Psychopharmacology Made Simple!

Britta Ostermeyer, MD, MBA
Professor and Chairman
Department of Psychiatry & Behavioral Sciences
University of Oklahoma
Objectives

By the end of the presentation, the audience will:

1. Understand the main classes of medications utilized in psychiatry
2. Can name at least two representatives in each medication class
3. Can name at least two benefits and two side-effects of the main medication representative in each medication class
4. Will be able to identify the child FDA-approved psychiatric medications in each medication class
Disclaimer

- Informational in order to better understand patients

- Slides reflect material from:
  - FDA information/package inserts
  - Psychopharm books
  - Individual experience
Overview

1. Antidepressants
2. Antipsychotics
3. Anxiolytics
4. Sedatives/Hypnotics
5. Mood Stabilizers
6. ADHD Medications
7. Dementia Medications
8. Substance Use Disorder Medications
Determinants of Treatment Choice

- Age
- Gender
- Diagnosis
- Specific symptoms
- Comorbid psychiatric symptoms
- Comorbid medical conditions
- Past medication trials and responses
- Family history of medication response

- Severity of current episode
- Phase of illness - acute vs chronic
- Single vs recurrent
- Access to health care
- Financial implications
- Patient choice
1. Antidepressants
Antidepressants

- SSRIs
- SNRIs
- TCAs
- MAOIs
- Others
FDA Warning: Suicidality and Antidepressants

ADs increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of MDD and other psychiatric disorders. Anyone considering the use of [name of AD] in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the suicidality risk with ADs compared to placebo in adults beyond age 24; there was a reduction in risk with ADs compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on ADs should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families/caregivers should be advised of the need for close observation and communication with the prescriber.
Questions You Must Answer
Prior To Treatment Of Depression

1) Safety concerns?
2) Due to medical?
3) Mania/hypomania?
4) Psychotic symptoms?
5) Substance abuse?
6) Insomnia?
7) Also significant anxiety?
8) Also personality problems or stressors?
Indications/Use of ADs

- MDD
- Premenstrual Dysphoric Disorder
- Bipolar, Depressed
- Bulimia
- GAD
- PTSD
- Social Anxiety Disorder
- Panic Disorder
- OCD
- Dysthymia
- Premature Ejaculation
- Enuresis (IMP)
- ADHD (Bupropion)
- Neuropathic pain, migraine
- Urticaria/pruritis (Doxepin cream)
Antidepressant Choice by Symptom Complex

- Norepinephrine
  - Energy
  - Interest
- Serotonin
  - Anxiety
  - Irritability
- Dopamine
  - Drive
- Mood, Emotion, Cognitive Function
  - Impulse
  - Appetite
  - Aggression

- Motivation
Pharmacological Profile of ADs

Antidepressant

- Reduce depression
- Psychomotor activation
- Parkinsonian effects
- DA reuptake inhibition

5HT reuptake inhibition
- Reduce depression
- Antianxiety effect
- GI disturbance
- Sexual dysfunction

5HT₂ block
- Reduce depression
- Reduce suicidality
- Antipsychotic effect
- Hypotension
- Ejaculatory dysfunction
- Sedation

NE reuptake inhibition
- Reduce depression
- Tremors
- Tachycardia
- Erectile/ejaculatory dysfunction
SSRIs
Selective Serotonin Reuptake Inhibitors (the “Gold Standard”)

- Citalopram (Celexa®)
- Escitalopram (Lexapro®)
- Fluoxetine (Prozac®)
- Fluvoxamine (Luvox®)
- Paroxetine (Paxil®)
- Sertraline (Zoloft®)
SSRIs General Remarks

- Not lethal in overdose
- Black box on suicidality in minors
- CI with MAOIs
- Start lower dose, then increase
- Dose reduction in liver disease
- Potential risk of bleeding
- P 450 2D6 inhibitors, ↑ TCAs
- Pregnancy category C (Paxil was changed to D)
- Discontinuation syndrome (except Prozac)
SSRIs Side-Effects

- Psychomotor agitation
- Anxiety, insomnia
- Sedation
- Headache, worsening of migraines
- N/V, loose stools
- ↑ Sweating
- Rhinitis
- Sexual SEs, hypo Na, SIADH
- ↓ REM sleep w/ nightmares, dreams
- Myoclonus, EPS, bruxism
- Serotonin Syndrome (AMS, temp, abn VS, EPS)
- Bradycardia
- Problems in exposed neonates (w/ SNRIs too) requiring hospitalization
Antidepressants SSRI
Paroxetine (Paxil®)

General: Most sedating, qhs, most w/d, best for anxiety

FDA I: MDD, SAD, OCD, GAD, PD, PTSD, PMDD

Dose: Start 10-20 mg, max 60-80 mg

SEs: Most anticholinergic, most weight gain, do not use in pregnancy
Antidepressants SSRI
Fluvoxamine (Luvox®)

**General:** CR preparation, drug interactions

**FDA I:** CR: OCD, Social A; regular: adult and Pedi OCD

**Dose:** 50 mg qhs, max 300 mg
Child start 25 mg qhs, max 200 mg (8-11), 300 mg (12-17)

**SEs:** Contra I with a number of other meds
Antidepressants SSRI
Citalopram (Celexa®)

General: Little drug interaction,
Dose dependent QT prolongation (8/24/11)

FDA I: MDD

Dose: Start 10-20 mg, max 40 mg
Max dose is 20 mg in:
> age 60
D/C in persistent QTc > 500msec

SEs: Dose-dependent QT prolongation
Antidepressants SSRI

Escitalopram (Lexapro®)

**General:** More stimulating, more potent than Celexa (1.5 to 2 X), cleanest SSRI, qam, little drug interactions like Celexa

**FDA I:** MDD, GAD

**Dose:** Start 10 mg, max 20 mg

**SEs:** Anxiety, insomnia
Antidepressants SSRI
Sertraline (Zoloft®)

**General:** Better in the am

**FDA I:** MDD, PMDD, PTSD, PD, SAD, OCD, Pedi OCD

**Dose:** Start 25-50 mg, max 200 mg

**SEs:** Rarely tremors
Antidepressants SSRI

**Fluoxetine (Prozac®)**

**General:** Stimulating, qam, no w/d, weekly Prozac, washout 5 wks (norfluoxetine 330 h)

**FDA I:** MDD, OCD, PD, Bulimia, PMDD
Pedi MDD + OCD
Fluoxetine/Olanzapine (TRMDD, bipolar depression)

**Dose:** Start 10 mg, max 80 mg

**SEs:** Anxiety, insomnia
SNRIs
Serotonin Norepinephrine Reuptake Inhibitors

- Venlafaxine XR (Effexor XR®)
- Duloxetine (Cymbalta®)
- Desvenlafaxine (Pristiq®)
Antidepressants SNRI
Serotonin Norepinephrine Reuptake Inhibitor

Venlafaxine XR
(Effexor XR®)

General: Good for anxiety, significant w/d, once qam

FDA I: MDD, SAD, GAD, PD

Dose: Start 37.5 mg, max 375 mg

SEs: Elevation BP, not in narrow angle glaucoma (mydriasis)
Antidepressants SNRI
Serotonin Norepinephrine Reuptake Inhibitor

Duloxetine (Cymbalta®)

**General**: Withdrawal

**FDA I**: MDD, GAD, fibromyalgia

- Diabetic peripheral neuropathic pain
- Chronic musculoskeletal pain

**Dose**: Start 30-60 mg; 60 mg recommended, max 120 mg

**SEs**:
- **Warning**: liver damage
- **Do not use in**: alcohol use/liver disease, severe renal disease, narrow angle glaucoma (mydriasis)
Antidepressants SNRI
Serotonin Norepinephrine Reuptake Inhibitor

Desvenlafaxine (Pristiq®)

**General:** Similar to Venlafaxine

**FDA Indication:** MDD

**Dose:** 50 mg daily (higher dose no added benefit)
ESRD/severe renal failure: 50 mg QOD,
moderate renal failure: No more than 50 mg daily

**SEs:** Like Venlafaxine
TCAs
Tricyclic Antidepressants

- Amitriptyline (Elavil®)
- Nortriptyline (Pamelor®)
- Imipramine (Tofranil®)
- Clomipramine (Anafranil®)
Antidepressants
TCAs

General: **Lethal in overdose** (usually 1 week supply)
(class 1A, like Quinidine, AV↓)
Anxious/panic: Imipramine
Depression: NTP
OCD: Clomipramine
Inhibit reuptake of NE and 5-HT

**EKG:** Age 40 or older or suspect heart condition

**SEs:**
• Significantly more, incl cardiac
• Contra I in heart block or s/p MI
• Relatively Contra I: BBB
SSRIs vs. TCAs

**Advantages**
- Not anti-cholinergic*
- Not anti-histaminic
- Not alpha₁ antagonistic
- Unlikely to cause
  - Hypotension
  - Tachycardia
  - Delayed cardiac conduct.
  - Blurred vision
  - Dry mouth*
  - Sedation*
- * Except Paroxetine (Paxil®)

**Disadvantages**
- Nervousness, agitation
- Insomnia
- Nausea, diarrhea
- Headache
- Sexual dysfunction
TCAs

Tertiary Amines

• 5-HT >> NE
• More anti-cholinergic
• More orthostasis

Secondary Amines

• NE >> 5-HT
• Less anti-cholinergic
• Less orthostasis

Imipramine

Desipramine
TCAs Side Effects

- **Cardiovascular**
  - Tachycardia
  - Hypotension
  - Quinidine-like effect

- **Anti-muscarinic**
  - Blurred vision
  - Constipation
  - Confusion, delirium
  - Dry mouth
  - Urinary retention

- **Anti-histaminic**
  - Sedation
  - Weight gain

- **Sexual dysfunction**
- **Mania**
- **Peripheral edema**
- **Seizures**
Antidepressants TCAs

Amitriptyline (Elavil®)

- Oral/IM
- 75 to 200 mg qhs, (max dose is 300 mg)
- Sedating
- Depression
- Chronic pain
Avoid Elavil® In Psychiatric Patients For Sleep and Pain!
Antidepressants TCAs

Nortriptyline (Pamelor®)

- 25 mg tid or QID or once daily, max 150 mg/d
- Elderly, max 30 to 50 mg/d
- Depression
- Chronic pain, migraine
Antidepressants TCAs
Imipramine (Tofranil®)

- Adults: 50 to max 300 mg/d
- Children: 25 to 75 mg 1 h prior to bedtime or divided dose of one in the afternoon and one 1h prior to bedtime
- Depression, childhood enuresis age 6 and older
- Panic Disorder
Antidepressants TCAs
Clomipramine (Anafranil®)

- Oral/IV
- Adults: 100 to 250 mg qhs
- Children: up to 100 to 200 mg qhs
- OCD in adults and children
- Depression
NDRIs

Norepinephrine Dopamine Reuptake Inhibitors

• Bupropion SR or XL (Wellbutrin SR or XL®)
Antidepressants NDRI
Norepinephrine Dopamine Reuptake Inhibitors

**Bupropion SR or XL**
(Wellbutrin SR or XL®)

**General:** Very stimulating, not for anxious/panic, qam, good for attention, least sexual SEs, dose-dep seizures

**FDA I:** MDD (mild to moderate), smoking cessation
Seasonal Affective Disorder (XL)

**Dose:** Start 100-150 mg, max 400 (SR) + 450 (XL) mg

**SEs:**
- Contra in seizure disorder, eating disorder, alcohol w/d, benzo w/d,
- Worsens OCD and tics
- Insomnia, anxiety
NaSSADs
Noradrenergic/Specific Serotonergic ADs

• Mirtazapine (Remeron®)
Antidepressants NaSSAD
Noradrenergic/Specific Serotonergic AD
Alpha-2, H1, 5-HT2 and 5-HT3 Antagonism

Mirtazapine (Remeron®)

General: Very sedating, Sol Tabs, for poor eaters, always qhs

FDA Indications: MDD

Dose: Start 15 mg, max 45 mg as per PI

SEs: Weight gain, ↑ appetite
SARIs
Serotonin-2 Antagonists/Reuptake Inhibitors

• Trazodone (Desyrel®)
• Nefazodone (Serzone®)
Trazodone (Desyrel®)

General: Blocks 5-HT2 receptors, antagonist of alpha 1 adrenergic receptors, poor antidepressant efficacy, used for sleep

FDA I: MDD

Dose: Start 25-50 mg, max 400 mg qhs

SEs:
- Sedation, orthostatic hypotension
- Priapism (warn men)
- Arrhythmias in preexisting heart conditions
Nefazodone (Serzone®)

General: Rarely used, analogue of Trazodone

FDA I: MDD

Dose: 200-600 mg, bid or qhs

SEs:
- Sedation, helps sleep and anxiety
- Black box warning: liver failure (rare but catastrophic)
MAOIs
Irreversible Monoamine Oxidase Inhibitors

- Isoxcarboxazid (Marplan®)
- Phenelzine (Nardil®)
- Tranylcypromine (Parnate®)
Indications/Uses of MAOIs

- Major depression
- Atypical Depression
- Anxiety
  - Panic disorder
  - Phobias
MAO I Blocks Monoamine Oxidase

- Breakdown of monoamine neurotransmitters and increasing their availability

- 2 isoforms of monoamine oxidase:
  - MAO-A (Brain, GI): Serotonin, melatonin, epinephrine, norepinephrine, dopamine
  - MAO-B (Brain, Platelets): Phenylethylamine, dopamine
MAOIs: Food & Drug Interactions

Hypertensive Crisis ("The Cheese Reaction")

Foods: Tyramine (exogenous monoamine with vasopressor actions; displaces norepinephrine from storage vesicles, accumulation of catecholamines with increase of BP)

No dietary amines (Tyramine)!

- Cheese (cottage OK)
- Chianti wine
- Vermouth
- Sausage
- Pickled herring
- Yeast & meat extracts
- Fava beans

Contraindicated Drugs

- SSRIs, SNRIs (serotonin syndrome)
- TCAs
- Buspirone (Buspar®)
- Nefazodone (Serzone®)
- Meperidine (Demerol®)
- Decongestants
MAOIs
Irreversible Inhibitor of MAO A and B

Phenelzine (Nardil®)
- 30-90mg
- Sedation
- Hypotension
- 1/2 life 2 hours

Tranylcypromine (Parnate®)
- 30-60mg
- Stimulating
- Less hypotensive
- 1/2 life 2 hours

General Side Effects
- Postural hypotension
- Insomnia, agitation
- Pyridoxine deficiency
- Sexual dysfunction
- Edema
- Delirium

Contra Indicated:
- With long list of meds/foods
- Pheochromocytoma
- CHF
- Hepatic failure
- Parnate: cerebrovascular and cardiovascular disease and HTN

MAOI-A: Reduces breakdown of serotonin, norepinephrine dopamine, requires diet
MAOI-B: Reduces breakdown of dopamine, no diet in low dose, eg Selegiline
Washout Starting or Stopping

- MAOI to SSRI - 2 week washout
- Diet: Continue for 2 weeks after stopping MAOI
- SSRI to MAOI
  - Fluoxetine: 5-6 week washout
  - Clomipramine: 3 weeks
  - Sertraline: 3 weeks
  - Other SSRIs: 2 weeks
MAOI-B Inhibitor
Monoamine Oxidase B Inhibitors

- Selegiline Transdermal (EMSAM®)
MAOI-B Inhibitor

Selegiline Transdermal (EMSAM®)

**General:** Selective, irreversibly inhibits MAOI-B, no diet required, at high dose inhibits both MAO-A and B requiring diet

**FDA I:** MDD

**Dose:** 6 mg/24h (no diet, for elderly); 9 mg/24h and 12 mg/h (with diet)

**SEs:**
- Contra I: Serotonin drugs (14 day wash-out prior to starting another serotonin drug)
- Drug abuse concern
- Headache, insomnia
- Reactions to patch
New AD
Vilazodone (Viibyrd®)

5-HT1A receptor partial agonist/5-HT RI

General: More rapid effect, give with food

FDA I: MDD

Dosing: Start 10 mg X 7, then 20 mg X 7 days, then 40 mg

SEs: Drug interactions
Augmenting Agents

- Add antidepressant (Wellbutrin®)
- Add Lithium
- Add atypical antipsychotics (Abilify®, Seroquel®)
Compliance: Explain To Patient!

• Not to expect anything after taking the pill that day
• Starts working after 2-4 weeks
• Has to be gradually increased
• Has to be taken daily
Response vs. Remission

- > 50% decrease in HAM-D score
- Clinically significant improvement in symptoms
- Residual symptoms present

- Minimal or no symptoms
- No longer meets syndromal criteria
- $\text{HAM-D}_{17} < 7$
- Return to “functional normality”
  - Restoration of optimal daily functioning
  - Typically, cannot be distinguished from those without depression
  - Better prognosis
Risk of Recurrence of Depression

1 episode: 50%

2 episodes: 80–90%

3 episodes: > 90%
Depression Treatment guidelines

Continue for > 4-9 months

Continue indefinitely for > 3 episodes or 2 episodes with risk factors
Discontinuation Syndrome

- Paxil, Luvox, Effexor > Celexa > Zoloft
- Prozac very unlikely
- Can be seen in TCAs and MAOs
- Tx Prozac, slower taper
- Dizziness
- Nausea, vomiting
- Anxiety, irritability
- Flulike symptoms
- Insomnia
- Electric shocks sensations
Treatment-Resistant Depression

- DDX
- Diagnosis
- Non-compliance
- Inadequate dose
- Co-morbidity
  - Substance use
  - Medications
  - Medical conditions
  - Psychosocial stressors
  - Personality Disorder

Strategies
- Optimize
  - Longer duration, higher dosages
- Augment or combine
- Switch
  - Within same class
  - Across classes
- Antidepressants + psychotherapy
2. Antipsychotics
First Generation: Typical Antipsychotics

**Low Potency**
- Chlorpromazine (Thorazine®)
- Chlorprothixene (Taractan®, Truxal®)
- Levomepromazine (Levoprome®)
- Mesoridazine (Serentil®)
- Thioridazine (Mellaril®)

**Medium Potency**
- Loxapine (Loxitane®)
- Molindone (Miban®)
- Perphenazine (Trilafon®)
- Thiothixene (Navane®)

**High Potency**
- Droperidol (Dehydrobenzperidol®)
- Fluphenazine (Prolixin®)
- Haloperidol (Haldol®)
- Pimozide (Orap®)
- Prochlorperazine (Compro®)
- Trifluoperazine (Stelazine®)
Second Generation: Atypical Antipsychotics

- Aripiprazole (Abilify®)
- Asenapine (Saphris®)
- Clozapine (Clozaril®)
- Iloperidone (Fanapt®)
- Lurasidone (Latuda®)
- Olanzapine (Zyprexa®)
- Paliperidone (Invega®)
- Quetiapine (Seroquel®)
- Risperidone (Risperdal®)
- Ziprasidone (Geodon®)
What Else To Address

1) Safety, Suicidal? Homicidal?
2) Living arrangements?
3) Substance abuse referral?
4) Depression? Schizoaffective Disorder?
5) Insomnia?
6) Anxiety?
First Generation: Typical Antipsychotics SEs

- All black box on increased mortality in elderly with dementia-related psychosis
- EPS: Acute dystonia, akathisia, parkinsonism, tardive dyskinesia
- Neuroleptic malignant syndrome
- Seizures
- Arrhythmias, EKG changes
- Anticholinergic (dry mouth, constipation, urinary retention, blurry vision)
- Hyperprolactinemia
- Abnormal blood counts
- Sexual SEs
Second Generation
Atypical Antipsychotics

- All black box on increased mortality in elderly with dementia-related psychosis
- Weight gain, most Zyprexa, least Abilify, Latuda
- Metabolic syndrome and diabetes
- EPS & TD & NMS, least Seroquel, Clozaril no TD
- Somnolence, least Abilify
- Hyperprolactinemia, except Seroquel, Clozaril
- ↑ Transaminases, liver/biliary problems
- Sexual side-effects
- Abnormal blood counts
Tardive Dyskinesia
Tardive Dystonia: Torticollis
AIMS Evaluation

(Abnormal Involuntary Movement Scale)

Twice Yearly to Monitor For Tardive Dyskinesia:

1. Facial Muscles
2. Lips/Perioral Area
3. Jaws
4. Tongue
5. Upper Extremities
6. Lower Extremities
7. Neck/Shoulders/Hips
Treatment of Tardive Dyskinesia

- Taper antipsychotic
- Caution b/c of withdrawal dyskinesias
- Switch to Seroquel
- Clozaril
Metabolic Syndrome

- Abdominal obesity
- Elevated triglycerides
- Low HDL
- Elevated blood pressure
- Elevated fasting glucose
Long Acting Therapy: Injectable Depot Antipsychotics

- Haldol Decanoate®
- Prolixin Decanoate®
- Risperdal Consta®
- Invega Sustenna®
- Abilify Maintena®
- Zyprexa Relprevv®
Long Acting Therapy
Invega Sustenna®

**General:** Single po test dose if no hx of prior tx, missed dosing schedule, no oral supplementation, efficacy on day 1 due to higher initial dose, refilled syringes, no refrigeration, stays up to 6 months in patient, active drug

**FDA I:** Schizophrenia, acute + maintenance

**Dosing:** Day 1, Day 7, then monthly; switching from another depot injection: Inject desired monthly maintenance dose the day the old medication is due

**SEs:** Metabolic syndrome
3. Sedatives/Hypnotics
Sedatives/Hypnotics

- Benzodiazepines
- Barbiturates
- Antihistamines
- Partial agonist at 5-HT$_{1A}$ receptor
- Non-Benzodiazepine Hypnotics
- Selective Melatonin Agonist
- Others
Concept For Medication Treatment of Anxiety Disorders

• Gold standard:
  - SSRI or SNRI or TCA

• If needed as PRN:
  - Hydroxyzine (Atarax®, Vistaril®)

• Avoid: Benzos

• Not indicated: Barbiturates
Selective Serotonin Reuptake Inhibitors (the “Gold Standard”)

- Citalopram (Celexa®)
- Escitalopram (Lexapro®)
- Fluoxetine (Prozac®)
- Fluvoxamine (Luvox®)
- Paroxetine (Paxil®)
- Sertraline (Zoloft®)
Other ADs Used For Anxiety

**SNRIs:**
Venlafaxine (Effexor®)
Duloxetine (Cymbalta®)

**TCAs:**
Imipramine (Tofranil®, Panic Disorder)
Clomipramine (Anafranil®, OCD)

**Avoid:**
Buproprion (Wellbutrin®)

**MAOI:**
Tranylcypromine (Parnate®)
Phenelzine (Nardil®)
Barbiturates and Benzodiazepines

Most Are:
- Anxiolytics
- Sedatives
- Hypnotics
- Anticonvulsants
- Muscle relaxers
Barbiturates

Long-acting (12 - 24 hours):
- Phenobarbital (Luminal®)
- Mephobarbital (Mebaral®)

Short and intermediate acting (3 to 8 hours):
- Amobarbital (Amytal®)
- Butabarbital (Butisol®)
- Pentobarbital (Nembutal®)
- Secobarbital (Seconal®)

Ultrashort-acting (minutes):
- Thiopental (Pentothal®)
- Thiamylal (Surital®)
- Hexobarbital (Sombulex®)

Adolf von Baeyer, Germany
1st Barbiturate, Nobel Prize, 1905
Barbiturates

- Bind within the GABA-mediated chloride ion channel increasing chloride ion conductance
- Increases the duration of opening, thereby hyperpolarizing the neuron
- Reduction in excitability of neuron and CNS depression
- Increases chloride ion conductance independently of GABA
- DANGEROUS, LETHAL in overdose!!! CNS depression and respiratory depression
- Significant and fast tolerance
- Very high potential for dependence
Barbiturates

- Paradoxical excitation
- REM sleep suppression
- Motor incoordination
- Not indicated in treatment of anxiety disorders
- Powerful inducers of hepatic cytochrome P450 enzymes
- Important drug interactions with Warfarin, Phenytoin, Valproic Acid
- Contra l in porphyria
Benzodiazepines

- Clonazepam (Klonopin®)
- Oxazepam (Serax®)
- Lorazepam (Ativan®)
- Chlordiazepoxide (Librium®)
- Clorazepate (Tranxene®)
- Diazepam (Valium®)
- Nitrazepam (Mogadon®)
- Alprazolam (Xanax®)
- Flurazepam (Dalmane®)
- Temazepam (Restoril®)
- Estazolam (ProSom®)
- Halazepam (Paxipam®)
- Quazepam (Doral®)
- Triazolam (Halcion®)
- Midazolam (Versed®)
Benzodiazepines

- GABA availability is the rate-limit step!
- Thus, much less dangerous than barbiturates
- **DANGEROUS** when with other CNS depressants like alcohol
- CNS depression and respiratory depression
- Avoid in patients with alcohol problems
- Ataxia and falls in the elderly
- Confusion, memory impairment
- Paradoxical excitation
- REM suppression
- Dependence and abuse potential
- Tolerance
Benzodiazepines

- Alprazolam (Xanax®)
- Diazepam (Valium®)
- Clonazepam (Klonopin®)

Onset of Action
Duration of Effect

Time
Relative Potency of BZDs

- Clonazepam (Klonopin®) 0.25 mg
- Alprazolam (Xanax®) 0.50 mg
- Lorazepam (Ativan®) 1.0 mg
- Diazepam (Valium®) 5.0 mg
- Chlordiazepoxide (Librium®) 10.0 mg
You Will Be Asked For Xanax…
Say “No” To Xanax!
Antihistamine Used As Anxiolytics/Hypnotics

- Hydroxyzine (Atarax®, Vistaril®)
Non-BZD, Non-Barbiturate Anxiolytics

Buspirone (Buspar®)

General: Partial agonist at 5-HT$_{1A}$ receptor, delayed onset of action, no abuse potential, minimal drug interactions, efficacy?

FDA I: Anxiety Disorders

Dose: Start 15 mg or 7.5 mg bid, max 60 mg

SEs: Dizziness, headache, nausea
Non-Benzo Hypnotics
Zolpidem (Ambien®),
Eszopiclone (Lunesta®)

General: Potentiates GABA by binding to GABA A receptors at the same location as benzos, quick onset 15 min

FDA I: Insomnia, Ambien: short-term treatment

Dose: Ambien 5-10 mg, Sonata 1-3 mg

SEs:
• Drowsiness, day time impairment
• Headache, dizziness, ataxia
• Abnormal thinking, behavioral changes
• Amnesia, hallucinations (1%)
• Abuse/dependence?
• W/d, carefully monitor patient with SUD
Selective Melatonin MT1 and MT2 Agonist

Ramelteon (Rozerem®)

**General**: Reduces sleep latency,

**Not**: Controlled substance, abuse, rebound insomnia, confusion in elderly, motor problems, or exacerbation of sleep apnea/COPD

**FDA I**: Insomnia with difficulty of sleep onset

**Dose**: 8 mg, not after a meal

**SEs**: Headache, fatigue, dizziness, nausea
Other Agents Used For Anxiety

Beta-Blockers for Stage Fright:

- Propranolol (Inderal®)
- Metoprolol (Lopressor®, cardioselective)

Others (not FDA approved):

- Gabapentin (Neurontin®)
- Quetiapine (Seroquel®)
4. Mood Stabilizers
Mood Stabilizers

- Lithium
- Anticonvulsants
- (Second Antipsychotics)
- (Antipsychotic/Antidepressant Combinations)
Lithium

General: Narrow therapeutic range, modulates intracellular signaling, 95% renal excretion, 1) mania; 2) anti-suicidal; 3) augmentation in depression

FDA I: Manic episodes, maintenance tx

Dose: Start 300 mg tid, level 0.8-1.2 mmol, measure 5 d after starting; once stable dose q 3-6 months; acute 900-2400 mg; maintenance 400-1200 mg
SEs: Toxicity, teratogenic, GI, weakness, fatigue, cognitive blunting, tremor, EKG changes, weight gain, hypothyroidism, polyuria/polydipsia, renal disease, sodium ↓ → Li ↑

Contra I:
- Not in 1st trimester (Epstein)
- Brain damage, severe debilitation
- Severe renal ds
- Severe CVD
Anticonvulsants

- Divalproex Sodium (Depakote®)
- Carbamazepine (Tegretol®)
- Lamotrigine (Lamictal®)
Divalproex Sodium (Depakote®)

General: Sedation

FDA I: Mania, more in mixed/rapid cycling, epilepsy, prophylaxis of migraine

Dose: Start 250-500 mg, 750-3000 mg

SEs:
- Liver damage, pancreatitis,
- Low platelets
- Encephalopathy with elevated ammonia
- Birth defects
Carbamazepine (Tegretol®)

**General:** Dizziness, start on low dose, induces its own metabolism

**FDA I:** Seizures, trigeminal neuralgia, no psych I

**Dose:** Start gentle, therapeutic 400-800 mg

**SEs:**
- Black box warning: serious skin reaction, Steven-Johnson Syndrome, 1-6/10,000, abn blood counts
- Not in pts with bone marrow suppression
- Birth defects (spinal bifida)
- Drug interactions
- Liver damage, pancreatitis
- Hyponatremia (SIADH)
Lamotrigine (Lamictal®)

General: No weight gain, better for depression in bipolar disorder

FDA I: Seizures, bipolar maintenance

Dose: Start gentle at 25 mg, 100-300 mg

SEs:
- Increase w/ Depakote,
- Black box warning: Rash/Steven-Johnson Syndrome, 0.8/1,000
Steven-Johnson Syndrome
5. ADHD Medications
ADHD Medications

- Stimulants
- Selective Norepinephrine Reuptake Inhibitor
- Alpha 2 Agonists
- (Certain ADs: Bupropion)
Stimulants

- **Methylphenidate**
  - Short: Ritalin®, Methylin®, Metadate®, Focalin®
  - Mid: Ritalin LA®, Metadate CD®
  - Long: Concerta®, Daytrana® patch, Focalin XR®

- **Dextroamphetamine**
  - Short: Dexedrine¹
  - Long: Dextedrine spansule¹, Dextroamphetamine Sulfate ER, Vyvanse®

- **Mixed Amphetamines**
  - Short: Adderall¹ ®
  - Long: Adderall XR®

¹Approved age 3 and older

Short: 4-5h
Mid: 8h
Long: 10-12h
Mechanism

- Intra-synaptic DA >> NE
- Bind to DA transporter protein blocking DA reuptake
- In addition, amphetamines enter neuron and cause exit of NE, DA, ST from storage
Ritalin ® (CII)

**General**: Milder than Adderall

**FDA I**: ADHD (age 6 or older), narcolepsy

**Dose**: 5 mg (max 60 mg)

**SEs**:
- Black box warning: drug dependence
- Contra I: Tics, Tourette’s, glaucoma
- Growth suppression
- Sudden death in patients with heart disease
- Stroke, MI, HTN, seizures
Adderall® (CII)

General: Stronger

FDA I: ADHD (age 3 onwards), narcolepsy

Dose: 2.5 mg (max in child 40 mg, max 60 mg in narcolepsy)

SEs:
- Black box warning: High potential for abuse, dependence, misuse may cause sudden death/serious CV adverse events
- Contra I: Symptomatic CVD, mod-severe HTN, hyperthyroidism, glaucoma, hx of drug abuse
- Growth retardation, sudden cardiac death in those with heart problems, stroke, MI, seizures, worsening of tics
Selective Norepinephrine Reuptake Inhibitor

Atomoxetine (Strattera®)

**General**: Non-stimulant, black box suicide warning

**FDA I**: ADHD, age 6 and over

**Dose**: Start 40 mg, max 100 mg

**SEs**: “Severe liver injury”

**Contra I**: severe CVD
Alpha 2 Agonists

Guanfacine XR (Intuniv®)

General: Non-stimulant,
FDA I: ADHD, with or without stimulant
Dose: 1-4 mg
SEs:
• Sedation
• Hypotension, bradycardia, syncope
6. Dementia Medications
Dementia Medications

- **Cholinesterase Inhibitors**
  - Donepezil (Aricept®)
  - Tacrine (Cognex®)
  - Rivastigmine (Exelon®)
  - Galantamine (Razadyne®)
- **NMDA (N-methyl-D-aspartate) Receptor Antagonist**
  - Memantine (Namenda®)
Cholinesterase Inhibitors
Donepezil (Aricept®)

General: Dissolvable tab
FDA I: Alzheimer’s Dementia
Dose: Start 5 mg, 23 mg
SEs:
• N/V, diarrhea
• Peptic GI ulcer, GI bleed
• Bradycardia, heart block
• Weight loss
NMDA (N-methyl-D-aspartate) Receptor Antagonist

Memantine (Namenda®)

General:

**FDA I**: Mod-severe AD

**Dose**: Start 5mg, max 10 mg bid

**SEs**:  
- Dizziness, headache  
- Confusion  
- Constipation
7. Substance Use Disorder Medications
Meds For SUD

- Alcohol Use Disorder
  - Disulfiram (Antabuse®)
  - Acamprosate (Campral®)

- Alcohol/Opiate Use Disorder; Opiate Antagonist
  - Naltrexone (Vivitrol®)

- Opiate Use Disorder
  - Methadone (Dolophine®)
  - Buprenorphine/Naloxone (Suboxone®)
  - Buprenorphine (Subutex®)
Disulfiram (Antabuse®)

**General:** Inhibits alcohol metabolism, acetaldehyde accumulates causing reaction of flushing, headache, N/V, hypotension, tachycardia, sweating

**FDA I:** Alcohol abuse deterrent

**Dose:** 125-500 mg qhs

**SEs:**
- Black box warning: Do not give to intoxicated patient, and liver damage
- Drowsiness, restlessness, depression, psychosis
- Neurological toxicity
- Elevated liver enzymes
- Contra I: Liver/kidney/heart/lung ds, epilepsy, diabetes, psychotic conditions
Acamprosate (Campral®)

**General:** Requires psychosocial support, antagonizes NMDA (glutaminergic N-methyl-D-aspartate) receptors and agonizes GABA type A receptors

**FDA I:** Maintenance of alcohol abstinence

**Dose:** 666 mg bid or tid

**SEs:**
- Black box warning: Liver damage
- Contra I: Severe kidney disease
- Flatulence, diarrhea
Opiate Antagonist

**Naltrexone**

*Injection: Vivitrol® ; Pills: ReVia®*

**General:** With psychosocial program, reduces alcohol relapse, blocks “opiate high”

**FDA I:**
1) Abstain from alcohol
2) Prevention of opiate relapse

**Dose:** Injection of 380 mg IM every 4 weeks
Pill of 50 mg daily

**SEs:**
- Contra I: on opiates, in opiate w/d, positive opiate Utox
- GI cramping, diarrhea
- Liver damage, pneumonia
- Injection site reactions
- Monitor for depression, suicidality (1% in study)
Mu Receptor Agonist

Methadone
(Dolophine®)

General: Liquid, tabs, injection

FDA I: Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment, for which alternative treatment options are inadequate

Dose: Start 10-20 mg, 60-120 mg for opiate (1/2 life 24-36h)

SEs:
- Black box warning: Addiction, abuse, misuse; life-threatening respiratory depression; accidental ingestion; life-threatening QT prolongation; neonatal opiate w/d syndrome
- Contra I: sig respiratory depression, severe asthma, paralytic ileus
Partial Mu Receptor Agonist +
Kappa Receptor Antagonist

Buprenorphine/
Naloxone
(Suboxone®)

General: Requires psychosocial support, sublingual film, pills;
induction >12h after last short-acting, >24h after last
long-acting opiate dose, no QT
prolongation, CIII, office-based

FDA I: Opiate dependence

Dose: 2/0.5 mg; 4/1 mg; 8/2 mg;
12/3 mg; ½ life 24-36h

SEs:
• Can be abused
• Sedation, dizziness, ataxia

High

Wasted
Thank you!
Pregnancy Categories

A: Well-controlled human studies showed no risk
B: Animal reproduction studies showed no risk, no human studies
C: Animal reproduction studies showed adverse effect
D: **Positive** evidence of human fetal risk