1p5 and spares S-1p3 so spares the heart)</td>
<td>No serious side effects. No macular edema. Mainly headache and pharyngitis</td>
<td>RADIANCE: reduced number of Gd enhancing lesions compared with 11 in placebo after 24w. ARR 0.15 after 72w. Doesn’t prolong QT - Shorter half-life (19h) compared with fingolimod (1w).</td>
</tr>
<tr>
<td>Siponimod</td>
<td>SPMS</td>
<td>Oral</td>
<td>Selective sphingosine-1-P receptor modulator (similar to fingolimod but specific to S-1P1 &amp; S-1p5 and spares S-1p3 so spares the heart)</td>
<td>No serious side effects. No macular edema. Mainly headache and pharyngitis</td>
<td>BOLD</td>
</tr>
<tr>
<td>Ponesimod</td>
<td>RRMS</td>
<td>Oral</td>
<td>Selective sphingosine-1-P receptor modulator (similar to fingolimod but specific to S-1P1 &amp; S-1p5 and spares S-1p3 so spares the heart)</td>
<td>No serious side effects. No macular edema. Mainly headache and pharyngitis</td>
<td>BOLD</td>
</tr>
<tr>
<td>Masitinib AB science</td>
<td>PPMS - SPMS</td>
<td>Oral</td>
<td>Blocks KIT Rc (stem cell Rc), platelet derived growth factor, inhibits mast cell degranulation slowed cognitive decline in Alzheimer.</td>
<td>Nausea, abdominal pain, diarrhea, neutropenia</td>
<td>Masitinib in PPMS, SPMS: still pending</td>
</tr>
<tr>
<td>Laquinimod</td>
<td>RRMS</td>
<td>Oral</td>
<td>Suppresses gene expression related to antigen presentation and inflammation</td>
<td>Abdominal pain, elevated LFT</td>
<td>ARPEGGIO – CONCERTO: pending ALLEGRO: compared with placebo 23% reduction in the ARR (0.30 versus 0.39) and a reduction in disease progression (11.1% versus 15.7%). Marked improvement in EDSS which raise concerns about being neuroprotective.</td>
</tr>
<tr>
<td>Neuro-Pharmacology</td>
<td>Immuno-modulatory Therapy</td>
<td></td>
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<td>--------------------</td>
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<tr>
<td><strong>Idebenone</strong></td>
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<tr>
<td>(Roxane)</td>
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<tr>
<td>Takeda</td>
<td></td>
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</tr>
<tr>
<td>PPMS Oral</td>
<td>Works on reactive oxygen species, increase ATP synthesis, electron transport in cells with depressed mitochondrial functions → approved for Leber optic atrophy in EU.</td>
<td>Fatigue, headache, diarrhea</td>
<td>IPPOMS: pending</td>
<td></td>
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<tr>
<td><strong>Dronabinol</strong></td>
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<tr>
<td>SPMS for spasticity</td>
<td>Cannabinoid receptor agonist Decrease accumulation of cAMP, thought to be neuroprotective. Reduces signs of inflammation in animals.</td>
<td>Amnesia, ataxia, asthenia, euphoria, diarrhea, paranoid reactions</td>
<td>CUPID: not effective CAMS: didn’t affect spasticity but increased patient’s walking speed. Ungerleider et al: improved spasticity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Dose</td>
<td>Effect</td>
<td>Side effects</td>
<td>Monitoring</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------------------------------------------</td>
<td>-------------------</td>
<td>--------------------------------------------------------------------------------</td>
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<tr>
<td><strong>Injections</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>PO (daily): 1-2mg/kg/day</td>
<td>Alkylating agent</td>
<td>Hemorrhagic cystitis, alopecia, infertility</td>
<td>Monthly CBC, UA Daily CBC, UA</td>
<td></td>
</tr>
<tr>
<td>Cytoxan</td>
<td>IV (pulse): 1gm/m² then 600mg/m² every 2 months</td>
<td>interferes with DNA duplication</td>
<td>Infusion reaction: headache, nausea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methyl-prednisone</td>
<td>IV: 1gm/day for 3-5 days</td>
<td>Anxiety, insomnia</td>
<td>BP, FSBS, K</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solumedrol</td>
<td></td>
<td>psychosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVIG</td>
<td>IV: 2gm/kg over 3-5 days then 1gm/kg every 1-2 months</td>
<td>Infusion reaction: hypotension, arrhythmia, flushing</td>
<td>Creatinine – BUN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gammagard</td>
<td></td>
<td>Hypokalemia, gastritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carimune</td>
<td></td>
<td>Nephrotoxicity, aseptic meningitis, blood clots</td>
<td>Avoid Carimune in low GFR patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>IV infusion: 2 doses of 1gm 2weeks apart, Repeated every 6 months</td>
<td>Ab against CD20</td>
<td>Infusion reaction: fatal arrhythmia, angina, hypotension, nausea, flushing PML, HBV reactivation</td>
<td>Screening: Hepatitis panel, CBC, HCG, creatinine Premedication: Tylenol 650, Benadryl 50, Solumedrol 100mg IV Monitoring: Monthly CD19 level by flowcytometry (target &lt;5%) &amp; IgG level (target to keep 30% above LLN)</td>
<td></td>
</tr>
<tr>
<td>Rituxan</td>
<td></td>
<td></td>
<td>&gt;Avoid live vaccines during therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;Non-live vaccines will have reduced efficacy</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;Avoid in HBV infection, active infection</td>
<td></td>
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</tr>
<tr>
<td>Tocilizumab</td>
<td>SC: 162mg weekly with steroid taper</td>
<td>IL-6 Rc blocker</td>
<td>Avoid with active infections, live vaccines.</td>
<td>CBC, LFT after 4Wks then Q3 months ANC: hold if &lt; 1000 – Dc if &lt; 500 Plat: hold if &lt; 100k – Dc if &lt; 50K</td>
<td></td>
</tr>
<tr>
<td>Actemra</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eculizumab</td>
<td>IV Infusion: 900mg weekly x4 then 1200mg q2weeks</td>
<td>Complement CS Ab</td>
<td>High risk for meningococcal infections Risk for encapsulated bacterial infection</td>
<td>Vaccinate for meningococcus before starting Soliris.</td>
<td></td>
</tr>
<tr>
<td>Soliris</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infliximab</td>
<td>IV infusion: 3mg/kg at 0,2,6, 8 weeks then q8weeks</td>
<td>TNF inhibitor</td>
<td>Infusion reactions Increases risk of solid malignancies and infections</td>
<td>Evaluate immunization status (flu, hepatitis B, HPV) Screening: TB (QuantiFERON gold or Tuberculin skin test + Chest X ray), hepatitis panel, HIV, LFT, Cr, CBC, CRF Premedication: Tylenol 650, Benadryl 50, Solumedrol 100mg IV</td>
<td></td>
</tr>
<tr>
<td>Remicade</td>
<td></td>
<td></td>
<td>&gt;Caution in patients with mild HF, demyelinating diseases, at risk of infections (DM, COPD ...)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Neuro-Pharmacology

<table>
<thead>
<tr>
<th>Treatments</th>
<th>PO: 2-3mg/kg/day (QD)</th>
<th>PO: 4-6mg/kg/day (BID)</th>
<th>PO: 1-1.5gm BID (take it the same way in relation to food, either before or after food)</th>
<th>PO: 0.1-0.2mg/kg/day (BID)</th>
<th>PO: 100mg daily for 2wks then EOD for 4wks then gradual taper every 4wks</th>
<th>PO/IM: 7.5mg weekly x 4Wks then 10mg weekly x 4Wks then 15mg weekly, taper steroids after 4 months of MTX.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azathoprine</td>
<td>Inhibits purine synthesis</td>
<td>Calcineurin inhibitor, ↓ cytokines</td>
<td>Inosine-1P-dehyd inhibitor. Inhibits lymphocyte proliferation</td>
<td>Calcineurin inhibitor, ↓ cytokines</td>
<td></td>
<td>Dihydrofolate inhibitor</td>
</tr>
<tr>
<td>Immuran</td>
<td>Hepato-toxicity, Pancreatitis, leukopenia, anemia, risk of malignancy</td>
<td>Nephrotoxicity, hepatotoxicity, hypertension, hirsutism, tremors, gum hyperplasia, malignancy</td>
<td></td>
<td>Nausea, vomiting, abdominal pain, diarrhea Fever, peripheral edema, malignancy (lower risk)</td>
<td></td>
<td>Hepato-toxicity, Pulmonary fibrosis, gastritis, stomatitis, alopecia, infertility</td>
</tr>
<tr>
<td>Cyclosporin</td>
<td>Takes up to 6 months before it shows an effect</td>
<td>Takes up to 6 months before it shows an effect</td>
<td>Takes up to 6 months before it shows an effect</td>
<td>Takes up to 6 months before it shows an effect</td>
<td></td>
<td>Give daily folate (4mg) to reduce side effects</td>
</tr>
<tr>
<td>Sandimmune</td>
<td>Never give with allopurinol (myelotoxic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Pre: test for TPMT activity assay first</td>
<td>Monthly LFT, BUN/Cr, cyclosporine trough level (70–120 µg/l)</td>
<td>Monthly CBC</td>
<td>Monthly BUN/Cr, electrolytes, trough level (weekly x4 then q3months)</td>
<td></td>
<td>Monthly LFT, CBC</td>
</tr>
<tr>
<td>Cellcept</td>
<td>Monthly CBC</td>
<td>BP monitoring</td>
<td>BP monitoring</td>
<td>BP monitoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tacrolimus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prograf, Protopic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Immuno-modulatory Therapy

- Avoid in patients with moderate/severe HF, hematological or solid malignancy, active systemic infection, untreated latent TB
- Live vaccines: contraindicated with anti-TNF agents
- Monitoring: CBC, ALT, Cr before infusions- Annual TB testing

### Side Effects

- Hepato-toxicity
- Pancreatitis
- Leukopenia
- Anemia
- Nephrotoxicity
- Hypertension
- Hirsutism
- Tremors
- Gum hyperplasia
- Nausea
- Vomiting
- Abdominal pain
- Diarrhea
- Fever
- Peripheral edema
- Malnutrition
- Hypertension
- Electrolyte imbalance
- Mg imbalance
- Tremors
- Nausea
- Vomiting
- Abdominal pain
- Diarrhea
- Fever
- Peripheral edema
- Malnutrition
- Hypertension
- Electrolyte imbalance
- Mg imbalance
- Tremors
- Nausea
- Vomiting
- Abdominal pain
- Diarrhea
- Fever
- Peripheral edema
- Malnutrition
- Hypertension
- Electrolyte imbalance
- Mg imbalance
- Tremors

### Monitoring

- CBC, ALT, Cr before infusions
- Annual TB testing

### Additional Information

- Taper steroids after 4 months of MTX.
- Give daily folate (4mg) to reduce side effects.
- Liver biopsy at 2gm accumulative dose.

### Other Side Effects

- Anxiety, insomnia, psychosis
- Hyponatremia, hypokalemia, gastritis
- Hyperglycemia
- Hypokalemia
- Gastritis
- Stomatitis
- Alopecia
- Infertility

### Monitoring

- BP, FSBS, K, body weight, Dexascan, monitor for cataract formation.
### Neuro-Pharmacology

**Preferred agents:**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Chronic (maintenance) immunotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIDP</td>
<td>Steroids, azathioprine, mycophenolate, cyclosporine</td>
</tr>
<tr>
<td>MMN</td>
<td>Monthly IVIG, rituximab, cyclophosphamide</td>
</tr>
<tr>
<td>Anti-Mag</td>
<td>Rituximab, cyclophosphamide</td>
</tr>
<tr>
<td>Polymyositis</td>
<td>Steroids, azathioprine, rituximab</td>
</tr>
<tr>
<td>Myasthenia</td>
<td>Steroids, azathioprine, mycophenolate, cyclosporine, eculizumab (if AChR positive), rituximab</td>
</tr>
<tr>
<td>NMO</td>
<td>Rituximab, mycophenolate, azathioprine, eculizumab (mayo clinic trial)</td>
</tr>
<tr>
<td>Paraneoplastic</td>
<td>Steroids, monthly IVIG, rituximab</td>
</tr>
<tr>
<td>GCA (arteritis)</td>
<td>Steroids – add tocilizumab if steroid resistant</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Steroids, methotrexate, azathioprine, cyclophosphamide, infliximab</td>
</tr>
</tbody>
</table>

**Pregnancy category:**

<table>
<thead>
<tr>
<th>Class</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class B</td>
<td>Infliximab</td>
</tr>
<tr>
<td>Class C</td>
<td>Rituximab, Steroids, IVIG, Cyclosporine, Tacrolimus</td>
</tr>
<tr>
<td>Class D</td>
<td>Cyclophosphamide, Azathioprine, Mycophenolate</td>
</tr>
<tr>
<td>Class X</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Not assigned</td>
<td>Tocilizumab</td>
</tr>
</tbody>
</table>

### Immuno-modulatory Therapy

**Rituximab:**
- Used for: CIDP, Anti-Mag, MMN, inflammatory myopathies, Myasthenia gravis, RRMS, NMO & paraneoplastic syndromes.
- Phase I and II studies on rituximab for MS patients showed marked success, however manufacturer didn’t seek FDA approval
- Infusion related reaction are thought to be related to its cytolytic effect on CD20 cells with release of cytokines

**Eculizumab:**
- Approved in U.S. for seropositive generalized MG, however it is used mainly for treatment-resistant MG (failed 2 immunomodulating agents).
- Don’t stop other immunomodulating agents, rather taper them gradually to lowest possible dose once symptoms are controlled.

**Tocilizumab:**
- Used for giant cell arteritis that is either steroid-resistant or steroid-intolerant patients.
- Steroid is the mainstay for initial treatment, if tocilizumab is needed then it is added to steroids then steroids can be tapered down typically over 6 months.

**Infliximab:**
- Used for steroid-resistant sarcoidosis
- Don’t stop other immunomodulating agents, rather keep patients on lowest possible dose (5mg prednisone and 50mg azathioprine).
- Main concerns while on treatment are risk of infection and malignancy. Periodically screen for systemic infections & malignancy.
**Rituximab Protocol**

**Indication:**
- [] Relapsing remittent MS
- [] Neuromyelitis Optica
- [] Myasthenia Gravis
- [] CIDP
- [] Inflammatory myopathy
- [] Paraneoplastic neurological disorders

**Screening labs:**
- [] HCG (for women)
- [] Hepatitis B screen
- [] CBC with differential
- [] Creatinine, BUN
- [] CD19 flow cytometry

**Pre-medicate patient with:**
- [] Acetaminophen 650mg PO
- [] Benadryl 50mg IV
- [] Solumedrol 100mg IV

**Administration:**

**Dose:** 1000mg Rituximab (Rituxan) in 250ml of NS

**First infusion:** start at 50ml/h then increase by 50ml/hr every 30 minutes to target of 400mg/hr. Slow infusion if patient developed mild infusion reactions (nausea, flushing, mild hypotension), stop if patient developed severe infusion reactions (marked drop in BP, arrhythmia, chest pain).

**Next infusions:** start at 100mg/hr and increase by 100mg/hr every one hour to target of 400mg/hr. Slow infusion if patient developed mild infusion reactions (nausea, flushing, mild hypotension), stop if patient developed severe infusion reactions (marked drop in BP, arrhythmia, chest pain).

**Timing after starting infusion**

<table>
<thead>
<tr>
<th>Timing after starting infusion</th>
<th>Total dose given so far</th>
<th>Increase Infusion rate to</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 minute (start time)</td>
<td>0 mg</td>
<td>Start at 50mg/hr</td>
</tr>
<tr>
<td>30 minutes</td>
<td>25mg</td>
<td>100mg/hr</td>
</tr>
<tr>
<td>60 minutes</td>
<td>75mg</td>
<td>150mg/hr</td>
</tr>
<tr>
<td>1.5 hr</td>
<td>150mg</td>
<td>200mg/hr</td>
</tr>
<tr>
<td>2 hr</td>
<td>250mg</td>
<td>250mg/hr</td>
</tr>
<tr>
<td>2.5 hr</td>
<td>325mg</td>
<td>300mg/hr</td>
</tr>
<tr>
<td>3 hr</td>
<td>425mg</td>
<td>350mg/hr</td>
</tr>
<tr>
<td>3.5 hr</td>
<td>650mg</td>
<td>400mg/hr</td>
</tr>
<tr>
<td>4 hr</td>
<td>850mg</td>
<td>400mg/hr</td>
</tr>
<tr>
<td>4hr 22 minutes</td>
<td>1000mg</td>
<td>Stop</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Timing after starting infusion</th>
<th>Total dose given so far</th>
<th>Increase Infusion rate to</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 minute (start time)</td>
<td>0 mg</td>
<td>Start at 100mg/hr</td>
</tr>
<tr>
<td>30 minutes</td>
<td>50mg</td>
<td>200mg/hr</td>
</tr>
<tr>
<td>60 minutes</td>
<td>150mg</td>
<td>300mg/hr</td>
</tr>
<tr>
<td>1.5 hr</td>
<td>300mg</td>
<td>400mg/hr</td>
</tr>
<tr>
<td>2 hr</td>
<td>500mg</td>
<td>400mg/hr</td>
</tr>
<tr>
<td>2.5 hr</td>
<td>700mg</td>
<td>400mg/hr</td>
</tr>
<tr>
<td>3 hr</td>
<td>900mg</td>
<td>400mg/hr</td>
</tr>
<tr>
<td>3hr 15 minutes</td>
<td>1000mg</td>
<td>Stop</td>
</tr>
</tbody>
</table>
# Migraine Preventive Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual Effective Dose</th>
<th>Mechanism</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CGRP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erenumab (Aimovig)</td>
<td>70mg subcutaneous monthly</td>
<td>CGRP receptor antagonist</td>
<td>Injection site reaction</td>
</tr>
<tr>
<td>Galcanezumab (Emgality)</td>
<td>240mg initial then 120mg subcutaneous monthly</td>
<td>CGRP ligand antagonist</td>
<td>Injection site reaction</td>
</tr>
<tr>
<td>Fremanezumab (Ajovy)</td>
<td>225mg SC monthly or 675mg SC every 3 months</td>
<td>CGRP ligand antagonist</td>
<td>Injection site reaction</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topiramate</td>
<td>50mg BID</td>
<td>VG Na Channel blocker ↑ GABA-A Rc activity ↓ AMPA Rc (glutamate Rc)</td>
<td>Naming and cognitive impairment - Weight loss – kidney stones</td>
</tr>
<tr>
<td>Valproate</td>
<td>500-1000mg BID</td>
<td>Sodium channel blocker</td>
<td>Sedation – weight gain – PCOS – teratogenic</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>50-150mg QHS</td>
<td>Tricyclic antidepressant</td>
<td>Sedation, dry mouth, weight gain</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>75-150mg daily (ER)</td>
<td>Selective serotonin norepinephrine reuptake inhibitor</td>
<td>Nausea - weight loss - elevated blood pressure</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>30-60mg daily</td>
<td>Selective serotonin norepinephrine reuptake inhibitor</td>
<td>Nausea - weight loss - elevated blood pressure</td>
</tr>
<tr>
<td><strong>BP medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nadolol</td>
<td>160-240mg Daily</td>
<td>Nonspecific beta blocker</td>
<td>Depression, dizziness, bradycardia</td>
</tr>
<tr>
<td>Losartan</td>
<td>4-8 mg Daily</td>
<td>Angiotensin receptor blocker</td>
<td>Dizziness – muscle cramps</td>
</tr>
<tr>
<td><strong>Antihistamines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>2-4mg TID</td>
<td></td>
<td>Sedation – weight gain</td>
</tr>
<tr>
<td><strong>Supplements</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td>500mg TID</td>
<td></td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>50-100 mg daily</td>
<td></td>
<td>Urine discoloration (orange color)</td>
</tr>
</tbody>
</table>
# Neuro-Pharmacology

## CGRP ANTAGONISTS

**Mechanism:**
Calcitonin gene-related protein is a potent vasodilator protein secreted by the neurons in the trigeminal ganglia through their nerve endings in the meninges. CGRP can induce migraine attacks when injected in patients with migraine.

**Side effects:**
Injection site reactions, otherwise it is very well tolerated

### CGRP drugs approved by FDA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation/Dose</th>
<th>Mechanism</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erenumab (Aimovig)</td>
<td>Syringe 70mg subcutaneous monthly</td>
<td>CGRP receptor antagonist</td>
<td>Headache days: ↓ 2.5 days/month &gt; 50% intensity reduction: in 17% more than placebo</td>
</tr>
<tr>
<td>Galcanezumab (Emgality)</td>
<td>Syringe 240mg initial then 120mg subcutaneous monthly</td>
<td>CGRP ligand antagonist</td>
<td>Headache days: ↓ 2 days/month &gt; 50% intensity reduction: in 20% more than placebo MSQ increase from Placebo: 7.7</td>
</tr>
<tr>
<td>Fremanezumab (Ajovy)</td>
<td>Syringe 225mg SC monthly or 675mg SC every 3 months</td>
<td>CGRP ligand antagonist</td>
<td>Headache days: ↓ 2.1 days/month &gt; 50% intensity reduction: in 20% more than placebo</td>
</tr>
</tbody>
</table>

### CGRP drugs in progress

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Company</th>
<th>Mechanism</th>
<th>Stage</th>
<th>Expected FDA filing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rimegepant</td>
<td>Oral</td>
<td>Biohaven</td>
<td>CGRP receptor antagonist</td>
<td>Phase III</td>
<td>2019</td>
</tr>
<tr>
<td>Eptinezumab</td>
<td>Intravenous</td>
<td>Alder</td>
<td>CGRP ligand antagonist</td>
<td>Phase III</td>
<td>2019</td>
</tr>
<tr>
<td>Atogepant</td>
<td>Oral (prophylactic)</td>
<td>Allergan</td>
<td>CGRP receptor antagonist</td>
<td>Phase III</td>
<td>2019</td>
</tr>
<tr>
<td>Ubrogepant</td>
<td>Oral (acute migraine)</td>
<td>Allergan</td>
<td>CGRP receptor antagonist</td>
<td>Phase III</td>
<td>2019</td>
</tr>
<tr>
<td>Neuro-Pharmacology</td>
<td>Migraine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Neuro-Pharmacology**

**Migraine**

### Triptans

**Mechanism:** Triptans (5HT 1b/1d agonists → inhibit release of CGRP & sub P → inhibit meningeal vasodilatation and trigeminal activation)

**Side effects:** Vasoconstriction - Chest tightness

**Precautions:** Avoid in: CAD – Arrhythmia - Peripheral vascular disease - Basilar or hemiplegic migraine - With ergots/MAOI/SSRI - Pregnancy

**Rapidly acting Triptans:**
- Non-oral: Nasal (sumatriptan – zolmitriptan) – SC (sumatriptan)
- Fast acting oral: Eletriptan – Rizatriptan – Zolmitriptan
- Add prokinetic: Sumatriptan + Domperidone

**Long acting Triptans:**
- Best for recurrent or long headaches, also least in side effects: Frovatriptan (26h) – Almotriptan (4h) – Naratriptan (6h)

**Nausea with Triptans, use:**
- Non-oral: Nasal (sumatriptan – zolmitriptan) – SC (sumatriptan)
- Dissolving wafers: Sumatriptan – Zolmitriptan
- Add anti-emetic: domperidone – prochlorperazine

### Formulations

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation/Dose</th>
<th>T-half</th>
<th>Response (headache relief at 2h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan</td>
<td>(Imitrex) Tab 25, 50, 100 mg</td>
<td>2h</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>(Imitrex Nasal Spray) Nasal spray 20 mg</td>
<td>1h</td>
<td>30-55%</td>
</tr>
<tr>
<td></td>
<td>(Onzetra Xsail) Nasal powder 22 mg</td>
<td>15min</td>
<td>15-25%</td>
</tr>
<tr>
<td></td>
<td>(Imitrex Statdose) SC 6mg</td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td>(Zomig) Tab 2.5, 5mg</td>
<td>1-2h</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>(Zomig-ZMT) Dissolving wafer 5mg</td>
<td></td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td>(Zomig-nasal spray) Intranasal spray 5mg</td>
<td></td>
<td>40%</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>(Maxalt) Tab 10mg</td>
<td>1h</td>
<td>30-40%</td>
</tr>
<tr>
<td></td>
<td>(Maxalt-MLT) Dissolving wafer 10mg</td>
<td></td>
<td>20-40%</td>
</tr>
<tr>
<td>Eletriptan</td>
<td>(Relpax) Tab 40mg</td>
<td>1h</td>
<td>20-40%</td>
</tr>
<tr>
<td>Naratriptan</td>
<td>(Amerge) Tab 2.5mg</td>
<td>2h</td>
<td>20%</td>
</tr>
<tr>
<td>Frovatriptan</td>
<td>(Frova) Tab 2.5mg</td>
<td>2h</td>
<td>20%</td>
</tr>
<tr>
<td>Almotriptan</td>
<td>(Axert) Tab 12.5mg</td>
<td>2h</td>
<td>20-30%</td>
</tr>
<tr>
<td>Sumatriptan + Naproxen</td>
<td>(Treximet) Tab 85/500mg</td>
<td>2h</td>
<td>50%</td>
</tr>
</tbody>
</table>
**NSAIDs**

**Mechanism:** Cyclo-oxygenase inhibitors → Inhibit prostaglandin synthesis which is the main pain mediator

**Side effects:** Medication overuse headache – Rebound headache – gastritis – asthma exacerbation (COX1 inhibitors) – interfere with platelet functions

**Precautions:** Avoid in: peptic ulcer patients – severe asthma

**Rapidly acting:** Best for brief severe headache: Cambia (Diclofenac packets)

**Gastritis:** COX2 selective: Meloxicam

**Combinations:** Vimovo (Naproxen/Esomeprazole) – Duexis (Ibuprofen/Famotidine) – Arthrotec (Diclofenac sodium + misoprostol tab)

### Formulations

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation/Dose</th>
<th>Price</th>
<th>OTC/Prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen Sodium</td>
<td>Tab 250 – 500mg</td>
<td>OTC &amp; Prescription</td>
<td></td>
</tr>
<tr>
<td>Anaprox</td>
<td>Tab 250 – DS tab 500mg</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Naprelan</td>
<td>Tab 375, 500, 750mg</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Naprosyn</td>
<td>Tab 250, 375, 500 - Susp (25mg/ml)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Naproxen</td>
<td>Tab 250, 375, 500 - Susp (25mg/ml)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Combinations</td>
<td>Naxproen/Somprazole (500/20mg)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Naproxen sodium/Sumatriptan tab (60/10mg) or (500/85mg)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Ibuprofen Sodium</td>
<td>Tab 200mg</td>
<td>OTC</td>
<td></td>
</tr>
<tr>
<td>Advil (Ibuprofen Sodium)</td>
<td>Tab 200mg</td>
<td>OTC</td>
<td></td>
</tr>
<tr>
<td>Ibuprofen (acid)</td>
<td>Liquid gels 200mg – Chewable tab (50, 100mg) - Susp (20mg/ml)</td>
<td>OTC</td>
<td></td>
</tr>
<tr>
<td>Combinations</td>
<td>IV infusion 400mg vial (over 30 minutes)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ibuprofen/Famotidine tab (800/26mg)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Diclofenac Sodium</td>
<td>Tab 50, 75mg</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Dyloject</td>
<td>IV injection 37.5mg vial (over 15 seconds)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Diclofenac Potassium</td>
<td>Cambia Packets 50mg (mix in 30ml of water)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Diclofenac Epolamine</td>
<td>Tab 50mg</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Combinations</td>
<td>Patch (180mg) daily</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac sodium + misoprostol tab (50/0.2mg)</td>
<td>Prescription</td>
<td></td>
</tr>
<tr>
<td>Neuro-Pharmacology</td>
<td>Migraine</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Parkinsonism Medications (Motor Manifestations)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Initial dosage</th>
<th>Max dose</th>
<th>Indications/Precautions</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopamine</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td><strong>LevoDopa/Carbidopa</strong></td>
<td>Sinemet tab (10/100 – 25/100 – 25/250)</td>
<td>25/100 half tab TID</td>
<td>25/250 per day</td>
<td>- Take 30m before food  - Sudden interruption will cause hyperpyrexia and delirium  - Caution in patients with arrhythmia</td>
<td>Common Dopaminergic Side Effects Falling asleep during ADL – Impulse control disorders – Hallucination/confusion – Dyskinesia - Nausea – Dizziness - Constipation - Orthostatic hypotension – Anxiety - Confusion - Hallucination – Dyskinesia</td>
</tr>
<tr>
<td></td>
<td>Parcopa ODT tab (10/100 – 25/100 – 25/250)</td>
<td>25/100 half tab TID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sinemet CR tab (25/100 – 50/200)</td>
<td>25/100 BID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rytari ER capsules</td>
<td>23.75/95 TID</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>MAO B inhibitors</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Selegellin</td>
<td>Eldepryl – Carbex tab (5mg)</td>
<td>5mg BID</td>
<td>5mg BID</td>
<td>Adjunct to levodopa (patients with long Off periods)</td>
<td>Dopaminergic Side Effects (as Sinemet)</td>
</tr>
<tr>
<td></td>
<td>Zelapar ODT (1.25mg)</td>
<td>1.25 mg Daily</td>
<td>1.25mg Daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rasagellin</td>
<td>Azilect tab (0.5 – 1 mg)</td>
<td>0.5mg Daily</td>
<td></td>
<td>Adjunct to levodopa or monotherapy</td>
<td>Dopaminergic Side Effects (as Sinemet)</td>
</tr>
<tr>
<td><strong>Safinamide</strong></td>
<td>Xadago tab (50 – 100 mg)</td>
<td>50mg daily</td>
<td>100mg daily</td>
<td>Adjunct to levodopa for patients with Off periods</td>
<td>Dopaminergic Side Effects (as Sinemet) Less dyskinesia</td>
</tr>
<tr>
<td><strong>COMT inhibitors</strong></td>
<td>Comtan tab (200mg)</td>
<td>200mg with each dose of levodopa</td>
<td>8 Tab per day</td>
<td>Adjunct to levodopa (patients with long Off periods)</td>
<td>Dopaminergic Side Effects (as Sinemet) + Diarrhea – Abdominal pain – Orange colored urine</td>
</tr>
<tr>
<td><strong>Dopamine agonists</strong></td>
<td>Apokyn solution (10 mg/mL) with multi-use injector.</td>
<td>0.2 ml daily prn then TID prn off state</td>
<td>0.6 ml (6mg) PRN</td>
<td>Antiemetic trimethobenzamide (300 mg three times a day) should be started 3 days prior to the initial dose of Apokyn</td>
<td>Dopaminergic Side Effects (as Sinemet) + Hallucinations – Impulse control disorders - Dyskinesia (20%) – Angina/MI (4%) – QTc prolongation</td>
</tr>
<tr>
<td>Neuro-Pharmacology</td>
<td>Parkinsonism</td>
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<tr>
<td><strong>Bromocriptine</strong></td>
<td>Parlodel tab (2.5mg – 5mg) 2.5mg TID</td>
<td>Dopaminergic Side Effects (as Sinemet)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pramipexole</strong></td>
<td>Mirapex tab (.125, .25, .5, 1, 1.5 mg) Pramipex ER tab (.375, .75, 1.5, 3, 4.5 mg) 0.125mg TID 0.375mg daily 4.5mg/day</td>
<td>Dopaminergic Side Effects (as Sinemet) + Hallucinations – impulse control disorder – irresistible sleepiness – leg edema</td>
<td></td>
<td></td>
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<tr>
<td><strong>Ropinirole</strong></td>
<td>Requip tab (.25, .5, 1, 2, 3, 4.5 mg) Requip XL tab (2.4, 6, 8, 10, 12, 14, 16, 18, 20, 24 mg) 0.25mg TID 2mg daily 24mg/day</td>
<td>Binds to Melanin in animals, longer duration in patients with darker skin. Same as pramipexole</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Rotigotine</strong></td>
<td>Neupro patches (1, 2, 4, 6, 8 mg patches) 2mg patch daily 8mg/24h</td>
<td>Avoid in sulfite allergic patients Same as pramipexole (less severe)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Anticholinergics</strong></td>
<td></td>
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<tr>
<td><strong>Benzztropine</strong></td>
<td>Cogentin tab 0.5mg 0.5mg BID 6mg /day</td>
<td>Confusion – Hallucination – Dry mouth – Blurred vision – Urine retention</td>
<td></td>
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<tr>
<td><strong>Other Medications</strong></td>
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<tr>
<td><strong>Amantadine</strong></td>
<td>Symmetrel tab 100mg 100mg BID 400mg/day</td>
<td>Caution in patients with seizures, RF or CHF Suicide ideations – Lowers seizure threshold – Confusion – Hallucinations - Nausea – Dizziness – Insomnia – Dry mouth – Peripheral edema – Livedo reticular</td>
<td></td>
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<tr>
<td><strong>Amantadine ER</strong></td>
<td>Gocovri capsule 68.5, 137mg 137mg QHS x 7d then 274mg HS 274mg QHS 129mg QAM 274mg QHS 322mg QAM</td>
<td>Caution in patients with seizures, RF or CHF Same as amantadine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Carbidopa/Levodopa/Entacapone</strong></td>
<td>Stalevo tab (12.5/50/200 – 18.75/75/200 – 25/100/200 – 37.5/150/200 – 50/200/200) as Sinemet</td>
<td>as Sinemet</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Symptom</td>
<td>Drug of choice</td>
<td>Max dose</td>
<td>Side effects</td>
<td>Notes</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------</td>
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</tr>
<tr>
<td><strong>Neurogenic orthostatic hypotension (NOS)</strong></td>
<td><strong>Droxidopa</strong> (Northera tab 100, 200, 300 mg)</td>
<td>600mg TID</td>
<td>Supine hypertension (monitor supine BP) – Nausea – Dizziness</td>
<td>Mechanism: norepinephrine precursor ↑ symptoms of Ischemic heart disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Midodrine</strong> (ProAmatine 2.5, 5, 10mg)</td>
<td>10mg TID</td>
<td>Supine hypertension (monitor supine BP) – paresthesia – piloerection</td>
<td>Mechanism: α1 agonist (don’t give at night to avoid supine hypertension)</td>
<td></td>
</tr>
<tr>
<td><strong>Psychosis</strong> (hallucinations/delusions)</td>
<td><strong>Pimavanersin</strong> (Nuplazid tab 17mg)</td>
<td>34mg daily (two tabs)</td>
<td>Peripheral edema – Confusion</td>
<td>Atypical antipsychotic (inverse agonist and antagonist activity at serotonin 5-HT2A)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Quetiapine</strong> (Seroquel 25, 50, 100)</td>
<td></td>
<td>Agranulocytosis – QT prolongation – Hypothyroidism - Tardive dyskinesia</td>
<td>Atypical antipsychotic</td>
<td></td>
</tr>
<tr>
<td><strong>Dementia</strong></td>
<td><strong>Rivastigmine</strong> (Exelon cap 1.5,3,4,5,6mg) (Exelon patch 10, 20)</td>
<td>6mg BID</td>
<td>Nausea – Loss of appetite – Weight loss</td>
<td>Acetylcholinesterase inhibitors</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Donepezil</strong> (Aricept tab 5,10,23 mg) (Aricept ODT 5,10mg)</td>
<td>23mg daily</td>
<td>Bradycardia – Heart block – Nausea – Vomiting – Diarrhea – Worsens GERD/PU – Worsens asthma/COPD</td>
<td>Start with 5mg qhs for 4 weeks then 10mg. The 23mg tab shouldn’t be used till the patient has been on 10mg for 3 months.</td>
<td></td>
</tr>
<tr>
<td><strong>REM behavior disorder</strong></td>
<td><strong>Clonazepam</strong> (Klonopin 0.5,1,2mg qhs)</td>
<td></td>
<td></td>
<td>Anti-muscarin that doesn’t cross BBB</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Melatonin</strong> 3,6mg qhs</td>
<td></td>
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</tr>
<tr>
<td><strong>RLS/PLM</strong></td>
<td><strong>Dopamine agonists</strong> (Pramipexole, Ropinirole, Rotigotine)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td><strong>Opioids, Gabapentin, Clonazepam</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>Drooling</strong></td>
<td><strong>Glycopyrrolate</strong> (Robinul tab 1, 2 mg)</td>
<td>2mg TID</td>
<td>Anticholinergic side effects</td>
<td>Anti-muscarin that doesn’t cross BBB</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Ipratropium bromide</strong> (Atrovent spray)</td>
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<tr>
<td></td>
<td><strong>Clonidine</strong></td>
<td></td>
<td></td>
<td>α1 agonist</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Modafinil</strong></td>
<td></td>
<td></td>
<td>α2 agonist</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Botox injection in salivary glands</strong></td>
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</tbody>
</table>
### Neuro-Pharmacology

#### Management of motor Symptoms:

<table>
<thead>
<tr>
<th>Situation</th>
<th>Approach</th>
</tr>
</thead>
</table>
| **Initiating treatment** | Mild symptoms: MAO-B or Dopa agonist  
Marked symptoms: Sinemet ½ tab 25/100 TID                                                   |
| **Marked tremors** | Add Cogentin if young patient (< 60)  
Increase Sinemet if older patient (>60)                                                   |
| **Wearing off (<2h)** | ↑ dosing frequency – use Rytari - add COMT or MAO-B – add Dopa agonist.               |
| **Delayed On (>20min)** | Sinemet before meals – suspension of crushed Sinemet – domperidone                        |
| **Dyskinesia**     | ↑ dosing frequency – use Rytari  
Add amantadine (Gocovri or Osmolex)  
Duodopa, apomorphine pump or DBS                                                             |

#### Management of non-motor symptoms:

<table>
<thead>
<tr>
<th>Situation</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychosis</strong></td>
<td>↓ anticholinergics, amantadine then Dopa agonists. Add pimivanersin or quetiapine.</td>
</tr>
</tbody>
</table>
| **Orthostasis**       | If related to Dopa -> ↑ dosing frequency  
If not related -> ↑ fluids, add droxidopa                                                        |
| **RBD (REM behavior disorder)** | Melatonin is first choice then clonazepam                                                   |
| **ICD (impulse control disorder)** | ↓ dopaminergic agents, quetiapine, CBT                                                     |

#### Rytari dose calculation:

<table>
<thead>
<tr>
<th>Total L-dopa dose</th>
<th>Rytari conversion</th>
<th>Rytari L-dopa dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>400-549mg</td>
<td>23.75/95 3capsules TID</td>
<td>866mg</td>
</tr>
<tr>
<td>550-749mg</td>
<td>23.75/95 4capsules TID</td>
<td>1140mg</td>
</tr>
<tr>
<td>750-949mg</td>
<td>36.25/145 3 capsules TID</td>
<td>1305mg</td>
</tr>
<tr>
<td>950-1249mg</td>
<td>48.75/195 3 capsules TID</td>
<td>1755mg</td>
</tr>
<tr>
<td>&gt;1250mg</td>
<td>48.75/196 4 capsules TID</td>
<td>2340mg</td>
</tr>
</tbody>
</table>

**Example:** patient currently takes Sinemet 50/200 tablet QID → total daily L-dopa dose is 800mg → Rytari equivalent is 36.25/145 3 capsules TID.

### Parkinsonism

#### Rotigotine (Neupro):
- Advantage: No interaction with meals, no adjustment for mild-moderate hepatic disease, no adjustment for renal impairment,
- Application: use different spot every day, avoid using in same spot more than once every 14 days. It should be pressed firmly in place for 30 seconds after application.

#### Entacapone:
- COMT and non-selective MAO inhibitors (Phenelzine “Nardil” – tranylcypromine “Parnate”) can’t be given together, they will prevent catecholamine metabolism.
- Be cautious when administering epinephrine, norepinephrine, dopamine, dobutamine or alpha-methylldopa in patients taking COMT inhibitor.
- Diarrhea present in 10% of patients on Entacapone due to lymphocytic activation causing microscopic colitis. Usually starts after 4 weeks of initiation of therapy.
Adverse effects associated with dopaminergic medications:

All dopaminergic medications cause:
- **Impulse control disorders** (urge to gamble, have sex, and to spend money), sudden falling asleep during ADL (as driving or working on machinery), confusion & hallucination.
- **Dopamine dysregulation syndrome**: craving for dopaminergic medications. Patient will self-administer extra doses, if can’t get more medications then patient will simulate worsening symptoms to get more medications otherwise will go in aggressive outburst (addiction for dopamine).
- **Dopamine agonist withdrawal syndrome (DAWS)**: may occur with abrupt discontinuation of dopamine agonists. It manifests with lack of energy, anxiety, insomnia, dysphoria and depression that may persist for months or years. Symptoms are not controlled with increasing L-dopa or antidepressants. Only dopamine agonists restitution may help.

MAOI cause:
- **Serotonin syndrome** if given with: opioids (e.g., meperidine and its derivatives, methadone, tramadol); SNRIs; TCAs; cyclobenzaprine; methylphenidate, amphetamine; or St John’s wort.
- **Psychosis** if given with dextromethorphan.

Augmentation, tolerance and rebound in restless leg syndrome:
- **Tolerance**: patient requires increasing doses to get the same effect.
- **Rebound**: marked worsening of symptoms by the end of the dose effect
- **Augmentation**: Patient develops worsening of symptoms with the medication. Observed only with dopaminergic therapy for RLS (dopamine agonists and Levodopa). Management is a dopaminergic holiday of at least 3 months.
<table>
<thead>
<tr>
<th>Neuro-Pharmacology</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dementia Medications</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Cholinesterase Inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Donepezil</strong></td>
<td>Aricept:</td>
</tr>
<tr>
<td><strong>Formulation</strong></td>
<td>Tab (5, 10, 23 mg)</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>ODT (5, 10 mg)</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>5mg QHS, increase to 10mg after 4 weeks</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>Can be increased to 23mg/day in severe dementia</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td>-Causes hypotension &gt; take at bedtime</td>
</tr>
<tr>
<td></td>
<td>-Lowers seizure threshold</td>
</tr>
<tr>
<td></td>
<td>-Caution in patients with Peptic ulcer</td>
</tr>
<tr>
<td></td>
<td>-Caution in patients with COPD</td>
</tr>
<tr>
<td></td>
<td>-Caution in patients with arrhythmia</td>
</tr>
<tr>
<td></td>
<td>-Increases QT interval</td>
</tr>
<tr>
<td></td>
<td>-Causes delayed recovery after succinylcholine anesthesia</td>
</tr>
<tr>
<td></td>
<td>-Nausea, vomiting, diarrhea, colic</td>
</tr>
<tr>
<td></td>
<td>-Headache, insomnia</td>
</tr>
<tr>
<td></td>
<td>-Syncope</td>
</tr>
<tr>
<td><strong>Rivastigmine</strong></td>
<td>Exelon:</td>
</tr>
<tr>
<td><strong>Formulation</strong></td>
<td>Tab (1.5, 3, 4.5, 6 mg)</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>Patch (4.6,9.5,13.3 mg)</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Tab: 1.5mg BID, increase q2weeks, max 6mg BID</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>Patch: 4.6 mg daily, increase every 4 weeks</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td>Tab → patch conversion:</td>
</tr>
<tr>
<td></td>
<td>Tab &lt; 6mg/day → 4.6mg patch</td>
</tr>
<tr>
<td></td>
<td>Tab &gt; 6mg/day → 9.5mg patch</td>
</tr>
<tr>
<td></td>
<td>-Caution in patients with Peptic ulcer</td>
</tr>
<tr>
<td></td>
<td>-Caution in patients with COPD</td>
</tr>
<tr>
<td></td>
<td>-Caution in patients with Sick Sinus Syndrome</td>
</tr>
<tr>
<td></td>
<td>-Causes delayed recovery after succinylcholine anesthesia</td>
</tr>
<tr>
<td></td>
<td>-Nausea, vomiting, diarrhea, colic</td>
</tr>
<tr>
<td></td>
<td>-Headache, insomnia, nightmares</td>
</tr>
<tr>
<td><strong>NMDA antagonists</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Memantine</strong></td>
<td>Namenda:</td>
</tr>
<tr>
<td><strong>Formulation</strong></td>
<td>Tab (5, 10 mg)</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>ER Cap (7,14,21,28 mg)</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Solution (2mg/ml)</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>Tab: 5mg daily, increased weekly to 20mg QD</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td>-Headache, Dizziness, Confusion</td>
</tr>
<tr>
<td></td>
<td>-Constipation</td>
</tr>
<tr>
<td></td>
<td>-Doesn’t lower seizure threshold</td>
</tr>
<tr>
<td></td>
<td>-Nausea, Dizziness</td>
</tr>
<tr>
<td></td>
<td>-Renal constipation</td>
</tr>
<tr>
<td></td>
<td>-Headache, Confusion</td>
</tr>
</tbody>
</table>
## Drugs for Symptomatic treatment in Dementia & Neurodegenerative diseases

<table>
<thead>
<tr>
<th>Agitation/Depression •</th>
<th>Citalopram</th>
<th>Celexa: Tab (10, 20, 40mg)</th>
<th>10mg daily – Max 20mg daily</th>
<th>QT prolongation, Suicidal ideation</th>
<th>CNS: insomnia – drowsiness</th>
<th>Bleeding: impairs platelet functions</th>
<th>CVS: QT prolongation, Orthostatic hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Withdrawal symptoms: Taper down over several weeks.</td>
<td>GI: nausea, anorexia, diarrhea</td>
<td>Serotonin syndrome (triptans, TCAs, fentanyl, lithium, tramadol, buspirone)</td>
<td>Endo: SIADH</td>
</tr>
<tr>
<td></td>
<td>Quetiapine</td>
<td>Seroquel: Tab (25, 50, 100, 200) XR (50, 150, 200, 300)</td>
<td>25mg QHS – Max 150mg/day</td>
<td>Death: risk of death in dementia patients (OR 1.6, use only in severe cases of agitation)</td>
<td>CNS: Drowsiness, Extrapyramidal (1-10%)</td>
<td>QT prolongation, Suicidal ideation</td>
<td>CVS: Hypertension, Orthostatic hypotension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Withdrawal symptoms: Taper down over several weeks.</td>
<td>GI: Xerostomia, increased appetite, Constipation</td>
<td>Neuroleptic syndrome</td>
<td>Endo: Weight gain, Increase LDL, TGD &amp; FSBS.</td>
</tr>
<tr>
<td>Insomnia/Sleep disturbances</td>
<td>Melatonin</td>
<td>Tab (1mg) PR Tab (2, 3mg)</td>
<td>0.5mg – 1mg QHS</td>
<td>Avoid high dosage melatonin in elderly</td>
<td>CNS: Somnolence: avoid driving after taking Ramelteon</td>
<td>Inhibits hepatic metabolism: interacts with warfarin, Plavix, etc</td>
<td>CNS: Headache – drowsiness – dizziness</td>
</tr>
<tr>
<td></td>
<td>Ramelteon</td>
<td>Rozerem: Tab (8mg)</td>
<td>8mg QHS</td>
<td>Somnolence: avoid driving after taking Ramelteon</td>
<td>CNS: Headache – drowsiness – dizziness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM Disorders***</td>
<td>Melatonin</td>
<td>Tab (6mg)</td>
<td>High dose (6mg QHS)</td>
<td>Avoid high dosage melatonin in elderly</td>
<td>CNS: Headache – drowsiness – dizziness</td>
<td>Inhibits hepatic metabolism: interacts with warfarin, Plavix, etc</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clonazepam</td>
<td>Tab (0.5mg)</td>
<td>0.5mg QHS (only if severe RBD, if melatonin fails)</td>
<td>Worsens dementia symptoms (not preferable for use in dementia patients)</td>
<td></td>
<td>lowers seizure threshold</td>
<td></td>
</tr>
</tbody>
</table>

• **Agitation**: SSRI takes a long time to start working, you may add quetiapine for few weeks in patients with severe agitation till SSRI starts working.

**Ramelteon** is a melatonin MT1, MT2 receptor agonist, approved for insomnia and ICU related delirium. Not approved in EU. There is no generic form, price is 427$/30 pills

***RBD (REM behavior disorder): first step is to stop medications that worsen RBD (SSRI, SNRI & TCA).
# New Oral Anticoagulants

## The New Oral Anticoagulant Drugs (NOADs)

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Warfarin</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
</table>

### Dose

<table>
<thead>
<tr>
<th>Normal individual</th>
<th>DVT Prophylaxis</th>
<th>DVT/PE treatment</th>
<th>Costs (monthly)</th>
<th>Reversal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>220mg daily</td>
<td>10mg Daily</td>
<td>8$ (5mg)</td>
<td>Vitamin K</td>
</tr>
<tr>
<td>150mg BID</td>
<td>150mg, BID</td>
<td>15mg BID x 21d then 20mg QD</td>
<td>357$</td>
<td>Praxbind (idarucizumab)</td>
</tr>
<tr>
<td>20mg Daily (with evening meal)</td>
<td>10mg Daily</td>
<td>15mg BID x 7d then 5mg BID</td>
<td>357$</td>
<td>Andexanet (pending FDA)</td>
</tr>
<tr>
<td>5mg BID</td>
<td>2.5mg BID</td>
<td>60mg Daily</td>
<td>300$</td>
<td>Andexanet (pending FDA)</td>
</tr>
</tbody>
</table>

### Interaction

- Multiple P-glycoprotein inhibitors**
- CYP 3A4 inhibitors & P-glycoprotein inhibitors**
- CYP 3A4 inhibitors & P-glycoprotein inhibitors**

### Comparative Information

- Risk of Stroke (RRR): ↓ (34%)  Non-inferior  ↓ (20%)
- Risk of ICH (RR): ↓ (0.4)  ↓  ↓
- Risk of GI bleed (RR): ↑ (1.5)

### Details

- **Avoid in Child Pugh B & C due to increased risk of hemorrhage**
- **P-glycoprotein inhibitors: include verapamil – Amiodarone – Clarithromycin**
### Drugs that interact with warfarin
(Patient friendly format, including all names of each class)

<table>
<thead>
<tr>
<th>Severe Interaction:</th>
<th>Drugs That Increase INR (Increase Risk of Bleeding)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood thinners</td>
<td>Aspirin - Clopidogrel (Plavix) - Dabigatran (Pradaxa) - Apixaban (Eliquis) - Rivaroxaban (Xarelto)</td>
</tr>
<tr>
<td></td>
<td>Sulfa/TMP (Bactrim) - Antifungal agents (ending with -azole)</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>Celecoxib (Celebrex) – Naproxen (Naprosyn) – Ibuprofen (Motrin) – Ketorolac (Flector) – Diclofenac (Voltaren)</td>
</tr>
<tr>
<td>Pain Meds (NSAIDS)</td>
<td>Amiodarone (Cordarone) - Ropinirole (Requip) - Acetaminophen (Tylenol) - Tamoxifen (Nolvadex)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate Interaction:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobials</td>
</tr>
<tr>
<td>Stomach (Gastric)</td>
</tr>
<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>Cholesterol</td>
</tr>
<tr>
<td>Brain (Nervous)</td>
</tr>
<tr>
<td>HIV</td>
</tr>
<tr>
<td>Gout</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>
### Neuro-Pharmacology

#### Drugs to Avoid in Myasthenia

<table>
<thead>
<tr>
<th>Severe Interaction:</th>
<th>Drugs That Decrease INR (Increase Risk of Blood Clots)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain (Nervous)</td>
<td>Barbiturates – Phenobarbital – Phenytoin (Dilantin) – St. John’s Wort</td>
</tr>
<tr>
<td>Anti-TB</td>
<td>Rifampin (Rifadin)</td>
</tr>
<tr>
<td>Moderate Interaction:</td>
<td></td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>Dicloxacillin – Grisofulvin -</td>
</tr>
<tr>
<td>Stomach (Gastric)</td>
<td>Sucralfate (Carafate)</td>
</tr>
<tr>
<td>Heart (Cardiac)</td>
<td>Bosentan (Tracleer)</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Colestipol (Colestid)</td>
</tr>
<tr>
<td>Brain (Nervous) Antivirals</td>
<td>Carbamazepine (Tegretol) – Primidone (Mysoline)</td>
</tr>
<tr>
<td>Herbal - Vitamins</td>
<td>Darunavir (Prezista) – Ribavirin (Rebetol) – Nevirapine (Viramune)</td>
</tr>
<tr>
<td>Other</td>
<td>Ginseng – Green tea – Vitamin K (Mephyton) – Coenzyme Q</td>
</tr>
<tr>
<td></td>
<td>Azathioprine (Imuran) – Cholestyramine (Questran) – Estrogen - Isotretinoin - Raloxifene (Evista) - Spironolactone (Aldactone) – Sulfasalazine (Azulfadine) – Mesalamine – Propylthiouracil – Methimazole</td>
</tr>
</tbody>
</table>

### Dietary Modification

#### Foods to Watch While on Warfarin (Not To Avoid)

There is no problem of consuming foods rich in vitamin K, however you must be consistent with the amount you eat on daily basis to avoid fluctuations in INR. Again, no need to avoid these foods as long as you keep your daily consumption constant.


#### Foods That Increase The Effect Of Warfarin (Increase INR)

Alcohol – Grape fruit (Try to avoid both or at least consume small amounts).
# Drugs to Avoid with Myasthenia Gravis

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Heart Medications</th>
<th>Anesthesia</th>
<th>Brain/nerve</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>ampicillin</td>
<td>Quinidine</td>
<td>Procainamide</td>
<td>Lithium</td>
<td>Timolol eye drops</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Quinine</td>
<td>Succinylcholine</td>
<td>Phenytoin</td>
<td>Cortisones</td>
</tr>
<tr>
<td>Penicillin</td>
<td>Procainamide</td>
<td>Curare derivatives</td>
<td>Gabapentin</td>
<td>Penicillamine</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Statins</td>
<td></td>
<td>Botox</td>
<td>Iodinated contrast</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Atenolol</td>
<td></td>
<td>Nicotine</td>
<td>Magnesium</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Metoprolol</td>
<td></td>
<td>Methocarbamol</td>
<td>Interferon alpha</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>Sotalol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofloxacin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Propranolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Pindolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Nebivolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Nadolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Labetalol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>Esmolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gentamycin</td>
<td>Carvedilol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobramycin</td>
<td>Bisoprolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kanamycin</td>
<td>Acebutolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neomycin</td>
<td>Amlodipine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Verapamil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diltiazem</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nifedipine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Felodipine</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NB:** to make it a patient friendly list, names of all common individual medications were listed instead of pharmaceutical group listing so you can copy this page and give it to the patient as a reference.

**Red:** Strong evidence of harmful effect  
**Yellow:** Few case reports of harmful effect  
**Blue:** Should be avoided in spite of weak clinical evidence
Drugs to avoid in patients with seizures

- Although the list of medications that lower seizure threshold is huge, most of these medications cause seizures only in rare occasions.
- Example; all cephalosporins have the potential of inducing seizures, however only cefepime was found to be commonly implicated and rest of cephalosporins are rarely associated with seizures.
- Here, we included only drugs that known to commonly induce seizures.

<table>
<thead>
<tr>
<th>Group</th>
<th>Family</th>
<th>Drugs shown to lower seizure threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>4th generation cephalosporins</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Carbapenems</td>
<td>Cefepime</td>
</tr>
<tr>
<td></td>
<td>Penicillin</td>
<td>Imipenem</td>
</tr>
<tr>
<td></td>
<td>Quinolones</td>
<td>Ampicillin – Ampicillin/Sulbactam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ciprofloxacin – Levofloxacin</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Atypical antipsychotics</td>
<td>Clozapine</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Typical antipsychotics</td>
<td>Chlorpromazine</td>
</tr>
<tr>
<td></td>
<td>Aminoketones</td>
<td>Bupropion</td>
</tr>
<tr>
<td></td>
<td>Serotonin agonists</td>
<td>Buspirone</td>
</tr>
<tr>
<td></td>
<td>Serotonin antagonist</td>
<td>Trazodone</td>
</tr>
<tr>
<td></td>
<td>SNRI</td>
<td>Venlafaxine</td>
</tr>
<tr>
<td></td>
<td>Tricyclics</td>
<td>Amitriptyline – Nortriptyline – Clomipramine</td>
</tr>
<tr>
<td>Mood stabilizers</td>
<td>Lithium</td>
<td>Lithium</td>
</tr>
<tr>
<td>Analgesics</td>
<td>Narcotics</td>
<td>Fentanyl – Tramadol – Meperidine</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>Calcineurin inhibitor</td>
<td>Cyclosporine – Tacrolimus</td>
</tr>
</tbody>
</table>
# Vasopressors & Inotropes

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>MOA</th>
<th>Heart rate</th>
<th>Systolic function</th>
<th>Diastolic function</th>
<th>SVR</th>
<th>PVR</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>0.01-3 mcg/kg/min</td>
<td>α and β1 agonist (α&gt;β)</td>
<td>Some increase</td>
<td>No effect</td>
<td>Increase</td>
<td>Significant increase</td>
<td>Minimal increase</td>
<td>Shock (vasodilatory, cardiogenic)</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>0.5-9 mcg/kg/min</td>
<td>α agonist</td>
<td>Decrease</td>
<td>No effect</td>
<td>No effect</td>
<td>Significant increase</td>
<td>No effect</td>
<td>Hypotension (vagal &amp; medication)</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>0.04 U/min</td>
<td>V1 Rc (vascular) V2 Rc (renal)</td>
<td>No effect</td>
<td>No effect</td>
<td>No effect</td>
<td>Significant increase</td>
<td>Unknown</td>
<td>Shock (vasodilatory, cardiogenic)</td>
</tr>
<tr>
<td>Milrinone</td>
<td>50mcg load, 0.375-0.75 mcg/kg/min</td>
<td>PDE inhibitor</td>
<td>No effect</td>
<td>Increase</td>
<td>Increase</td>
<td>Decrease</td>
<td>Decrease</td>
<td>Hypotension, Cardiac ischemia, Torsade des pointes</td>
</tr>
<tr>
<td>Dopamine</td>
<td>5-20 mcg/kg/min</td>
<td>Dopamine agonist</td>
<td>Increase</td>
<td>Increase</td>
<td>No effect</td>
<td>Increase</td>
<td>Increase</td>
<td>Shock (vasodilatory, cardiogenic), HF, resistant bradycardia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug of choice</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic shock</td>
<td>Norepinephrine – Phenylephrine – 2\textsuperscript{nd} line: Vasopressin</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Dopamine – 2\textsuperscript{nd} line: Milrinone</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>Norepinephrine – Dobutamine</td>
</tr>
<tr>
<td>Anaphylactic shock</td>
<td>Epinephrine – 2\textsuperscript{nd} line: Vasopressin</td>
</tr>
<tr>
<td>Neurogenic shock</td>
<td>Phenylephrine</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Phenylephrine</td>
</tr>
</tbody>
</table>
## DRIPS FOR HYPERTENSION/TACHYCARDIA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dose</th>
<th>Max Dose</th>
<th>MOA</th>
<th>Dilator</th>
<th>Onset (min)</th>
<th>Duration</th>
<th>Metabolism</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>10mg q10min</td>
<td>8mg/min</td>
<td>α and β blocker</td>
<td>Arterial</td>
<td>2</td>
<td>2-4 hours</td>
<td>Hepatic</td>
<td>Avoid in bradycardia &amp; decompensated HF</td>
</tr>
<tr>
<td></td>
<td>then 1-2mg/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esmolol</td>
<td>500mcg/kg load</td>
<td>300mcg/kg/min</td>
<td>β1 blocker</td>
<td>↓COP</td>
<td>1</td>
<td>15 min</td>
<td>RBC esterase</td>
<td>Avoid in bradycardia &amp; decompensated HF</td>
</tr>
<tr>
<td></td>
<td>25-50mcg/kg/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicardipine</td>
<td>5mg/hr</td>
<td>15mg/hr</td>
<td>CCB</td>
<td>Arterial</td>
<td>10</td>
<td>4-6 hours</td>
<td>Hepatic</td>
<td>DOC in ischemic stroke and HTN encephalopathy</td>
</tr>
<tr>
<td>Sodium Nitroprusside</td>
<td>0.5mcg/kg/min</td>
<td>5mcg/kg/min</td>
<td>Nitrate</td>
<td>Arterial/Venous</td>
<td>1</td>
<td>1 min</td>
<td>Kidney</td>
<td>Causes coronary steal, tolerance, cyanide toxicity</td>
</tr>
<tr>
<td>Nitroglycerine</td>
<td>5mcg/min</td>
<td>400mcg/min</td>
<td>Nitrate</td>
<td>Venous</td>
<td>3</td>
<td>15 min</td>
<td>Hepatic</td>
<td>Tolerance in 24h</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>10-20mg boluses</td>
<td></td>
<td>Arterial</td>
<td></td>
<td>10</td>
<td>3 hours</td>
<td>Hepatic</td>
<td>Variable effect – avoid in acute conditions</td>
</tr>
<tr>
<td>Fenoldopam</td>
<td>0.1mcg/kg/min</td>
<td>1.6mcg/kg/min</td>
<td>D1 agonist</td>
<td>Arterial</td>
<td>5</td>
<td>1 hour</td>
<td>Hepatic</td>
<td>Sulfa allergy</td>
</tr>
<tr>
<td>Clevidipine</td>
<td>1mg/hr</td>
<td>16mg/hr</td>
<td>CCB</td>
<td>Arterial</td>
<td>1</td>
<td>10 min</td>
<td>RBC esterase</td>
<td>Lipid emulsion Can’t use &gt; 96h</td>
</tr>
</tbody>
</table>

MOA: mechanism of action – DOC: drug of choice
### Empirical Antibiotic Coverage in ICU

<table>
<thead>
<tr>
<th>Disease</th>
<th>Definition</th>
<th>1st Line</th>
<th>2nd Line</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAP/VAP</td>
<td>HAP: occurring &gt; 48h after admission</td>
<td>Vancomycin + Pip/Tazo or</td>
<td>Vancomycin + Aztreonam +</td>
<td>7 days</td>
</tr>
<tr>
<td></td>
<td>VAP: occurring &gt; 48h after intubation</td>
<td>Vancomycin + Cefepime</td>
<td>Tobramycin</td>
<td>Stop Vanc if MRSA not isolated after 72h</td>
</tr>
<tr>
<td>UTI</td>
<td>1-4 days since admission:</td>
<td>Ceftriaxone</td>
<td>Aztreonam</td>
<td>Uncomplicated: 7 days</td>
</tr>
<tr>
<td></td>
<td>&gt; 4 days since admission:</td>
<td>Pip/tazo</td>
<td>Aztreonam</td>
<td>Complicated: 7-14 days</td>
</tr>
<tr>
<td>C. Diff</td>
<td>Initial (mild): WBCs &lt; 15k &amp; Cr is normal</td>
<td>Metronidazole 500mg tid</td>
<td>Same as first episode</td>
<td>14 days</td>
</tr>
<tr>
<td></td>
<td>Initial (severe): WBCs &gt; 15k or Cr 1.5 times baseline</td>
<td>Vanc PO 125mg q6h</td>
<td>Vanc PO 500mg q6h + Metronidazole</td>
<td>14 days</td>
</tr>
<tr>
<td></td>
<td>Initial (complicated): Hypotension, ileus</td>
<td>IV: Nafcillin 2gm q4h or Cefazolin</td>
<td>PO: Cephalexin 500mg q6h or Clindamycin</td>
<td>Till Sx resolve</td>
</tr>
<tr>
<td></td>
<td>1st Recurrent:</td>
<td>2gm q8h</td>
<td>300 q8h</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2nd Recurrence:</td>
<td>Vanc taper or pulse regimen</td>
<td>Same as first episode</td>
<td></td>
</tr>
<tr>
<td>Cellulitis</td>
<td>No abscess or penetrating trauma (consider strept)</td>
<td>IV: Nafcillin 2gm q4h or Cefazolin</td>
<td>PO: Sulpha/Trimethoxazole DS 2tabs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abscess or penetrating trauma (consider MRSA)</td>
<td>2gm q8h</td>
<td>bid</td>
<td></td>
</tr>
<tr>
<td>Surgical site</td>
<td>Clean wound:</td>
<td>Nafcillin 2gm q4h or Cefazolin</td>
<td>Metronidazole 500 IV q6h +</td>
<td></td>
</tr>
<tr>
<td>infection</td>
<td></td>
<td>2gm q8h</td>
<td>Cefazolin or Ceftriaxone</td>
<td></td>
</tr>
</tbody>
</table>

HAP: hospital acquired pneumonia – VAP: ventilator acquired pneumonia

### Surgical Prophylaxis

<table>
<thead>
<tr>
<th>Surgery</th>
<th>1st line</th>
<th>2nd line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurosurgery</td>
<td>Cefazolin or Cefuroxime</td>
<td>Vancomycin or Clindamycin</td>
</tr>
<tr>
<td>Head &amp; Neck</td>
<td>Cefazolin or Cefuroxime or Unasyn</td>
<td>Vancomycin or (Clindamycin + Gentamicin)</td>
</tr>
</tbody>
</table>

Price of commonly used antibiotics:
Vancomycin 1 gm: $4.28, Metronidazole 500 mg: $1.10; Ciprofloxacin 400 mg: $1.70; Levofoxacin 500 mg: $3.84; Cefazolin 2 gm: $2.00; Cefoxitin 2 gm: $6.10;
Cefuroxime 1.5 gm: $3.57; Clindamycin 900 mg: $7.85; Ertapenem 1 gm: $77.94; Gentamicin 80 mg: $0.69;
<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Mechanism</th>
<th>Formulation</th>
<th>Dose</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tegsedi (inotersen)</td>
<td>Neuropathy due to hereditary amyloidosis</td>
<td>Antisense oligonucleotide that binds to TTR mRNA preventing TTR protein synthesis</td>
<td>SC injection</td>
<td>284mg SC weekly</td>
<td>Thrombocytopenia (avoid if platelets &lt; 100k) Glomerulonephritis (avoid in patients with proteinuria or GFR &lt; 45%). Lowers vitamin A level (prescribe supplements). Increased risk of stroke in first 2 days of treatment. Monitoring: LFT q4m, Cr, GFR, platelet count q2w.</td>
</tr>
<tr>
<td>Onpattro (Patisiran)</td>
<td>Neuropathy due to hereditary amyloidosis</td>
<td>Double stranded siRNA against TTR mRNA</td>
<td>0.3mg/kg IV infusion every 3 weeks</td>
<td></td>
<td>Infusion related reactions: pre-medicate with 10mg dexamethasone, 50mg diphenhydramine &amp; 500mg acetaminophen. Upper respiratory tract infections.</td>
</tr>
<tr>
<td>Emgality (galcanezumab)</td>
<td>Migraine prevention</td>
<td>CGRP antagonist</td>
<td>SC injection</td>
<td>240mg initial dose then 120mg monthly</td>
<td>Injection site reaction.</td>
</tr>
<tr>
<td>Ajovy (fremanzumab)</td>
<td>Migraine prevention</td>
<td>CGRP antagonist</td>
<td>SC injection</td>
<td>225mg SC monthly or 675mg SC every 3 months</td>
<td>Injection site reaction.</td>
</tr>
<tr>
<td>Aimovig (erenumab)</td>
<td>Migraine prevention</td>
<td>CGRP antagonist</td>
<td>SC injection</td>
<td>70mg SC monthly</td>
<td>Injection site reaction.</td>
</tr>
<tr>
<td>Epidiolex (cannabidiol)</td>
<td>Seizures associated with LGS and Dravet.</td>
<td>Cannabinoid R agonist</td>
<td>Oral solution (100mg/ml)</td>
<td>10mg/kg/d (Maximum 20mg/kg/d)</td>
<td>Transaminase elevation (13%), especially if given with valproic acid. Somnolence, sedation, weight loss.</td>
</tr>
<tr>
<td>Diacomit (stiripentol)</td>
<td>Seizures associated with Dravet syndrome</td>
<td>Capsule 250, 500 Powder 250, 500</td>
<td>50mg/kg/d</td>
<td>Neutropenia, thrombocytopenia Somnolence and sedation.</td>
<td></td>
</tr>
<tr>
<td>Galafold (migalastat)</td>
<td>Fabry disease (specific variants)</td>
<td>Alpha galactosidase enzyme chaperone</td>
<td>Oral</td>
<td>123mg PO every other day</td>
<td>Headache, insomnia, fever.</td>
</tr>
<tr>
<td>Neuro-Pharmacology</td>
<td>ICU: Vasopressors &amp; Inotropes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td><strong>Soliris</strong>&lt;br&gt;(eculizumab) 2017</td>
<td><strong>Myasthenia</strong>&lt;br&gt;(AchR positive)</td>
<td>Monoclonal Ab against complement (C5)</td>
<td>IV infusion</td>
<td>900mg weekly for 4 weeks then 1200mg 1 week later then then 1200 mg every 2 weeks thereafter</td>
<td>High risk for meningococcal infections Vaccinate for meningococcus 2 weeks before starting Soliris. (risk is 1% in vaccinated patients) Risk for encapsulated bacterial infection</td>
</tr>
<tr>
<td><strong>Radicava</strong>&lt;br&gt;(edaravone) 2017</td>
<td><strong>ALS</strong></td>
<td>Free radical scavenger</td>
<td>IV infusion</td>
<td>60mg IV QD x 14d then 2 weeks off then 10 days every 4 weeks.</td>
<td>Allergic reactions Sula allergy</td>
</tr>
<tr>
<td><strong>Actemra</strong>&lt;br&gt;(tocilizumab) 2017</td>
<td><strong>Giant Cell Arteritis</strong></td>
<td>IL-6 Rc blocker</td>
<td>Subcutaneous</td>
<td>162mg weekly with steroid taper.</td>
<td>Avoid with active infection, live vaccines Hold if ANC &lt; 1000 – Stop if ANC &lt; 500</td>
</tr>
<tr>
<td><strong>Emflaza</strong>&lt;br&gt;(deflazacort) 2017</td>
<td><strong>Duchenne Dystrophy</strong></td>
<td>Corticosteroid</td>
<td>Tab 6,18,30,36 mg&lt;br&gt;Susp 22.75/ml</td>
<td>0.9 mg/kg/day daily</td>
<td>Steroids side effects</td>
</tr>
<tr>
<td><strong>Austedo</strong>&lt;br&gt;(deutetrapanabenzine) 2017</td>
<td><strong>Huntington's chorea</strong>&lt;br&gt;Tardive Dyskinesia</td>
<td>Vesicular monoamine transporter 2 inhibitor</td>
<td>Tab 6,9,12 mg</td>
<td>6-48mg daily</td>
<td>Depression &amp; suicidality (2%) Don’t use with MAOI or Reserpine (wait 14 days) NMS, Parkinsonism, QTc prolongation (8msec)</td>
</tr>
<tr>
<td><strong>Ingrezza</strong>&lt;br&gt;(valbenazine) 2017</td>
<td><strong>Tardive Dyskinesia</strong></td>
<td>Vesicular monoamine transporter 2 inhibitor</td>
<td>Cap 40 mg&lt;br&gt;80mg daily</td>
<td>40mg daily x 1W then</td>
<td>Somnolence Don’t use with MAOI QT prolongation</td>
</tr>
<tr>
<td><strong>Gocovri</strong>&lt;br&gt;(amantadine) 2017</td>
<td><strong>Parkinson's Dyskinesia</strong></td>
<td>Long acting amantadine</td>
<td>Cap 68.5, 137 mg&lt;br&gt;274 qhs</td>
<td>137mg qhs x 1W then</td>
<td>Orthostatic hypotenstion, Falling asleep, somnolence Hallucinations/psychosis, Impulse control disorder Withdrawal-Emergent Hyperpyrexia and Confusion</td>
</tr>
<tr>
<td><strong>Xadago</strong>&lt;br&gt;(safinamide) 2017</td>
<td><strong>Parkinson's disease</strong></td>
<td>MAO-B inhibitor</td>
<td>Tab 50, 100 mg</td>
<td>50mg daily x 2W then</td>
<td>Don’t use with opioids, TCA, SNRI, cyclobenzaprine Hypertension, Falling asleep, somnolence Hallucinations/psychosis, Impulse control disorder Withdrawal-Emergent Hyperpyrexia and Confusion</td>
</tr>
<tr>
<td><strong>Brineura</strong>&lt;br&gt;(cerliponase) 2017</td>
<td><strong>NCL type II</strong>&lt;br&gt;(infantile)</td>
<td>Lysosomal peptidase</td>
<td>Intraventricular infusion every 2W</td>
<td>300mg intraventricular infusion every 2W</td>
<td>Allergic reactions Arrhythmia</td>
</tr>
<tr>
<td><strong>Exondys 51</strong>&lt;br&gt;(eteplirsen) 2016</td>
<td><strong>Duchenne Dystrophy amenable to exon-51 skipping</strong></td>
<td>Antisense oligonucleotide (binds to exon 51 of dystrophin pre-mRNA resulting in exclusion of this exon in protein synthesis)</td>
<td>Infusion</td>
<td>30mg/kg weekly infusion</td>
<td>Dizziness, nausea, vomiting</td>
</tr>
<tr>
<td>Neuro-Pharmacology</td>
<td>ICU: Vasopressors &amp; Inotropes</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>-------------------------------------------</td>
<td>---------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Spinraza</strong> (nusinersen) 2016</td>
<td>Spinal Muscle Atrophy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nuplazid</strong> (pimavanersin) 2016</td>
<td>Parkinson related psychosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Briviact</strong> (brivaracetam) 2016</td>
<td>Partial Seizures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Carnexiv</strong> (carbamazepine) 2016</td>
<td>Seizures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Keveyis</strong> (dichlorphenamide) 2016</td>
<td>Periodic Paralysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neudexta</strong> (dextromethorphan + quinidine) 2011</td>
<td>Pseudo-bulbar Affect (PBA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neudexta alternative:</strong> a combination of “Robitussin 12 Hour Cough Relief” 5ml = 30mg of dextromethorphan BID or “DAYQUIL HBP COLD &amp; FLU” capsule = 30mg dextromethorphan + Fluoxetine 20mg daily (CYP450 2D6 inhibitor).</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Dextromethorphan**: NMDA receptor antagonist and sigma-1 agonist

**Quinidine**: CYP450 2D6 inhibitor

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Dose</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinraza</td>
<td>Spinal Muscle Atrophy</td>
<td>Intrathecal</td>
<td>12mg ever 2W x 4 then every 4 months</td>
</tr>
<tr>
<td>Nuplazid</td>
<td>Parkinson related psychosis</td>
<td>Tab 17mg</td>
<td>34mg daily (2 tablets)</td>
</tr>
<tr>
<td>Briviact</td>
<td>Partial Seizures</td>
<td>Tab 25,50,75,100 Susp 10mg/ml IV 10mg/ml</td>
<td>50-100 mg BID</td>
</tr>
<tr>
<td>Carnexiv</td>
<td>Seizures</td>
<td>Na Channel Blocker (IV Carbamazepine)</td>
<td>IV dose = 70% of usual oral dose divided q6h</td>
</tr>
<tr>
<td>Keveyis</td>
<td>Periodic Paralysis</td>
<td>Tablets 50mg</td>
<td>50mg BID (Max 100mg BID)</td>
</tr>
</tbody>
</table>

**Neudexta**: Capsules 20/10mg

One capsule daily for 1 week then BID

Avoid in: liver disease, sulfa allergy, concomitant use of aspirin (CAI shifts aspirin from blood to CNS causing neurotoxicity). Hypokalemia, metabolic acidosis, falls, paresthesia, dysgeusia.

**Neudexta alternative**: a combination of “Robitussin 12 Hour Cough Relief” 5ml = 30mg of dextromethorphan BID or “DAYQUIL HBP COLD & FLU” capsule = 30mg dextromethorphan + Fluoxetine 20mg daily (CYP450 2D6 inhibitor).
Neurological Workup
(Laboratory – Neurophysiology – Imaging)
### Basic Workup Schemes

#### Neurology Workup

<table>
<thead>
<tr>
<th>Neuropathy Based on Exam</th>
<th>Differentials</th>
<th>Workup</th>
<th>Optional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symmetric Sensory-Motor</td>
<td>Acute: GBS - Chronic: CIDP</td>
<td>CSF – SPEP or Sr IFA – HIV</td>
<td>VEGF for POEMS</td>
</tr>
<tr>
<td>Symmetric Predominantly Sensory</td>
<td>Acute: Chronic: DM, B12 deficiency, alcohol, Sjogren’s syndrome, Sensory CIDP, CISP, CSPN, DADS, Drugs, Chemicals (arsenic, thallium, mercury), Hereditary neuropathy</td>
<td>A1C or GTT – B12 with MMA – SPEP or Sr IFA – RPR – SS-1/SS-B – ACE</td>
<td>Celiac panel (if hx of diarrhea) HIV (if hx suggestive) Heavy metal screen (if hx suggestive)</td>
</tr>
<tr>
<td>Symmetric Predominantly Motor</td>
<td>Acute: AMAN Chronic: CIDP, porphyria, lead toxicity, Hereditary motor neuropathy, SMA</td>
<td>Acute: CSF Chronic: CSF for CIDP, Gene testing (SMN, HMN, Kennedy’s gene)</td>
<td>Lead (wrist extensors) Porphyria panel</td>
</tr>
<tr>
<td>Asymmetric Predominantly Sensory</td>
<td>Ganglionopathy, CISP</td>
<td>SS-A/B – ACE – Anti Hu – RPR</td>
<td>CSF, MRI (enhancement in CISP)</td>
</tr>
<tr>
<td>Asymmetric Predominantly Motor</td>
<td>MMN, MND (ALS, PLS)</td>
<td>GM1 – B12 &amp; MMA</td>
<td></td>
</tr>
</tbody>
</table>

**Differentials:**
- GBS: Gillian Bare syndrome
- CIDP: Chronic inflammatory demyelinating polyradiculoneuropathy
- CISP: Chronic immune sensory polyradiculoneuropathy
- CSPN: Cryptogenic sensory polyneuropathy
- DADS: Distal acquired demyelinating sensory neuropathy
- MADSAM: Multifocal acquired demyelinating sensory and motor neuropathy
- MMN: Multifocal motor neuropathy
- AMAN: Acute motor axonal neuropathy
- SMA: Spinal muscle atrophy
- HNPP: Hereditary neuropathy with liability to pressure palsy
- MND: Motor neuron disease
- ALS: Amyotrophic lateral sclerosis
- PLS: Primary lateral sclerosis

**Workup:**
- SPEP: Serum protein electrophoresis
- IFA: Serum immunofixation
- VEGF: Vascular endothelial growth factor
- POEMS: Polynueropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes
- GTT: Glucose tolerance test
- MMA: Methylmalonic acid
### Neurology Workup

<table>
<thead>
<tr>
<th>Neuropathy with UMN signs</th>
<th>Neuro-Physiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory neuropathy + UMN signs</td>
<td>B12 deficiency, Copper deficiency, Friedrich’s ataxia, adrenomyeloneuropathy</td>
</tr>
<tr>
<td>Motor neuropathy + UMN signs</td>
<td>ALS, PLS</td>
</tr>
</tbody>
</table>

### Myopathy:

**Acute**

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Electrolytes: hypo/hyperkalemia, hypermagnesemia, hypophosphatemia</th>
<th>Endocrine: Thyroid, Parathyroid, Cushing, Conn’s (hypokalemia), Vitamin D deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxins</td>
<td>Barium, Buffalo fish toxin, Amanita mushrooms, Snake, Wasp &amp; African bee venoms</td>
<td>Drugs/Toxins: Alcohol, Statins, Fibrates, Steroids, Amiodarone, Chloroquine, Colchicine, Zidovudine</td>
</tr>
<tr>
<td>Drugs</td>
<td>Statins, antipsychotics (NMS), propofol</td>
<td>Channelopathies:</td>
</tr>
<tr>
<td>Channelopathies</td>
<td>Primary periodic paralysis, hyperthyroid periodic paralysis, malignant hyperthermia,</td>
<td>Inflammatory: Polymyositis, Dermatomyositis, Inclusion body myositis, Paraneoplastic</td>
</tr>
<tr>
<td>Immune</td>
<td>Polymyositis, Dermatomyositis, Necrotizing myopathy,</td>
<td>Hereditary:</td>
</tr>
<tr>
<td>Other</td>
<td>Critical illness myopathy, HIV myopathy</td>
<td></td>
</tr>
</tbody>
</table>

**Chronic**

<table>
<thead>
<tr>
<th>Workup</th>
<th>Step 1: Screening workup</th>
<th>Step 2: Specific workup</th>
<th>Step 3: Advanced workup</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK, Aldolase, LDH, AST/ALT/GGT, Sr K, Mg, PO4</td>
<td>CK, Aldolase, LDH, AST/ALT/GGT, Sr K, Mg, PO4</td>
<td>EMG</td>
<td>Muscle biopsy: for inflammatory and hereditary myopathies (muscle has to be at least grade 4/5 in power), Gene testing: for hereditary myopathies.</td>
</tr>
<tr>
<td></td>
<td>CSF: for immune mediated</td>
<td>TSH, T4, Ca, Parathyroid hormone, Sr. Cortisol, Vitamin D HIV, Lyme if history is suggestive</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Workup</th>
<th>Step 1: Screening workup</th>
<th>Step 2: Specific workup</th>
<th>Step 3: Advanced workup</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK, Aldolase, LDH, AST/ALT/GGT, Sr K, Mg, PO4</td>
<td>CK, Aldolase, LDH, AST/ALT/GGT, Sr K, Mg, PO4</td>
<td>EMG</td>
<td>Muscle biopsy: for inflammatory and hereditary myopathies (muscle has to be at least grade 4/5 in power), Gene testing: for hereditary myopathies.</td>
</tr>
<tr>
<td></td>
<td>CSF: for immune mediated</td>
<td>TSH, T4, Ca, Parathyroid hormone, Sr. Cortisol, Vitamin D HIV, Lyme if history is suggestive</td>
<td></td>
</tr>
</tbody>
</table>
# Neurology Workup

## Confusion/Encephalopathy:

<table>
<thead>
<tr>
<th>Step 1 (screening workup)</th>
<th>Step 2 (Specific workup)</th>
<th>Step 3 (Advanced workup)</th>
</tr>
</thead>
</table>
| Serum Glucose - Electrolytes - Liver function - Ammonia - Kidney function - TSH - CBC (WBCs) - Lactate - Urinalysis - Chest X-ray - TSH - Urine drug screen - Serum alcohol level. | **Thiamine level:** if history of alcoholism  
**ABG for CO2 level:** if history of COPD  
**MRI brain:**  
• **Without contrast:** if exam suggestive of multiple strokes (embolic shower), PRES  
• **With contrast:** if exam suggestive of meningo-encephalitis, autoimmune disease or brain tumors.  
**CSF:**  
• **Basic:** cell count, cell differential, protein, glucose, smear, culture, lactate, HSV PCR.  
*(Lactate is increased in early bacterial & fungal infections before glucose level drops)*  
**EEG:** If there is concerns about intermittent seizures, non-convulsive status, CNS infection (LPDs in HSV, 1Hz GPDs in CJ, periodic complex q5 seconds in SSPE)* | **CSF: Add as needed**  
• **Infectious:** PCR (HSV, Cryptococcus, T. Whippleii, JC virus, CMV, VZV, Influenza), Ab titer (VZV, Cryptococcus, Adenovirus, Coxsackie, Toxoplasma), CJD testing (14-3-3, Tau, RT-QuIC)  
• **Immune:** IgG index, Oligoclonal bands, Antibodies (NMDA, AMPA, VGKC, Thyroglobulin, Thyroperoxidase)  
• **Paraneoplastic:** Paraneoplastic panel  
• **Malignancy:** cytology  
• **Mitochondrial:** lactate, pyruvate  
**Blood:**  
• **ACE:** if MRI concerning for sarcoidosis ± CT chest.  
**Cerebral Angiography:** If MRI concerning for vasculitis |

## Hints:

- **CSF Lactate:** is usually elevated earlier than the decline in glucose level in bacterial & fungal meningitis.  
- **Oligoclonal bands:** Requires a sample in both serum and CSF in same time (preferred) or at least within 2 weeks (half-life of IgG is 23 days). Considered positive if more than 2 bands found in CSF and not found in serum. Can be positive in different disorders (MS, Neurosarcoid, Neurosyphilis, HHV6, SSPE & other CNS infections.)
# Autoantibodies

## Associated with central-demyelinating disorders

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Disease</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AQP4 Ab</td>
<td>NMO</td>
<td>Aquaporin-4</td>
</tr>
<tr>
<td>MOG Ab</td>
<td>Childhood MS, ADEM, AQP4 negative NMO, AQP4 negative optic neuritis</td>
<td>Myelin oligodendrocyte glycoprotein</td>
</tr>
</tbody>
</table>

## Associated with neuromuscular disorders

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Disease</th>
<th>Description</th>
</tr>
</thead>
</table>
| AChR Ab    | Myasthenia | Acetylcholine Rc Ab  
Positive in 85% of myasthenia patients  
**Binding:** causes endocytosis of the receptor – 99.6 sensitive & specific. Positive if > 0.4 nmol/L  
**Blocking:** prevents ACh from binding to the receptor – positive if represent > 40%  
**Modulating:** causes endocytosis of receptors – positive if represents > 45%, only present if binding Ab is positive. |
| MUSK Ab    | Myasthenia | Muscle specific kinase Ab -> inhibits AChR clustering in the motor end plate  
Positive in 50% of the AChR negative patients  
More common in women, African Americans, no eye involvement, more neck and bulbar involvement, less responsive to anticholinesterase medications or thymectomy. |
| LRP4 Ab    | Myasthenia | LDL receptor-related protein 4 acts as a receptor for neural agrin, activates MUSK  
Positive in 9% of double seronegative patients (negative AChR/MUSK) |
| Striational Ab (RyR Ab - Titin Ab) | Myasthenia | Against striated muscle proteins (titin and raynaudin)  
Present only in AChR positive myasthenia, usually in elderly > 60 and patients with thymoma.  
Sensitive but not specific for thymoma (50% of positives have thymoma, 95% of thymoma patients have titin Ab)  
Usually associated with more severe course of disease, respond to calcineurin inhibitors (tacrolimus and cyclosporine)  
Anti RyR can react against both skeletal RyR1 and the cardiac RyR2 receptors |
| Jo-1       | Polymyositis | Anti-histidyl–tRNA synthetase – Test only in patients with positive ANA  
Present in 30% of patients with inflammatory myopathy – typically polymyositis associated with interstitial lung disease. |
<table>
<thead>
<tr>
<th>Neurology Workup</th>
<th>Neuro-Physiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRP</td>
<td>Signal-Recognition-Protein</td>
</tr>
<tr>
<td>HMG CoA</td>
<td>Necrotizing myopathy</td>
</tr>
<tr>
<td>Mi-2</td>
<td>Dermatomyositis</td>
</tr>
<tr>
<td>TIF1</td>
<td>Dermatomyositis</td>
</tr>
<tr>
<td>VGCC Ab</td>
<td>Lambert Eaton</td>
</tr>
<tr>
<td>GAD</td>
<td>Stiff Person Syndrome</td>
</tr>
<tr>
<td>Glycine receptor</td>
<td>Stiff Person Syndrome Plus or &quot;PERM&quot;</td>
</tr>
<tr>
<td>GQ1b</td>
<td>Cranial variants of GBS</td>
</tr>
<tr>
<td>GM1</td>
<td>AMAN – MMN</td>
</tr>
<tr>
<td>GD1b</td>
<td>Pure sensory variant of GBS</td>
</tr>
<tr>
<td>MAG</td>
<td>Anti MAG neuropathy – Multiple sclerosis – SLE – MGUS - Waldestrom</td>
</tr>
<tr>
<td>Channels</td>
<td>Isaacs (neuromyotonia) – Morvan syndrome - Limbic encephalitis</td>
</tr>
</tbody>
</table>

**Associated with mainly neuropathic disorders (Glycoproteins)**

<table>
<thead>
<tr>
<th>Glycoprotein</th>
<th>Condition</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>GQ1b</td>
<td>Cranial variants of GBS</td>
<td>Positve in 90% of patients with MFS</td>
</tr>
<tr>
<td>GM1</td>
<td>AMAN – MMN</td>
<td>MMN (45% sensitivity – 98% specificity) - AMAN (motor variants of GBS)</td>
</tr>
<tr>
<td>GD1b</td>
<td>Pure sensory variant of GBS</td>
<td>Against gangliosides on sensory neurons in dorsal root ganglia</td>
</tr>
<tr>
<td>MAG</td>
<td>Anti MAG neuropathy – Multiple sclerosis – SLE – MGUS - Waldestrom</td>
<td>Myelin associated glycoprotein (present in peripheral and central myelin)</td>
</tr>
<tr>
<td></td>
<td>Anti MAD neuropathy is a chronic sensory-motor demyelinating neuropathy.</td>
<td>MAG Ab present in 50% of patients with monoclonal gammopathy (MGUS or Waldestrom) with peripheral neuropathy &gt;&gt; test for MAG in patients with MGUS/Waldestrom with neuropathy.</td>
</tr>
<tr>
<td>VGKC (CASPR2)</td>
<td>Isaacs (neuromyotonia) – Morvan syndrome - Limbic encephalitis</td>
<td>Contactin associated protein type 2 → peripheral motor hyperexcitability</td>
</tr>
</tbody>
</table>

**Channels**

- VGKC (CASPR2) Test in blood
  - Isaacs (neuromyotonia) – Morvan syndrome - Limbic encephalitis
<table>
<thead>
<tr>
<th>Neurology Workup</th>
<th>Neuro-Physiology</th>
</tr>
</thead>
</table>
| **VGKC (LGI-1)**  | **Leucine-rich, glioma Inactivated protein 1** → cognitive impairment and seizures  
Brief facio-brachial dystonic seizures, memory loss, disorientation, hyponatremia in 60%.  
CSF with lymphocytosis and OCB in 50% of patients |
| **Test in blood** | **Limbic Encephalitis** |
| **VGKC (DPPX)**  | **Dipeptidyl-peptidase–like protein 6, a peptide related to VGKC (Kv4) responsible for blocking of back-propagation of action potentials** → Triad of GI symptoms (diarrhea-weight loss), cognitive dysfunction, CNS excitability  
Starts with diarrhea, weight loss (average 20Kg) followed by CNS hyperexcitability (hyperekplexia, myoclonus, seizures) over a few months period. |
| **Test in blood** | **DPPX associated encephalitis** |
| **VGKC (Contactin-2)**  | **Found in sera of patients with variable CNS symptoms, not associated with a specific syndrome. Seen in some patients with multiple sclerosis but not related to disease activity.** |
| **NMDA (Contactin-2)**  | **NMDA Encephalitis**  
Psychiatric features, cognitive dysfunction, seizures  
May be associated with ovarian teratoma (get pelvic MRI) |
| **Test in CSF** | **Usually associated with cancers (Onconeural Ab)** |
| **Amphphysin** | **Stiff Person Syndrome (paraneoplastic)**  
Protein present on cytoplasmic surface of synaptic vesicles.  
SCLC & breast cancer |
| **Hu (ANNA-1)** | **Encephalomyelitis (limbic, brainstem or myelitis) – sensory neuronopathy – cerebellar degeneration**  
Anti-neuronal nuclear protein (present in all neurons).  
SCLC & Neuroblastoma |
| **Ri (ANNA-2)** | **Cerebellar degeneration – Opsoclonus**  
Ovarian, endometrial & breast cancer, directed against NOVA protein  
Most common cause of opscolonus in adults: Anti Hu, Ri, Yo (SCLC & breast)  
Most common cause of opscolonus in children: neuroblastoma with negative anti Hu, Ri, Yo |
| **Yo** | **Cerebellar degeneration**  
Ovarian, endometrial & breast cancer |
| **Ma2** | **Cerebellar degeneration – Limbic encephalitis – Stiff person syndrome**  
Testicular tumors |
| **CV2 (CRMP5)** | **Cerebellar degeneration – Limbic encephalitis – Peripheral neuropathy – optic neuropathy**  
Collapsin response-mediator protein  
SCLC, thymoma & uterine sarcoma. |
<table>
<thead>
<tr>
<th>Neurology Workup</th>
<th>Neuro-Physiology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mGluR5</strong></td>
<td>Ophilia Syndrome (limbic encephalitis in HD patients)</td>
</tr>
<tr>
<td></td>
<td>Hodgkin lymphoma</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td><strong>ANA</strong></td>
<td>Screening test for all antinuclear antibodies, if negative don’t test for specific antinuclear Abs.</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Endothelial cell Ab (AECA)</strong></td>
<td>Susac</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SSA (Ro) – SSB (La)</strong></td>
<td>Sjogren</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TPO, Thyroglobulin</strong></td>
<td>Hashimoto encephalopathy</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Anatomy

### Myotomes

### Muscles of The Upper Extremity

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Muscles</th>
<th>Action</th>
<th>Roots</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long Thoracic</strong></td>
<td>Serratus Anterior</td>
<td>Fix scapula to chest wall</td>
<td>C5-6-7</td>
</tr>
<tr>
<td><strong>Dorsal Scapular</strong></td>
<td>Rhomboids</td>
<td>Fix Scapula to the spine</td>
<td>C5</td>
</tr>
<tr>
<td></td>
<td>Levator Scapula</td>
<td>Elevates the Scapula</td>
<td></td>
</tr>
<tr>
<td><strong>Suprascapular</strong></td>
<td>Supraspinatus</td>
<td>Arm Abduction (15:30 degrees)</td>
<td>C5</td>
</tr>
<tr>
<td></td>
<td>Infraspinatus</td>
<td>Arm Adduction</td>
<td>C5-6</td>
</tr>
<tr>
<td><strong>Nerve to Subclavius</strong></td>
<td>Subclavius</td>
<td>Depress Shoulder</td>
<td>C5-6</td>
</tr>
<tr>
<td><strong>Lateral Pectoral</strong></td>
<td>Pectoralis Major</td>
<td>Arm Adduction/Flexion</td>
<td>C5-6</td>
</tr>
<tr>
<td><strong>Medial Pectoral</strong></td>
<td>Pectoralis Minor</td>
<td>Depress the Scapula</td>
<td>C8-T1</td>
</tr>
<tr>
<td><strong>Thoracodorsal</strong></td>
<td>Lattissimus Dorsi</td>
<td>Arm Adduction, Shoulder Extension</td>
<td>C6-7-8</td>
</tr>
<tr>
<td><strong>Axillary</strong></td>
<td>Deltoid</td>
<td>Arm Abduction (0-15 degrees)</td>
<td>C5-6</td>
</tr>
<tr>
<td></td>
<td>Teres Minor</td>
<td>Arm External Rotation</td>
<td>C5-6</td>
</tr>
<tr>
<td><strong>Musculocutaneous</strong></td>
<td>Biceps</td>
<td>Elbow Flexion (Supinated)</td>
<td>C5-6</td>
</tr>
<tr>
<td></td>
<td>Brachialis</td>
<td>Elbow Flexion</td>
<td></td>
</tr>
<tr>
<td><strong>Radial</strong></td>
<td>Brachioradialis</td>
<td>Elbow Flexion (Mid Position)</td>
<td>C5-6</td>
</tr>
<tr>
<td></td>
<td>Triceps</td>
<td>Elbow Extension</td>
<td>C7-8</td>
</tr>
<tr>
<td></td>
<td>Extensor Carpi Radialis</td>
<td>Wrist Extension &amp; Abduction</td>
<td>C6-7</td>
</tr>
<tr>
<td><strong>Posterior Interosseous</strong></td>
<td>Supinator</td>
<td>Forearm Supination</td>
<td>C6-7</td>
</tr>
<tr>
<td>(of Radial)</td>
<td>Extensor Carpi Ulnaris</td>
<td>Wrist Extension &amp; Adduction</td>
<td>C7-8</td>
</tr>
<tr>
<td></td>
<td>Extensor Digitorum</td>
<td>Wrist/Finger Extension</td>
<td>C7-8</td>
</tr>
<tr>
<td></td>
<td>Extensor Pollicis</td>
<td>Wrist/Index Extension</td>
<td>C7-8</td>
</tr>
<tr>
<td></td>
<td>Extensor Indices</td>
<td>Wrist/Thumb Extension</td>
<td>C7-8</td>
</tr>
<tr>
<td></td>
<td>Extensor Digiti Minimi</td>
<td>Wrist/Little finger Extension</td>
<td>C7-8</td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td>Pronator Teres</td>
<td>Forearm Pronation</td>
<td>C6-7</td>
</tr>
<tr>
<td></td>
<td>Flexor Carpi Radialis</td>
<td>Wrist Flexion &amp; Abduction</td>
<td>C7-8</td>
</tr>
<tr>
<td></td>
<td>Flexor Digitorum superficiales</td>
<td>Wrist/Finger Flexion (PIP)</td>
<td>C8-T1</td>
</tr>
<tr>
<td></td>
<td>Abductor Pollicis Brevis</td>
<td>Thumb Abduction</td>
<td>C8-T1</td>
</tr>
<tr>
<td></td>
<td>Opponens Pollicis</td>
<td>Thumb to oppose little finger</td>
<td>C8-T1</td>
</tr>
<tr>
<td></td>
<td>Lumbricals (1,2)</td>
<td>MCP flexion with PIP/DIP extended</td>
<td>C8-T1</td>
</tr>
<tr>
<td><strong>Anterior Interosseous</strong></td>
<td>Flexor Digitorum Profundus (1,2)</td>
<td>Wrist/Finger Flexion (DIP)</td>
<td>C8-T1</td>
</tr>
<tr>
<td>(of Median)</td>
<td>Flexor Pollicis Longus</td>
<td>Thumb Flexion</td>
<td>C8-T1</td>
</tr>
<tr>
<td></td>
<td>Pronator Quadratus</td>
<td>Pronation</td>
<td>C8-T1</td>
</tr>
<tr>
<td><strong>Ulnar</strong></td>
<td>Flexor Carpi Ulnaris</td>
<td>Wrist Flexion &amp; Adduction</td>
<td>C8-1-7</td>
</tr>
<tr>
<td></td>
<td>Flexor Digitorum Profundus (3,4)</td>
<td>Wrist/Finger Flexion</td>
<td>C8-1-7</td>
</tr>
<tr>
<td></td>
<td>Adductor Pollicis</td>
<td>Thumb Adduction</td>
<td>C8-1-7</td>
</tr>
<tr>
<td></td>
<td>Lumbricals (3,4)</td>
<td>MCP flexion with PIP/DIP extended</td>
<td>C8-1-7</td>
</tr>
<tr>
<td></td>
<td>Dorsal Interossei</td>
<td>Fingers Abduction</td>
<td>C8-1-7</td>
</tr>
<tr>
<td></td>
<td>Palmar Interossei</td>
<td>Fingers Adduction</td>
<td>C8-1-7</td>
</tr>
<tr>
<td></td>
<td>Flexor Digiti Minimi</td>
<td>Fifth Finger Flexion</td>
<td>C8-1-7</td>
</tr>
<tr>
<td></td>
<td>Abductor Digiti Minimi</td>
<td>Fifth Finger Abduction</td>
<td>C8-1-7</td>
</tr>
</tbody>
</table>

### Arm:
- Deltoid by Axillary – Biceps, Brachialis by Musculocutaneous – Triceps by Radial

### Forearm:
- Posterior Compartment (extensors): All by Radial & PIO
- Anterior Compartment (flexors): Flexor Carpi Ulnaris, Digit Profundus 3,4 by Ulnar - Rest are Median

### Hand:
- Thenar: All by Median except Adductor Pollicis by Ulnar
- Hypothenar: All by Ulnar
- In-between (Interossei & Lumbricals): All by Ulnar except Lumbricals 1,2 by Median
### Muscles of The Lower Extremity

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Muscles</th>
<th>Action</th>
<th>Roots</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior Gluteal</td>
<td>Gluteus Medius &amp; Minimums&lt;br&gt;Tensor Fascia Lata</td>
<td>Hip Abduction - Stabilizes the pelvis&lt;br&gt;Hip Abduction – External Rotation</td>
<td>L4-5 S1&lt;br&gt;L5 S1</td>
</tr>
<tr>
<td>Inferior Gluteal</td>
<td>Gluteus Maximus</td>
<td>Hip Extension – External Rotation</td>
<td>L5 S1-2</td>
</tr>
<tr>
<td>Obturator</td>
<td>Adductor Longus &amp; Brevis&lt;br&gt;Gracilis&lt;br&gt;Adductor Magnus</td>
<td>Hip Abduction&lt;br&gt;Hip Flexion – Medial Rotation&lt;br&gt;Hip Adduction</td>
<td>L2-4&lt;br&gt;L2-4&lt;br&gt;L2-4</td>
</tr>
<tr>
<td>Femoral</td>
<td>Iliopsoas&lt;br&gt;Pectineus&lt;br&gt;Sartorius&lt;br&gt;Quadriiceps Femoris</td>
<td>Hip Flexion&lt;br&gt;Hip Flexion - Adduction&lt;br&gt;Thigh Lateral Rotation&lt;br&gt;Hip Flexion – Knee Extension</td>
<td>L2-4&lt;br&gt;L2-4&lt;br&gt;L2-4&lt;br&gt;L2-4</td>
</tr>
<tr>
<td>Sciatic</td>
<td>Semitendinosus (Tibial part)&lt;br&gt;Semimembranosus (Tibial part)&lt;br&gt;Biceps Femoris Long head (Tibial)&lt;br&gt;Biceps Femoris Short Head (Fibular)&lt;br&gt;Adductor Magnus (Tibial part)</td>
<td>Hip Extension – Knee Flexion&lt;br&gt;Hip Extension – Knee Flexion&lt;br&gt;Hip Extension – Knee Flexion&lt;br&gt;Hip Extension – Knee Flexion&lt;br&gt;Hip Adduction</td>
<td>L5 S2&lt;br&gt;L5 S2&lt;br&gt;L5 S2&lt;br&gt;L5 S2&lt;br&gt;L5 S2</td>
</tr>
<tr>
<td>Superficial Peroneal</td>
<td>Peroneus Longus &amp; Brevis</td>
<td>Foot Eversion – Dorsi Flexion</td>
<td>L4 S2</td>
</tr>
<tr>
<td>Deep Peroneal</td>
<td>Tibialis Anterior&lt;br&gt;Extensor Digitorum Longus &amp; Brevis&lt;br&gt;Extensor Hallucis Longus &amp; Brevis&lt;br&gt;Peroneus Tertius</td>
<td>Foot Inversion – Dorsi Flexion&lt;br&gt;Toes/Ankle Extension&lt;br&gt;Hallux/Ankle Extension&lt;br&gt;Foot Eversion – Planter Flexion</td>
<td>L5&lt;br&gt;L4 S1&lt;br&gt;L4 S1&lt;br&gt;L4 S2</td>
</tr>
<tr>
<td>Tibial</td>
<td>Popliteus&lt;br&gt;Tibialis Posterior&lt;br&gt;Gastrocnemius&lt;br&gt;Soleus&lt;br&gt;Flexor Digitorum Longus&lt;br&gt;Flexor Hallucis Longus</td>
<td>Unlocks the knee to allow flexion&lt;br&gt;Foot Inversion – Planter Flexion&lt;br&gt;Planter Flexion&lt;br&gt;Planter Flexion&lt;br&gt;Toes/Ankle Flexion&lt;br&gt;Hallux/Ankle Flexion</td>
<td>L5 S1&lt;br&gt;L4 S3&lt;br&gt;S1-2&lt;br&gt;S1-2&lt;br&gt;S2-3&lt;br&gt;S2-3</td>
</tr>
</tbody>
</table>

### Brachial Plexus

<table>
<thead>
<tr>
<th>Cords</th>
<th>Divisions</th>
<th>Trunks</th>
<th>Roots</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsal scapular nerve&lt;br&gt;Suprascapular nerve</td>
<td>Long thoracic nerve</td>
<td>L1&lt;br&gt;L2&lt;br&gt;L3&lt;br&gt;L4&lt;br&gt;L5&lt;br&gt;S1&lt;br&gt;S2&lt;br&gt;S3&lt;br&gt;S4&lt;br&gt;S5</td>
<td>C5&lt;br&gt;C6&lt;br&gt;C7&lt;br&gt;C8&lt;br&gt;T1</td>
</tr>
<tr>
<td>Nerve to subclavius</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral pectoral nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculocutaneous nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axillary nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial cutaneous nerve of the forearm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial cutaneous nerve of the arm</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Dermatomes
# Stroke Alert Chart

**Last seen normal:**
**First time seen with stroke:**
**Past medical history:** DM – HTN – Cardiac – Hepatic - Other:
**Past surgical history:** any recent surgery?
**Medications:** Antiplatelets? Anticoagulants? Other home meds:
**Allergy to contrast? To drugs?**

<table>
<thead>
<tr>
<th>1a. <strong>Level of Consciousness (LOC)</strong></th>
<th>Alert 0</th>
<th>Drowsy 1</th>
<th>Obtunded 2</th>
<th>Comatose 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b. <strong>LOC - Questions</strong> Month? Age?</td>
<td>Both correct 0</td>
<td>One correct 1</td>
<td>Neither correct 2</td>
<td></td>
</tr>
<tr>
<td>1c. <strong>LOC - Commands</strong> Opens/closes eyes and hand</td>
<td>Both correct 0</td>
<td>One correct 1</td>
<td>Neither correctly 2</td>
<td></td>
</tr>
<tr>
<td>2. <strong>Eye Movements:</strong></td>
<td>Normal 0</td>
<td>Only to midline 1</td>
<td>Complete palsy 2</td>
<td></td>
</tr>
<tr>
<td>3. <strong>Visual fields:</strong></td>
<td>Normal 0</td>
<td>Quadrantanopia 1</td>
<td>Hemianopia 2</td>
<td>Bilateral hemianopia 3</td>
</tr>
<tr>
<td>4. <strong>Facial:</strong></td>
<td>Normal</td>
<td>Minor paralysis (flattening of nasolabial folds)</td>
<td>Partial paralysis (near or total paralysis lower face)</td>
<td>Complete paralysis (Of upper and lower face)</td>
</tr>
<tr>
<td>5a. <strong>Motor - Left Arm</strong></td>
<td>Normal (No drift at all)</td>
<td>Drift (Drifts downward but NOT to bed before 10 sec.)</td>
<td>Drifts to bed within 10 sec</td>
<td>Movement, but not against gravity</td>
</tr>
<tr>
<td>5b. <strong>Motor - Right Arm</strong></td>
<td>Normal (No drift at all)</td>
<td>Drift (Drifts downward but NOT to bed before 10 sec.)</td>
<td>Drifts to bed within 10 sec</td>
<td>Movement, but not against gravity</td>
</tr>
<tr>
<td>6a. <strong>Motor - Left leg</strong></td>
<td>Normal (No drift at all)</td>
<td>Drift (Drifts downward but NOT to bed before 5 sec.)</td>
<td>Drifts to bed within 5 sec</td>
<td>Movement, but not against gravity</td>
</tr>
<tr>
<td>6b. <strong>Motor - Right leg</strong></td>
<td>Normal (No drift at all)</td>
<td>Drift (Drifts downward but NOT to bed before 5 sec.)</td>
<td>Drifts to bed within 5 sec</td>
<td>Movement, but not against gravity</td>
</tr>
<tr>
<td>7. <strong>Limb Ataxia:</strong></td>
<td>Absent 0</td>
<td>One limb 1</td>
<td>Two limbs 2</td>
<td></td>
</tr>
<tr>
<td>8. <strong>Sensory:</strong> (on face, arm &amp; thigh)</td>
<td>Normal 0</td>
<td>Mild to moderate loss 1</td>
<td>Complete 2</td>
<td></td>
</tr>
<tr>
<td>9. <strong>Language/Aphasia</strong></td>
<td>Normal ability use words and follow commands</td>
<td>Mild to Moderate (Repeats / names with some difficulty)</td>
<td>Severe Aphasia (very few words correct or understood)</td>
<td>Mute (no ability to speak or understand at all)</td>
</tr>
<tr>
<td>10. <strong>Dysarthria (slurred)</strong></td>
<td>Normal 0</td>
<td>Mild to moderate 1</td>
<td>Non-understandable 2</td>
<td></td>
</tr>
<tr>
<td>11. <strong>Neglect:</strong> touch or vision</td>
<td>Normal 0</td>
<td>One modality 1</td>
<td>Both modalities 2</td>
<td></td>
</tr>
<tr>
<td><strong>Total Score</strong></td>
<td></td>
<td></td>
<td></td>
<td>0 = Best, 42 = Worst</td>
</tr>
</tbody>
</table>
You Know How.
Down to earth.
I got home from work.
Near the table in the dining room.
They heard him speak on the radio last night.

MAMA
TIP – TOP
FIFTY – FIFTY
THANKS
HUCKLEBERRY
BASEBALL PLAYER
Snellen’s Chart

Hold chart 6 feet (182 cm) from eyes in a good light.

Pupil Size:

<table>
<thead>
<tr>
<th>Pupil Size</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8 mm</th>
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<tr>
<td>1</td>
<td>20/200</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td>20/100</td>
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<td></td>
<td></td>
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<tr>
<td>3</td>
<td>20/70</td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>4</td>
<td>20/50</td>
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<td></td>
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<tr>
<td>5</td>
<td>20/40</td>
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<tr>
<td>6</td>
<td>20/30</td>
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<tr>
<td>7</td>
<td>20/25</td>
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<td>9</td>
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<tr>
<td>11</td>
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</tbody>
</table>