

## Parkinson's Disease

## I. Clinical Features

- A. Rigidity
- B. Bradykinesia
- C. Tremors
- D. Abnormal gait
- E. Dysautonomia
- F. Hallucinations

## II. Pathophysiology:

- A. ↓ dopamine prod from Sub Nigra
- B. ↓ Inhibition of neostriatum

## III. Drug Classes

- A. Levodopa/Carbidopa
- B. MAO Type B Inhibitors
- C. COMT Inhibitors
- D. Ergot Dopamine Receptor Agonists
- E. Non-Ergot Dopamine Receptor Agonists
- F. NMDA Receptor Antagonists
- G. Antimuscarinic Drugs

## Carbidopa/Levodopa

## I. Drugs

- A. Carbidopa > Parkinson's
  - i. Inhibits dopamine decarboxylase peripherally, allows more levodopa to reach CNS
- B. Levodopa > Parkinson's
  - i. Converted to dopamine in Sub Nigra & stimulates dopamine receptors

## II. Adverse Effects:

- A. Anorexia/Nausea
- B. Tachycardia/Hypotension
- C. HTN Crisis with MAOi
- D. Akinesia/Dyskinesia

## MAO Type B Inhibitors

## I. Drugs

- A. Selegiline
- B. Rasagiline

## II. MOA/Activity: Inhibits MAO Type B Enzyme

## III. Adverse Effects:

- A. Selegiline > HTN, Insomnia (amphetamine metabolite)
- B. Rasagiline > More selective for MAO B

## COMT Inhibitors

## I. Drugs

- A. Entacapone > Parkinson's
- B. Tolcapone > Parkinson's

## II. MOA/Activity: Inhibits COMT (↑ levodopa to CNS)

## III. Adverse Effects:

- A. Dyskinesia
- B. Hallucinations
- C. Orthostatic hypotension
- D. Tolcapone > Hepatic necrosis

## Ergot Dopamine Receptor Agonists

## I. Drugs

- A. Bromocriptine

## II. Applications

- A. Parkinson's
- B. Pituitary microadenomas
- C. Type II DM (unknown mech)
- D. Hyperprolactinemia (D2 stim ↓ prolactin)

## III. MOA/Activity: Stimulates dopamine receptors

## IV. Adverse Effects:

- A. Pulmonary and retroperitoneal fibrosis
- B. Hypotension
- C. Confusion/Hallucinations

## Non-Ergot Dopamine Receptor Agonists

## I. Drugs

- A. Apomorphine
- B. Pramipexole
- C. Ropinirole
- D. Rotigotine

## II. Applications

- A. Parkinson's

## III. MOA/Activity: Stimulates dopamine receptors

## IV. Adverse Effects:

- A. Hypotension
- B. Confusion/Hallucinations

## Multiple Sclerosis

## I. Clinical Features

- A. Vision Changes
- B. Weakness
- C. Pain/Fatigue/Cognitive Changes
- D. Abnormal gait

## II. Pathophysiology:

## A. Autoimmune disruption of myelin nerve sheaths

## MS Disease Modifying Drugs

## I. Drugs

- A. Interferon B1a & Interferon B1b
  - i. Reduces inflammatory response
- B. Glatiramer
  - i. Sacrificial protein
- C. Fingolimod
  - i. Slows lymphocyte migration
  - ii. Adv Rx: ↑ infection, macular edema
- D. Teriflunomide
  - i. Pyrimidine synthesis inh.
  - ii. Adv Rx: ↑ **Liv enzymes**

## E. Dimethyl Fumarate

- i. Alters cell resp to oxidative stress

## F. Natalizumab

- i. MAB targeting  $\alpha$ -4 integrin
- ii. Adv Rx: PML from JC virus link

## G. Mitoxantrone

- i. Anthracycline analog, kills T-cells

## Alzheimer's Disease Modifying Drugs

## I. Drugs

- A. Aducanumab

## II. MOA/Activity: MAB, ↓ amyloid plaques

## III. Adverse Effects: Cerebral edema, CNS microhemorrhages

## NMDA Receptor Antagonists

## I. Drugs

- A. Amantadine > Parkinson's, Influenza
- B. Memantine > Alzheimer's

## II. MOA/Activity: NMDA Receptor Antagonist

- A. Amantadine also stim dopamine release, anticholinergic

## III. Adverse Effects:

- A. Restlessness, confusion
- B. Amantadine > Anticholinergic, hypotension

## Benzodiazepines

### I. Short-Acting

- A. Midazolam
- B. Triazolam

### II. Intermediate-Acting

- A. Alprazolam
- B. Clonazepam
- C. Estazolam
- D. Lorazepam
- E. Oxazepam
- F. Temazepam

### III. Long-Acting

- A. Clorazepate
- B. Chlordiazepoxide
- C. Diazepam
- D. Quazepam

### IV. MOA/Activity: GABA-A receptor stimulation

@ different location than GABA binding site

### V. Class Applications

- A. Anxiolysis
- B. Sedative/hypnotic
- C. Anticonvulsant
- D. Muscle Relaxation
- E. Alcohol withdrawal

### VI. Adverse Effects:

- A. Drowsiness
- B. Confusion/Cognitive Impairment (Caution in elderly)
- C. Dependence (psychological & physiologic)
- D. Withdrawal (life-threatening)

## Benzodiazepine Antagonist

### I. Drugs

- A. Flumazenil > Benzodiazepine Reversal

### II. MOA/Activity: GABA receptor antagonist

### III. Adverse Effects: Seizures, agitation, vomiting

## Partial Serotonin Agonist

### I. Drugs

- A. Buspirone > Generalized anxiety disorder

### II. MOA/Activity: Partial (5-HT<sub>1A</sub>) receptor agonist

agonist

### III. Adverse Effects: HA, nausea

## Barbiturates

### I. Drugs

- A. Thiopental
- B. Pentobarbital
- C. Secobarbital
- D. Amobarbital
- E. Phenobarbital

### II. MOA/Activity:

- A. Potentiates GABA (prolongs chloride channel opening)
- B. Glutamate receptor inhibition
- C. ↓CO<sub>2</sub> response (respiratory depression)

### III. Class Applications

- A. Anesthesia
- B. Anticonvulsant

### IV. Adverse Effects

- A. Drowsiness/Hangover
- B. CYP450 induction
- C. Withdrawal (life-threatening)

## Other Hypnotics (Sleep)

### I. Drugs

- A. Zolpidem > BZ<sub>1</sub> receptor agonist
- B. Zaleplon > BZ<sub>1</sub> receptor agonist
- C. Eszopiclone > BZ<sub>1</sub> receptor agonist
- D. Ramelteon > Melatonin receptor agonist

### II. Adverse Effects:

- A. BZ<sub>1</sub> Agonists > Amnesia, nightmares
- B. Ramelteon > ↑Prolactin levels

## Selective Serotonin Reuptake Inhibitors (SSRIs)

### I. Drugs

- A. Citalopram
- B. Escitalopram
- C. Fluoxetine
- D. Fluvoxamine
- E. Paroxetine
- F. Sertraline

### II. Class Applications

- A. Anxiety/Depression
- B. OCD
- C. Panic Disorder
- D. Bulimia

### III. MOA/Activity: Blocks serotonin reuptake in CNS

### IV. Adverse Effects:

- A. Sleep disturbance

### B. Sexual Dysfunction

### C. Suicidal thoughts (children/teens)

### D. Discontinuation syndrome

### E. Overdose: Prolonged QT, seizures, serotonin syndrome

## Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

### I. Drugs

- A. Venlafaxine
- B. Desvenlafaxine
- C. Duloxetine

### II. Applications

- A. Depression
- B. Pain Syndromes

### III. MOA/Activity: Blocks serotonin & NE reuptake in CNS

### IV. Adverse Effects:

- A. Sexual dysfunction
- B. Discontinuation syndrome

## Atypical Antidepressants

### I. Drugs

- A. Bupropion > Depression, smoking cessation
- B. Mirtazapine > Depression

### II. MOA/Activity

- A. Bupropion > Dopamine & NE reuptake inh.
- B. Mirtazapine > Presynaptic α<sub>2</sub> receptor antagonist (↑NE & serotonin transmission)

### III. Adverse Effects:

- A. Bupropion > **Lowers seizure threshold**
- B. Less sexual dysfunction

## 5HT<sub>2</sub> Receptor Antagonists

### I. Drugs

- A. Trazodone
- B. Nefazodone

### II. MOA/Activity

- A. Serotonin reuptake inhibition
- B. Blocks post-synaptic 5HT<sub>2A</sub> receptors
- C. Antihistamine

### III. Adverse Effects:

- A. Trazodone > **Priapism**
- B. Nefazodone > **Hepatotoxicity**

## Tricyclic Antidepressants

## I. Drugs

- A. Amitriptyline
- B. Amoxapine
- C. Clomipramine
- D. Desipramine
- E. Doxepin
- F. Imipramine
- G. Maprotiline
- H. Nortriptyline
- I. Protriptyline
- J. Trimipramine

## II. MOA/Activity

- A. NE & Serotonin reuptake inhibition
- B. Blocks Serotonin, alpha, histamine & muscarinic receptors

## III. Class Applications

- A. Depression
- B. Sleep disorder
- C. Chronic pain syndromes

## IV. Adverse Effects:

- A. Anticholinergic
- B. Sodium Channel Blockade effects (cardiac arrhythmias in overdose)
  - 1. Tx: NaHCO<sub>3</sub> for QRS widening
- C. Alpha blocker effects
  - 1. Tx: Fluids/vasopressors
- D. Histamine effects
- E. Discontinuation syndrome
- F. Seizures
  - 1. Tx: Benzodiazepines
- G. Sexual dysfunction
- H. Suicidal ideation (pediatric & young adult)

## Lithium

## I. Lithium

## II. MOA/Activity: Unknown

## III. Class Application: Mania/Bipolar

## IV. Adverse Effects:

- A. Narrow therapeutic range
- B. Caution in renal dysfunction
- C. **Toxicity:** Confusion, tremor, slurred speech, ataxia, seizures, coma, death
- D. **Fetal congenital abnormalities**

## Non-Selective Monoamine Oxidase Inhibitors

## I. Drugs

- A. Phenelzine
- B. Tranylcypromine
- C. Isocarboxazid

## II. MOA/Activity

- A. MAO enzyme inhibition > ↑ NE, dopamine, serotonin levels

## III. Class Application: Depression

## IV. Adverse Effects:

- A. Food-food interactions: Aged/meats cheeses due to ↑ tyramine & ↑ release of neurotransmitters = **hypertensive crisis**
  - 1. Tx: alpha blockers
- B. Serotonin syndrome

## First Generation Antipsychotics

## I. Drugs

- A. Chlorpromazine
- B. Thioridazine
- C. Fluphenazine
- D. Haloperidol
- E. Loxapine
- F. Pimozide
- G. Thiothixene
- H. Trifluoperazine

## II. MOA/Activity: Competitive inh. of D2 receptors

## III. Class Applications

- A. Antipsychotic
- B. Antiemetic

## IV. Adverse Effects:

- A. Extra pyramidal side effects (EPS)
  - 1. Akathisia: restlessness
  - 2. Dystonia: prolonged muscle contraction
  - 3. Parkinsonism: bradykinesia, rigidity, tremor
- B. Tardive dyskinesia: long-term abnl repetitive movement (lip smacking, neck/limb movements)
- C. Neuroleptic Malignant Syndrome: Rigidity, fever, AMS, unstable BP
  - 1. Tx: Supportive care, bromocriptine
- D. Prolonged QT

## Second Generation Antipsychotics

## I. Drugs

- A. Aripiprazole (atypical)
- B. Asenapine
- C. Clozapine
- D. Iloperidone
- E. Lurasidone
- F. Olanzapine
- G. Paliperidone
- H. Quetiapine
- I. Risperidone
- J. Ziprasidone

## II. MOA/Activity:

- A. Competitive inh. of D2 receptors
- B. Serotonin receptor inhibition

## III. Class Applications

- A. Antipsychotic
- B. Antiemetic

## IV. Adverse Effects:

- A. Extra pyramidal side effects (EPS)
  - 1. Much less common than 1<sup>st</sup> gen
- B. Tardive dyskinesia: long-term abnl repetitive movement (lip smacking, neck/limb movements)
- C. Neuroleptic Malignant Syndrome: Rigidity, fever, AMS, unstable BP
  - 1. Tx: Supportive care, bromocriptine
- D. Prolonged QT
- E. Weight gain

## Inhaled Anesthetics

## I. Drugs

- A. Desflurane
- B. Halothane
- C. Isoflurane
- D. Sevoflurane

## II. MOA/Activity: Possibly ↑ sens. of GABA receptors

## III. Class Application: Induction of anesthesia

## IV. Adverse Effects:

- A. Bradycardia
- B. Hypotension
- C. **Malignant Hyperthermia** (autosomal dominant, uncontrolled ↑ metabolism in skeletal muscles)
  - 1. Tx: **Dantrolene**, cooling supportive care

## Antiepileptic Chart

| Drug Name              | Mechanism                                                                                                   | Application                                                                   | Adverse Effects                                                                | Other                                                                               |
|------------------------|-------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| <b>Carbamazepine</b>   | Sodium channel blocker                                                                                      | Seizures<br>Trigeminal neuralgia<br>Bipolar                                   | Erratic absorption<br><b>Stevens-Johnson Syndrome</b>                          | Do not use in absence seizures                                                      |
| <b>Divalproex</b>      | Sodium channel blocker<br>GABA blocker<br>↓Ganglionic low threshold<br>Ca current                           | Seizures<br>Bipolar Disorder<br>Headache                                      | <b>Teratogenic</b><br><b>Hepatotoxicity</b><br>Pancreatitis                    |                                                                                     |
| <b>Ethosuximide</b>    | T-type Ca Channel Inhibition                                                                                | <b>Absence Seizures</b>                                                       | <b>SLE</b>                                                                     |                                                                                     |
| <b>Phenobarbital</b>   | Enhances GABA inhibition                                                                                    | Status epilepticus                                                            | Impaired cognition; Precipitates acute intermittent porphyria                  |                                                                                     |
| <b>Primidone</b>       | Enhances GABA inhibition                                                                                    | Status epilepticus                                                            |                                                                                | Metabolized to phenobarbital                                                        |
| <b>Phenytoin</b>       | Blocks Na channels in inactive state                                                                        | Focal seizures<br>Tonic-clonic seizures<br>Status Epilepticus                 | CNS depression (vestibular)<br><b>Gingival hyperplasia</b><br>Nystagmus/ataxia | No IM: Necrosis/abscess formation<br>May precipitate with IV infusion               |
| <b>Fosphenytoin</b>    | Blocks Na channels in inactive state                                                                        | Focal seizures<br>Tonic-clonic seizures<br>Status Epilepticus                 | CNS depression (vestibular)<br><b>Gingival hyperplasia</b><br>Nystagmus/ataxia | Rapidly converted to phenytoin                                                      |
| <b>Eslicarbazepine</b> | Voltage gated sodium channel blocker                                                                        | Partial-onset seizures                                                        | Diplopia                                                                       |                                                                                     |
| <b>Ezogabine</b>       |                                                                                                             | Seizures                                                                      | QT Prolongation<br>Blue skin discoloration<br>Retinal abnormalities            |                                                                                     |
| <b>Felbamate</b>       | Voltage gated sodium channel blocker<br>Ca Channel Blocker<br>GABA potentiation<br>NMDA receptor antagonist | Refractory epilepsy                                                           | <b>Hepatic failure</b><br><b>Aplastic anemia</b>                               |                                                                                     |
| <b>Gabapentin</b>      |                                                                                                             | Adjunct for focal seizures<br>Post herpetic neuralgia                         |                                                                                |                                                                                     |
| <b>Lacosamide</b>      |                                                                                                             | Adjunct for focal seizures                                                    |                                                                                |                                                                                     |
| <b>Lamotrigine</b>     | Na Channel Blocker<br>High Voltage Ca Channel Blocker                                                       | Generalized, focal, & absence seizures<br><b>Bipolar disorder</b>             | <b>Stevens-Johnson Syndrome</b><br>Diplopia                                    |                                                                                     |
| <b>Levetiracetam</b>   |                                                                                                             | Generalized seizures<br>Focal onset seizure<br>Myoclonic seizures             |                                                                                |                                                                                     |
| <b>Oxcarbazepine</b>   | Na Channel Blocker<br>Converted to 10-MHD                                                                   | Partial onset seizures                                                        | Diplopia                                                                       |                                                                                     |
| <b>Perampanel</b>      | alpha-3-hydroxy-5-methyl-4-isoxazolepropionic acid antagonist                                               | Partial onset seizures                                                        | Gait disturbance<br>Behavioral reactions                                       |                                                                                     |
| <b>Pregabalin</b>      |                                                                                                             | Focal onset seizure<br>Diabetic neuropathy<br>Post-herpetic neuralgia         | Weight gain<br>Edema<br>Ataxia                                                 | Renal elimination                                                                   |
| <b>Rufinamide</b>      |                                                                                                             | Adjunct in Lennox-Gestaut syndrome in age >4                                  | <b>Short QT interval (don't give in patients with familial short QT)</b>       |                                                                                     |
| <b>Tiagabine</b>       | Blocks GABA uptake in presynaptic neurons                                                                   | Adjunct for partial onset seizures                                            |                                                                                |                                                                                     |
| <b>Topiramate</b>      |                                                                                                             | Partial onset epilepsy<br>Generalized seizures<br><b>Migraine prophylaxis</b> | Kidney stones<br>Glaucoma                                                      |                                                                                     |
| <b>Vigabatrin</b>      | Inhibits GABA-T (↑GABA levels)                                                                              | Lennox-Gestaut Syndrome                                                       | Visual field loss                                                              |                                                                                     |
| <b>Zonisamide</b>      | Sodium channel blocker<br>Blocks T-type calcium currents                                                    | Focal onset epilepsy                                                          | Kidney Stones<br>Oligohydrosis (↓Sweat)                                        | Contraindications:<br>Sulfonamide hypersensitivity<br>CA inhibitor hypersensitivity |

## Intravenous Anesthetics

## First Generation Antipsychotics

## I. Drugs

## A. Propofol

1. Activity: CNS Depressant
2. Adverse Effects
  - a) Respiratory depression
  - b) Pancreatitis (drug mixed in soybean oil and egg phospholipids)
  - c) Propofol infusion syndrome: heart failure, rhabdomyolysis, metabolic acidosis, renal failure
  - d) Hypotension ( $\downarrow$ SVR)

## B. Etomidate

1. Activity: Sedative/hypnotic
2. Adverse Effects
  - a)  $\downarrow$  Plasma cortisol
  - b)  $\downarrow$  Aldosterone levels

## C. Ketamine

1. Activity: Induces Dissociation, immobility,  **$\uparrow$  sympathetic outflow, bronchodilation**
2. Adverse Effects
  - a)  $\uparrow$  Secretions
  - b) Hallucinations
  - c) "Special K" – street drug

## D. Dexmedetomidine

1. Activity:  $\alpha_2$  receptor agonist
  - a) Sedative/Anxiolysis
  - b) Sympatholytic
  - c) Analgesia
2. Adverse Effects: Bradycardia, hypotension

## Amide Local Anesthetics

## I. Drugs

- A. Lidocaine
- B. Bupivacaine
- C.
- D. Mepivacaine
- E. Prilocaine

## II. MOA/Effects: Sodium ion channel blocker – blocks sensory impulses from reaching CNS

## III. Adverse Effects

- A. Seizures
- B. Cardiac arrhythmias
- C. Less allergenic than esters

## Ester Local Anesthetics

## IV. Drugs

- A. Procaine
- B. Tetracaine
- C. Chlorprocaine
- D. Cocaine
- E. Benzocaine

## V. MOA/Activity: Sodium ion channel blocker – blocks sensory impulses from reaching CNS

## VI. Adverse Effects

- A. Seizures
- B. Cardiac arrhythmias
- C. Benzocaine: methemoglobinemia

## Opioid Receptors

|          |                                                                                 |
|----------|---------------------------------------------------------------------------------|
| $\mu$    | Analgesia, respiratory depression, sedation, euphoria, dependence, constipation |
| $\delta$ | Analgesia                                                                       |
| $\kappa$ | Analgesia, dysphoria                                                            |

## Opioid Mechanisms

I. Pre-synaptic Neuron: Opioids  $\downarrow$   $\text{Ca}^{2+}$  influx  $\rightarrow$   $\downarrow$  glutamate release, reducing transmissionII. Post-synaptic Neuron: Opioids potentiates  $\text{K}^+$  channel opening  $\rightarrow$  hyperpolarizes post-junctional cellsIII. Activate  $\text{G}_i \rightarrow$  inhibits adenylyl cyclase  $\rightarrow$   $\downarrow$  cAMP and  $\downarrow$  protein phosphorylation

## Opioids

## I. Drugs

- A. Alfentanil
- B. Codeine
- C. Fentanyl
- D. Hydrocodone
- E. Hydromorphone
- F. Meperidine
- G. Methadone
- H. Morphine
- I. Oxycodone
- J. Oxymorphone
- K. Remifentanyl
- L. Sufentanil

## II. MOA/Effects:

- A. Analgesia
- B. Euphoria
- C. Anti-tussive
- D. Anti-diarrheal

## III. Adverse Effects

- A. Respiratory depression ( $\downarrow$  sensitivity to  $\text{CO}_2$ )
- B. Miosis
- C. Hypotension/bradycardia
- D. Histamine Release
- E. Opioid Withdrawal
- F. Opioid Epidemic

## Partial Opioid Agonists

## I. Drugs

- A. Buprenorphine

## II. MOA/Activity

- A. MAO enzyme inhibition: Partial  $\mu$  agonist

## III. Class Application: Opioid detoxification

## IV. Adverse Effects:

- A. Precipitation of withdrawal if given to patient without symptoms of withdrawal
- B. Respiratory depression/sedation less common

### Mixed Opioid Agonist/Antagonists

#### I. Drugs

- A. Pentazocine
- B. Nalbuphine
- C. Butorphanol

#### II. MOA/Activity

- A.  $\kappa$  agonist
- B.  $\Delta$  &  $\mu$  agonist/antagonist activity

#### III. Class Application: Analgesia

#### IV. Adverse Effects:

- A. Pentazocine: Nightmares/hallucinations, caution in CAD ( $\uparrow$ systemic and PA pressures)

### Other Opioid Analgesics

#### I. Drugs

- A. Tapentadol
- B. Tramadol

#### II. MOA/Activity

- A. Central  $\mu$  agonist
- B. Tapentadol: NE reuptake inhibitor
- C. Tramadol: NE & Serotonin reuptake inh.

#### III. Class Application: Analgesia

#### IV. Adverse Effects:

- A. Less respiratory depression than traditional opioids
- B. Confusion
- C. Serotonin syndrome

### Opioid Antagonists

#### I. Drugs

- A. Naloxone: Opioid reversal
- B. Naltrexone: Opioid/Alcohol dependence

#### II. MOA/Activity: Binds opioid receptors without activating receptor mediated response

#### III. Class Application: Opioid reversal

#### IV. Adverse Effects:

- A. Precipitates opioid withdrawal
- B. Naltrexone: Hepatotoxicity

### Methylxanthines

#### I. Drugs

- A. Caffeine: Stimulant/Neonatal apnea
- B. Theophylline: Asthma

#### II. MOA/Activity:

- A. Adenosine receptor blocker
- B. Increase in cAMP & cGMP

#### III. Effects:

- A. Stimulant
- B. Smooth muscle relaxation of bronchioles
- C. Cardiac inotropy/chronotropy
- D. Mild diuretic effects

#### IV. Adverse Effects:

- A. Anxiety/tremor
- B. Withdrawal syndrome
- C. Overdose: convulsions/cardiac arrhythmias

### Amphetamines - ADHD

#### I. Drugs

- A. Amphetamine
- B. Dexmethylphenidate
- C. Dextroamphetamine
- D. Lisdexamfetamine
- E. Methylphenidate

#### II. MOA/Activity: Stimulates release of dopamine and NE

#### III. Adverse Effects

- A. Addiction/tolerance
- B. Diversion
- C. Anorexia
- D. Palpitations/arrhythmias

### Amphetamines - Narcolepsy

#### I. Drugs

- A. Armodafinil
- B. Modafinil

#### II. MOA/Activity: Stimulates release of dopamine and NE

#### III. Adverse Effects

- A. Addiction/tolerance
- B. Diversion
- C. Anorexia
- D. Palpitations/arrhythmias