An Overview of Medications Commonly Used in I/DD Nursing

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Pharmacy Alternatives
Medications
Medication Usage in the I/DD Population

- Seizure Disorder
- Aggression
- SIB
- Anxiety
- Depression
- Psychosis
- Sleep
- Dementia
- ADHD
- GERD
- Osteoporosis
- Arthritis
- Spasticity
- Urinary Incontinence
- Constipation
- Diabetes
- Heart Disease
- HTN
- Hyperlipidemia
- Cancer
• Treatment of Seizure Disorder
MR/DD with Epilepsy

Population Characteristics

- Multiple seizure types
- Frequent prolonged seizures (status epilepticus)
- Refractory to treatment
- Cognitive, affective, behavior, neurologic problems
- With improved medical care the DD patient has significantly longer lifespan-elderly
- Life-long AEDs?

Mattson RH. The role of the old and the new antiepileptic drugs in special populations: Mental and multiple handicaps. Epilepsia 1996;37(Suppl.6):S45-53.
**Possible Aggravation of Seizures or Epilepsy Syndromes**

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<th>PHT</th>
<th>LTG</th>
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CBZ=carbamazepine; PHT=phenytoin; LTG=lamotrigine; GBP=gabapentin; VGB=vigabatrin; TGB=tiagabine; BDZ=benzodiazepine

Principles for Treatment of Epilepsy in Special Populations

• Efficacy
  – Attempt monotherapy whenever possible
  – Agent appropriate for the seizure type(s)
  – Broad spectrum agent when seizure types are mixed or unknown
  – Select an agent that will not exacerbate seizures
  – Minimize trough levels

• Safety
  – Minimize drug-drug interactions
  – Minimize side effects
  – Select an agent with known and manageable risks
  – Select an agent that will not exacerbate other conditions

• Simplification
  – Minimize number of agents used
  – Minimize number of daily doses
  – Simplify medication administration processes and costs
  – Improve quality of life
## Seizure Types: Established vs New AEDs

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+ = efficacy; ?+ = probably efficacy; 0 = ineffective; ?- = may worsen; - = worsen; ? = unknown

Clinical Challenges

- Side effects are tolerated (ignored?)
- Seizures are tolerated
- Polytherapy
- Social and economic realities
- Events are poorly recognized, frequently missed or mistaken
- Poor advocacy
- Non-epileptic movements that mimic seizures (stereotypes, tics, self-stimulating, muscle spasms, posturing)
- Access to EEGs/video EEG
Anticonvulsants

• Standard AEDs
  – Phenobarbital
  – Phenytoin
  – Carbamazepine
  – Divalproex Sodium

• New AEDs
  – Gabapentin (Neurontin)
  – Lamotrigine (Lamictal)
  – Levetiracetam (Keppra)
  – Oxcarbazepine (Trileptil)
  – Tiagabine (Gabatril)
  – Topiramate (Topamax)
  – Zonisamide (Zonegran)
  – Felbamate (Felbatol)
  – Pregabalin (Lyrica)
  – Vigrabatrin (Sabril)
  – Lacosamide (Vimpat)
  – Rufinamide (Banzel)
  – Clobazam (Onfi)
  – Ezogabine (Potiga)
  – Perampanel (Fycompa)
  – Eslicarbazepine (Aptiom)
Current Treatment Options

Partial
- Simple
- Complex
- Secondarily generalized

Generalized
- Tonic-clonic
- Tonic
- Myoclonic
- Atonic
- Infantile spasms
- Absence

- PHT, CBZ, PB, GBP, TGB, VGB
- ACTH, VGB
- ESX

- VPA, LTG, TOP (FBM)
# Established vs New AEDs

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Adverse Effects (AE) of AEDs

• AEs frequently lead to stopping medications (or holding and restarting)
• Dose-dependent AEs are common
  – Dizziness, lethargy, unsteady gait, visual disturbances
• Drug specific AEs are common
  – Hyponatremia, tremor, cardiotoxicity, ataxia, encephalopathies, neuropathies
• AEs occur at lower blood levels
General Information on Side Effects of AEDs

- All have side effects
- Some of the newer drugs are more specific in targeting mechanisms causing seizures and may have less widespread side effects
- Complicated Regimens: more side effects
General Information on Side Effects of AEDs

• Problems common to many AEDs:
  – Fatigue and sleepiness
  – Changes in appetite and weight
  – Loss of coordination
  – Gastrointestinal problems
  – Possible bone loss leading to osteoporosis (DPH, Pb, CBZ)
• Problems common to many AEDs:
  - Changes in skin (acne from CBZ)
  - Changes in hair (excessive: DPH and CBZ; loss VPA)
  - Reproductive problems (BC pills)
  - Severe allergic reactions including severe skin rashes, fever, inflammation of organs and lymph nodes (esp DPH, Pb, CBZ)
# CNS AEs: Established vs New AEDs

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## Other AEs: Established vs New AEDs

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AEDs and Drug / food Interactions

• Other AEDs
• Oral contraceptives
• Anti-infectives
• Cardiac meds: Calan, cardene, cardizem
• Take with food: Depakote, Gabbitril, Zarentin, others if N/V, newer meds with or without food
Phenobarbital

- Dose – 2 mg/kg/day
- 50% protein bound
- Long half-life
- Metabolized and eliminated in liver and kidney
- Side effects are significant in this population
Phenytoin

• Dose – 3mg/kg/day (blood level 10-20mcg/ml)

• 80 - 90% protein bound

• Metabolized in the liver

• Reduced protein stores may significantly affect free levels

• Watch interactions with tubing, formula
Divalproex Sodium

• Dose – 5-10 mg/kg/day
• 80 - 90% protein bound
• Metabolized in the liver
• Total protein stores can affect free levels
• Protein binding and metabolism are reduced in the elderly
• Liver function testing needed
Carbamazepine

- Dose – 4-6 mg/kg/day (blood level 8-14mcg/ml)
- 75 - 85% protein bound
- Metabolized in liver
- Side effects are caused by active metabolite, Stevens Johnson Syndrome (sore throat, easy bruising)
- Inducer of Hepatic enzymes; watch blood levels and decreased effectiveness of other drugs (examples)
- Elimination may be decreased in the elderly
- Sodium is often decreased
Tegretol (carbamazepine)

• Pharmacokinetics
  – Initiate at low doses (200-400mg/day) to allow tolerance to side effects
  – Increase by 200mg/day at 2-4 week intervals until therapeutic level of 4-14mcg/ml
  – Auto-Induction: Final dose dependant upon what extent carbamazepine induces its own metabolism
  – CBZ load=CBZ & CBZ epoxide
• Half-life: 8-72 hrs initially, and 12-17 hours with chronic usage
• Steady state: 4-6 weeks initially, after induction= 2-4 days
• Dosage strengths: 100mg chewable tabs, 200mg tabs and 100mg/5ml suspension
• Side effects:
  – Concentration dependant
    • Neurosensory: drowsiness, blurred vision, dizziness
Tegretol (cont)

• Side effects (cont)
  – Idiosyncratic (non-concentration dependant)
    • ADH like properties-watch sodium levels
    • Leukopenia
    • Skin rashes
Carbatrol and Tegretol XR

• Carbatrol
  – 200mg and 300mg sustained release capsule

• Tegretol XR
  – 100, 200, and 400mg sustained release tablets

• Advantages of both
  – Ease of dosing (bid)
  – Smoother blood level
  – Less potential side effects
Oxycarbazepine (Trileptal)

• Pharmacology
  – Similar to CBZ, although metabolized by a different pathway. Similar but milder side effect profile
  – Due to its alternative metabolic pathway, it also causes fewer idiosyncratic reactions and fewer interactions with other drugs
  – No auto-induction: blood levels maintained
  – Hyponatremia is potential side effect due to ADH properties-monitor sodium levels
Depakene (Valproic Acid) and Depakote (Valproate)

• Pharmacokinetics
  – Depakote tablets lag in absorption (1 hr on empty stomach, up to 8 hrs w/food)
  – Depakote tablets are coated to reduce possible GI side effects (Do not crush)
  – Depakene are liquid filled capsules, and appear to have more GI side effects
  – Dosage strengths: 125, 250 and 500mg tablets
Divalproate (cont)

- Levels increase when used with cimetidine and salicylates
- Decreased levels when given with phenobarbital, dilantin, carbamazepine and lamictal
- Half-life: 9-16 hours
- Therapeutic concentration: 50-125mcg/ml
Neurontin (gabapentin)

• Pharmacokinetics: initial dose of 900mg/day, may titrate up to 4800mg/day in 3-4 divided doses
• Dosage form: 100, 300, and 400mg capsules
• Drug is eliminated in kidney, not metabolized in the liver
• Half-life: 5-7 hours (normal renal function)
Neurontin (cont)

• Pharmacokinetics (cont)
  – No known drug interactions with other AEDs
  – Therapeutic range: not defined

• Side effects:
  – CNS: drowsiness and fatigue, which may be minimized by dosing patterns
Lamictal (lamotrigine)

• Pharmacokinetics:
  – Highly affected by concomitant use of other AEDs, so initial dose must be low, start slow, and titrate over several MONTHS. Initial dose if on Depakote and enzyme inducers is 25mg qod. If not on Depakote, but on enzyme inducer, use 50mg/day.
  • Inducers: CBZ, Phenobarbital, Dilantin
  – More than 95% metabolized, many metabolites, some active
  – Dosage form: 25, 100, 150, 200mg tabs
Lamictal (cont)

- Maintenance dose of 100-150mg/day if on Depakote, otherwise, 300-500mg/day dosed bid
- Half-life:
  - Ave 25hrs (monotherapy)
  - Ave 14hrs (inducers)
  - Ave 27hrs (inducers & VPA)
  - Ave 70 hrs (VPA)
Lamictal (cont)

• Side effects:
  – CNS: drowsiness, diplopia, dizziness, ataxia
  – RASH

• Drug interactions:
  – CBZ and Dilantin decrease half-life
  – VPA prolongs half-life
Topamax (topiramate)

- Dosage forms:
  - Sprinkles: 15, 25, 50mg
  - Tablets: 25, 100 and 200mg

- Dosage: start at 25-50mg at hs, adjust up to 400mg/day in divided dosing schedule

- Dosing schedule:
  - Week #1: 50mg hs
  - Week #2: 50mg bid
• Dosing schedule (cont)
  – Week #3: 50mg in am, 100mg hs
  – Week #4: 100mg bid
  – Week #5: 100mg in am, 150mg hs
  – Week #6: 150mg bid
  – Week #7: 150mg in am, 200mg hs
  – Week #8: 200mg bid
Topamax (cont)

• Side effects:
  – CNS: most notable: confusion, lethargy, ataxia, dizziness, difficulty in concentration and memory, psychomotor slowing, speech disorder, stupor
  – Hematologic: leukopenia
  – Weight loss (IDIOSYNCRATIC)

• Half-life: average 21 hrs
Topamax (cont)

• Drug interactions:
  – CBZ decreases topamax levels
  – DPH decreases topamax levels and increases DPH levels
  – VA decreases both topamax and VA levels

• Lab monitoring
  – Blood levels are not needed, monitor patient response to drug
  – LFT should be done routinely
  – CBC to monitor hemoglobin and WBC count
Gabitril (tiagabine)

• Dosage forms: 4, 12, 16, and 20mg tabs
• Dosage schedule: initial 4mg/d, increase by 4-8mg/week up to 56mg/d. divided doses bid-qid
• Side effects:
  – CNS: dizziness, lethargy, gait problems, nervousness, difficulty in concentration
  – GI: nausea, vomiting, diarrhea (take w/food)
Gabitril (cont)

• Drug interactions:
  – CBZ, DPH, Phenobarbital decrease blood levels of Gabitril-monitor patient

• Lab monitoring:
  – None needed, monitor clinical response of patient to medication
Keppra (levetiracetam)

• Dosage form: 250, 500, 750mg tablet
• Dosage: initial 250-500mg q 12 hrs, max 3000mg/day
• Side effects:
  – CNS: lethargy, dizziness, ataxia, coordination problems, agitation, mood lability (watch esp DD clients), anxiety
  – Hematologic: neutropenia, leukopenia
Discontinue AEDs?

• Few documented seizures in lifetime
• No gross neurological abnormalities
• Sub therapeutic levels of AEDs at time of discontinuance
• Persistently normal EEGs before and after discontinuance
• Discontinue Phenytoin over several months, Phenobarbital may take a year
• Treatment of Agitation, Aggression, and SIB
General Approach to Treating Behavioral Complications

1. Characterize target symptoms
2. Perform medical evaluation
3. Perform psychiatric evaluation
4. If due to medical disorder: treat and monitor behavioral symptoms
5. If due to psychiatric disorder: treat and monitor behavioral symptoms
6. Employ nonpharmacological approaches
7. Employ pharmacological approaches

Commonly Prescribed Medication Classes

- Antipsychotics
- Anxiolytics
- Antidepressants
- Anticonvulsants/Mood stabilizers
- Stimulants
- Opiate Receptor-Blocking Agents
- Beta-blockers
## Treatment of Psychiatric Problems in Mental Retardation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Preferred Medication Classes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-injurious behavior</td>
<td>Anticonvulsant/mood stabilizer</td>
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<tr>
<td></td>
<td>Atypical antipsychotic</td>
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<tr>
<td></td>
<td>Also consider SSRI</td>
</tr>
<tr>
<td>Physical aggression to people or property</td>
<td>Anticonvulsant/mood stabilizer</td>
</tr>
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<td></td>
<td>Atypical antipsychotic</td>
</tr>
<tr>
<td></td>
<td>Also consider SSRI</td>
</tr>
<tr>
<td>Nonaggressive agitation</td>
<td>Anticonvulsant/mood stabilizer</td>
</tr>
<tr>
<td></td>
<td>Also consider atypical AP, SSRI</td>
</tr>
</tbody>
</table>

Anticonvulsants/Mood Stabilizers

- Lithium-inexpensive, watch sodium, narrow therapeutic window, watch kidney function and drug interactions

- Divalproex (Depakote®)-may need higher dose to achieve blood level of 80-150ng/ml

- Carbamazepine (Tegretol®)-as above, watch sodium

- Lamotrigine (Lamictal®)-takes months for therapeutic dose to be reached, watch RASH

- Oxcarbazepine (Trileptal®)-see Tegretol notes
# Treatment of Psychiatric Problems in Mental Retardation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Preferred Mood stabilizer/opiate or beta blocker</th>
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<tbody>
<tr>
<td>Self-injurious behavior</td>
<td>Divalproex/valproic acid</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine</td>
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<tr>
<td></td>
<td>Naltrexone (ReVia) or propranolol etc.</td>
</tr>
<tr>
<td>For aggressive or destructive behavior</td>
<td>Divalproex/valproic acid</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine</td>
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<tr>
<td></td>
<td>Also consider Lithium</td>
</tr>
</tbody>
</table>
### Treatment of Psychiatric Problems in Mental Retardation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Preferred Antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-injurious behavior</td>
<td>Choice based on comorbid conditions and ease of dosing and potential side effects</td>
</tr>
<tr>
<td>For aggressive or destructive behavior</td>
<td>Choice based on co-morbid conditions and ease of dosing and potential side effects</td>
</tr>
</tbody>
</table>
• Treatment of Anxiety
Types

- Acute stress disorder
- Post-traumatic stress disorder
- Obsessive compulsive disorder
- Chronic generalized anxiety disorder
- Panic disorder
- Phobias
Barbiturates

- 30% of patients are non-responders
- Do not affect the core symptom of worry
- Cause a variety of adverse effects including disinhibition of the frontal lobe
- Potential for abuse, physical dependence and withdrawal, as well as high relapse rates when medication is withdrawn
Anti-anxiety medications

- Short acting barbiturates:
  Xanax (alprazolam)

- Mid acting barbiturates:
  Ativan (lorazepam)

- Long acting barbiturates:
  Valium (diazepam)
  Librium (chlordiazepoxide)
  Klonopin (clonazepam)
  Tranxene (chlonazepate)
Pharmacology

• Short acting:
  – Peak plasma level in 1-2 hours, half life 12-15 hours

• Moderate acting:
  – Peak plasma level in 1-6 hours, half life 10-20 hours

• Long acting:
  – peak plasma in 1/2 to 2 hours, half life 20-50 hours
Side Effects

• Skeletal muscle relaxation
• Dizziness
• Drowsiness
• Amnesia
• Increase in falls
Drug Interactions

• Additional sedating drugs including alcohol
• SSRIs like Prozac and Paxil may inhibit liver enzymes and prolong activity
Antidepressants

• Medication treatment of choice
• Drugs with primary effect on the serotonin system have become 1st line recommendations for the treatment of panic disorder, social phobia, OCD, and PTSD as well as generalized anxiety disorder
• Take longer to work than barbiturates
Antidepressants

- SSRIs like Prozac, Zoloft, Paxil, Celexa, Effexor, Serzone are probably more effective and easier to discontinue
- Tricyclics like Elavil and Tofranil may be useful for PTSD
Other agents

- Atarax (hydroxyzine)
- Buspar (buspirone)
- Catapres (clonidine)
- Inderal (propranolol)
- Tenormin (atenolol)
- Antipsychotics
• Treatment of Depression
Characteristics of Depression

• Five or more symptoms present nearly every day during same 2 week period:
  – A. Depressed mood
  – B. Markedly diminished interest or pleasure
  – C. Significant change in weight or appetite
  – D. Insomnia or hypersomnia
  – E. Fatigue or loss of energy
  – F. Feeling of worthlessness or excessive or inappropriate guilt
Characteristics of Depression

• Five or more symptoms

  – G. Decreased ability to think or concentrate, or inability to make decisions
  – H. Recurrent thought of death, or thoughts of suicide
Definitions

- Neurons
- Axon
- Dendrite
- Synapse
- Neurotransmitters
- Pre-synaptic
- Post-synaptic
- Synthesis
- Reuptake mechanism
Neurotransmitters

- Serotonin: problems with serotonin are associated with depressed mood, anxiety, insomnia, OCD, SAD, and violence
- Dopamine: Disruption in dopamine related to problems with attention, motivation, alertness, increased apathy, and difficulty in experiencing pleasure
- Norepinephrine: disorders in norepinephrine are associated with lack of energy, decreased alertness, and lethargy
- GABA: major calmative neurotransmitter
Tricyclic Antidepressants

• The most widely used class of antidepressants prior to SSRI class
• More general effects on neurotransmitters, less refined
• Out of favor because overdose can be fatal
• May be prescribed when other classes have not worked
Tricyclic Side Effects

• Orthostatic hypotension (watch elderly)
• Weight gain
• Dry mouth
• Blurred vision
• Constipation
• Sweating
• Sexual dysfunction
# Tricyclics

<table>
<thead>
<tr>
<th>Tricyclic</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anafranil (chlomipramine)</td>
<td>75-300mg</td>
</tr>
<tr>
<td>Ascendin (amoxapine)</td>
<td>150-600mg</td>
</tr>
<tr>
<td>Elavil (amitriptyline)</td>
<td>75-300mg</td>
</tr>
<tr>
<td>Ludiomil (maprotiline)</td>
<td>75-225mg</td>
</tr>
<tr>
<td>Norpramin (desipramine)</td>
<td>75-300mg</td>
</tr>
<tr>
<td>Pamelor (nortriptyline)</td>
<td>50-150mg</td>
</tr>
<tr>
<td>Sinequan (doxepin)</td>
<td>150-300mg</td>
</tr>
<tr>
<td>Surmontil (trimipramine)</td>
<td>75-300mg</td>
</tr>
<tr>
<td>Tofranil (imipramine)</td>
<td>75-300mg</td>
</tr>
<tr>
<td>Vivactil (protriptyline)</td>
<td>15-60mg</td>
</tr>
</tbody>
</table>
Selective Serotonin Reuptake Inhibitors (SSRIs)

• Came on the market in 1980s
• The most popular antidepressant
  – Side effects are less severe than older agents
  – Consequences of overdose are less severe
• Often first choice in antidepressant
SSRIs Pharmacology

- They “clog the pump” which normally tells first neuron to pump some of the released serotonin back into the cell as a measure of checks and balances.
- Therefore increased amount of serotonin hangs out in the synapse available for usage.
- Takes 1-4 weeks to become effective, 4-6 weeks before true evaluation of effectiveness.
- No dosage or drug changes should take place sooner than 1 month.
SSRIs Side Effects

- Increased anxiety
- Fatigue
- Upset stomach
- Insomnia
- Apathy
- Lack of sexual interest
- Inability to obtain orgasm
SSRIs Side Effects

- Dizziness
- Sweating
- Tremors
- Dry mouth
- Headache
- Weight loss
- Weight gain

- Side effects worse during the first couple of weeks and diminish with time
SSRI cautions

• Bipolar disease and increased activation of manic state
• Abrupt discontinuation: flu-like symptoms, vivid dreams and problems with sleep
• Black Box Warning for children and adolescents
• Avoid MAOIs
SSRIs

• Celexa (citalopram) usual dosage 10-60mg, may have fewer interactions with other drugs, and not particularly stimulating or sedating
• Lexapro (Escitalopram) usual dosage 10-20mg, chemically similar to Celexa, may work faster
SSRIs

• Luvox (fluoxamine) usual dosage 50-300mg, generally more sedating than the others, the first to be approved for OCD
• Paxil (paroxetine) usual dosage 20-60mg somewhat sedating, more drug interactions, weight gain, an more pronounced withdrawal symptoms
• Paxil CR usual dosage 12.5-62.5mg
SSRIs

• Prozac (fluoxetine) usual dosage 10-80mg, stimulating, may cause insomnia if taken late in the day, some report increase in anxiety, least withdrawal symptoms due to liver enzyme inhibition, but more drug interactions

• Zoloft (sertraline) usual dosage 50-200mg not as stimulating or sedating
Serotonin / Norepinephrine Reuptake Inhibitors (SNRIs)

• Cymbalta (duloxetine) usual dosage 30-120mg, although seldom effective >60mg, often used for pain
• Effexor (venlafaxine) usual dosage 75-375mg may have quicker action so good for severe depression, fewer drug interactions than most, may increase blood pressure in higher dosages
• Effexor XR as above
Serotonin-2 antagonists Reuptake Inhibitors (SARIs)

- Desyrel (trazadone) usual dosage 150-400mg sedating side effects, used mostly along with other antidepressants as a sleep aid
- Serzone (nafazadone) usual dosage 100-600mg may be sedating and help with anxiety 1 case liver failure resulting in death / transplant 250,000-300,000pt yrs, avoid if active liver disease
Noradrenergic / specific Serotonergic antidepressant (NaSSA)

- Enhances the release of norepinephrine and serotonin while blocking certain serotonin receptors
- Remeron (mitrazapine) usual dosage 15-45mg help when insomnia is a problem, may cause weight gain
Norepinephrine / Dopamine Reuptake Inhibitor (NDRI)

- Welbutrin (buproprion) usual dosage 150-450mg less likely to cause weight gain or sexual dysfunction, may initially increase anxiety, not for those with seizures
- Welbutrin SR (2 x daily dosing)
- Welbutrin XL (1 x daily dosing)
MAO Pharmacology

- Monoamine: neurotransmitters
- Oxidase: enzyme that breaks down monoamines
- MAO inhibitors: destroy this enzyme
- Allow for increased amount of neurotransmitters
- Work on norepinephrine, dopamine and serotonin
MAO I side effects

• Dangerous sudden increase in blood pressure which may lead to death, cerebral hemorrhage
• Avoid tyramine, which also increases blood pressure
• Tyramine is a natural substance found in the body and food products, tyramine forms as proteins break down as they age
Drug Interactions

- Other antidepressants
- Most drugs for colds and asthma
- Drugs for the treatment of diabetes
- Blood pressure medications
- Some pain killers
MAO Inhibitors

- Marplan (isocarboxazid) 10-40mg
- Nardil (phenelzine) 45-90mg
- Parnate (tranylcypromine) 30-60mg
- Emsam patch (selegeline transdermal) bypasses the GI tract, and at 6 and 9mg no dietary restrictions, but use tryramine free diet at 12 mg
Antipsychotics

- **Abilify** (aripiprazole) 5-10mg, start at 2mg and increase to 5mg then 10mg, then 15 or 20mg as needed
- Seroquel now also has indication as adjunctive therapy
- Adjunctive treatment for major depressive disorder
- Has minimal tendency to cause weight gain, metabolic side effects, sedation or movement disorders
- Side effects and drug interactions: see atypical antipsychotics
• Treatment of Psychosis
Diseases

• Psychosis
• Schizophrenia
• Schizoaffective disorder
Neurotransmitters

• Cholinergic symptoms
  – Ach: stimulatory excess: parkinsonism
  – Dopamine decreases amount of Ach; blockage of dopamine=parkinsonism, gait disturbance and falls

• Monoamine systems
  – Dopamine, norepinephrine, epinephrine, serotonin, histamine
    schizophrenia: high levels of dopamine; high levels of norepinephrine and serotonin: depression; histamine blockade: sedation, weight gain

• Neuropeptides: act as neurotransmitters or hormones; pain, taste, olfactory perception

• Amino acids
  – GABA, glycine are inhibitory; glutamate, aspartate are excitatory
Clinical Implications of Receptor Activities of antipsychotics

• D-2 antagonism:
  – positive symptom efficacy, EPS, endocrine effects

• 5-HT 2a antagonism:
  – negative symptom efficacy, reduced EPS
Clinical Implications of Receptor Activities of antipsychotics

• High 5HT 2a/D-2 affinity ratio:
  – antipsychotic efficacy, reduced EPS (compared to D-2 antagonism alone)

• 5-HT 1a antagonism:
  – antidepressant and anxiolytic activity, improved cognition, reduced EPS

• 5-HT 1d antagonism:
  – antidepressant activity
Clinical implications (cont)

• Alpha 1 antagonism:
  – hypotension

• H-1 antagonism:
  – sedation, weight gain

• M-1 antagonism:
  – anticholinergic side effects
Antipsychotics

• Positive symptoms
  – Hostility
  – Excitability
  – Delusions
  – Suspiciousness/persecution
  – Hallucinatory behavior
  – Conceptual disorganization
  – Grandiosity
Antipsychotics

• Negative symptoms
  – Emotional withdrawal
  – Passive apathetic withdrawal
  – Difficulty in abstract thinking
  – Blunted affect
  – Lack of spontaneity/flow of conversation
  – Stereotyped thinking
  – Poor rapport
Antipsychotics

• Conventional agents (older drugs)
  – All were equally effective
  – Different subtypes of schizophrenics respond differently to different agents?
  – Agitated patients = more sedating
  – Withdrawn patients = less sedating drugs
  – Controlled trials failed to support
Antipsychotics

• Conventional agents
  – Differences confined to side effects, formulations available, cost
  – Examples:
    • Thorazine (chlorpromazine)
    • Mellaril (thioridazine)
    • Haldol (haloperidol)
    • Navane (thiothixene)
    • Stelazine (trifluoperazine)
    • Prolixen (luphenazine)
Atypical Antipsychotics

• Serotonin-dopamine antagonists, therefore broader coverage of symptoms
• Examples:
  – Clozaril (clozapine)
  – Risperdal (risperidol)
  – Seroquel (quetiapine)
  – Zyprexa (olanzapine)
  – Geodon (ziprasidone)
  – Abilify (aripiprazole)
  – Invega (paliperidone)
  – Risperdal Consta
  – Latuda (Lurasidone)
  – Saphris (Asenapine)
  – Fanapt (Iloperidone)
Atypical Antipsychotics

- Differ in having effects related to the ratios of dopamine and serotonin
- Antihistaminic - dry mouth sedation weight gain
- Muscarinic - dry mouth urinary retention constipation esophageal constriction
- Alpha adrenergic - heart block hypotension
Side Effect Considerations of Atypical Antipsychotics

- Sedation
- Orthostasis, esp upon arising
- EPS and TD (DISCUS and AIMES)
- Anticholinergic (constipation)
- Gait disturbance
- Metabolic abnormalities
- Cerebrovascular adverse events: stroke, TIA
- QT prolongation
- Neuroleptic malignant Syndrome
Clozapine (Clozaril)

- Primary importance: refractory patients
- Indications: schizophrenia, schizo-assoc. suicide risk reduction
- Dosage form: scored 25mg, 100mg tabs
- Dosage regimen: 1-3 times/day
- Dose: 150-300mg twice daily, max: 900mg/day
- Continue for 2 yrs, reassess and taper if possible
Clozapine

• Side effects:
  – Agranulocytosis
  – Sedation, constipation, glaucoma (high histamine blockade)
  – Orthostasis
  – Excessive drooling, increased sweating
  – Anticholinergic symptoms
  – Weight gain (high histamine blockade)
  – Hyperlipidemia, hypertension
  – Increased glucose levels
  – Lowers seizure threshold
Risperidone (Risperdal)

- Indications: schizophrenia, psychiatric dementia, bipolar mania, autism
- Dosage form: 0.25mg, 0.5mg, 1mg, 2mg, 3mg and 4mg tab, liquid 5mg/5ml (not to be mixed w/cola or tea), quick dissolving tab, depot available (Consta)
- Dosage schedule: 1-3 times daily, most often 1/day at hs
- Dosage range: 0.25-16mg, most common in I/DD 1-4mg/day
Risperidone

Side effects:

– Few anticholinergic, watch constipation
– EPS low except at high (>6mg/day) dose
– Sedation
– Agitation, anxiety, insomnia
– Increased prolactin levels
Risperidone

– Weight gain: moderate
– Not associated with the same degree of hyperlipidemia, increased glucose levels as other agents
– Decreases seizure threshold
– Cerebral vascular accident-watch modifiable risk factors
Olanzapine (Zyprexa)

- Indications: psychosis, bipolar disorder
- Dosage schedule: 1 time/day
- Dosage range: 2.5-20mg/day, usual DD range 1.25-15mg/day
- Side effects:
  - Sedation, hypotension
  - Anticholinergic-highly
  - EPS much higher than others
Olanzapine

- Side effects (cont):
  - Headache, dizziness, insomnia, agitation
  - Weight gain!!!
  - Hyperlipidemia
  - Increased glucose levels, risk for diabetes mellitus
  - Lowers seizure threshold
Quetiapine (Seroquel)

- Indications: psychosis
- Dosage form: 25mg, 100mg, 200mg, 300mg tabs, liquid or fast dissolving NOT available
- Dosage schedule: 1-4 times daily
- Dosage range: 100-800mg/day, usual DD dose of 50-300mg/day
- Side effects:
  - orthostasis
Quetiapine

• Side effects (cont)
  – Moderate to high sedation
  – Weight gain
  – EPS/TD: low
  – Cataract formation: initial and every 6 month eye exam
  – Lowers seizure threshold
  – Histaminic-like side effects
Ziprasidone (Geodon)

- Dosage form: 20mg, 40mg, 60mg 80mg capsules, liquid or quick dissolve tabs NOT available, IM formulation is available
- Dosage schedule: 1-2 times/day
- Dosage Range: 20-160mg/day, usual DD dose is 20-80mg/day
- Side effects:
  - Nausea, dyspepsia, abdominal pain
Ziprasidone

• Side effects (cont):
  – Constipation
  – Insomnia or sedation
  – Prolongation of QT interval: baseline and routine EKG monitoring
  – Weight gain: low
Aripiprazole (Abilify)

• Indications: schizophrenia in adults as well as 13-17yr old, acute and maintenance bipolar disorder in adults as well as acute bipolar disorder in 10-17 yr old, adjunctive treatment for major depression in adults, acute agitation associated with schizophrenia in adults, autism

• Dosage forms: 2mg, 5mg, 10mg, 15mg, 20mg, and 30mg tab, liquid, fast dissolving tab and depot formulation NOT available

• Dosage schedule: 1 time/day

• Dosage range: 2.5-30mg, usual I/DD dosage 10-15mg
Aripiprazole

• **Side effects:**
  – Sedation or ACTIVATION (akithesias)
  – Hypotension
  – Lowers seizure threshold
  – Weight gain: low

• **Drug interactions:**
  – Decrease dose by ½ if also using quinidine, ketoconazole, fluoxetine, or paroxetine
  – Double dose if using carbamazepine
Paliperidone (Invega and Invega Sustena)

- Indication: schizophrenia
- Dosage: 6mg qam, may need 9 or 12 mg long acting formulation
- Side effects: sedation, prolactin increase, hypotension
- Drug interactions: QT prolongtion drugs (Geodon)
Paliperidone

• Indication: schizophrenia
• Dosage: 6mg qam, may need 9 or 12 mg long acting formulation
• Side effects: sedation, prolactin increase, hypotension
• Drug interactions: QT prolongtion drugs (Geodon)
Saphris (asenapine)

• Dosage: 5-10mg bid SL
• MOA: antagonizes D2 receptors, serotonin 5-HT2A receptors
Fanapt (iloperidone)

Dosage: 1mg po bid x 1 day, then 2mg bid x 1 day, then increase by 4 mg/day qd, max 24mg/day

Same MOA as others
Latuda (lurasidone)

- Once daily
- Recommended dosage: 40mg
- Maximum dose: 80mg
- No titration
- Take with food
- Minimal metabolic issues
- New product.....better? The same?
• Treatment of Sleep Disorders
Sleep Disorders

- Primary Insomnia
- Primary Hypersomnia
- Narcolepsy
- Breathing related sleep disorder
- Circadian rhythm sleep disorder
- Nightmare disorder
- Sleep Terror disorder
- Sleepwalking
Medications

• Benadryl (diphenhydramine)
• Ambien and CR (zolpidem)
• Lunesta (eszopiclone)
• Rozerem (ramelteon)
• Sonata (zaleplon)
• Desyrel (trazadone)
• Melatonin
Medications

• Diphenhydramine
  – Pharmacology: antihistamine
  – Dose 25-50mg 30min prior to bedtime
  – Side effects: sedation, dizziness, hangover effect
Medications

• Ambien
  – Dose: 5-10mg at bedtime
  – Pharmacology: interacts with GABA-benzodiazepine receptors
  – No evidence of next day effects, half life 2 and 1/2 hours
  – Minor changes in REM sleep at usual doses
  – Side effects: headache, drowsiness, dizziness, aggressive behavior, sleep related behavior
Medications

• Lunesta
  – Dose: 2-3mg at bedtime
  – Pharmacology: GABA-benzodiazepine receptors
  – Peak plasma level in 1 hour, half life 6 hours
  – Extensively metabolized by CYP enzymes and metabolite has hypnotic activity
  – Unpleasant taste, dry mouth, dizziness, strange sleep behavior, insomnia, impaired memory, difficulty concentrating
Medications

• Rozerem
  – Dose: 8mg at bedtime, avoid high fat meal
  – Melatonin receptor agonist
  – Peak plasma levels in 1/2 to 1.5 hours
  – Half life: 1-2.6 hours
  – Side effects: headache, fatigue, dizziness, drowsiness, strange sleep complex
Medications

- **Sonata**
  - Dose: 5-10mg at bedtime, max. 20mg, avoid high fat meal
  - Pharmacology: GABA-benzodiazepine receptors
  - Decreases the time to get to sleep, does not increase sleep time or decrease awakenings
  - Peak plasma level 1 hour, half life 1 hour
  - Side effects: headaches, dizziness, nausea, strange sleep complex
Melatonin

- Over the counter product
- Naturally occurring hormone, increase in levels in lack of daylight
- Decreased amount in individuals with autistic spectrum?
- Dosage: 1-4 tablets
- Relaxes musculature to help one fall asleep
Sleep Disorders

• Avoid usage if at all possible
• Use only for short term (7-14 days)
• Use lowest dose possible
• Avoid abrupt withdrawal
• Remember they interrupt / change normal REM sleep patterns
Monitoring Hypnotics

• No blood levels are needed
• Evaluate side effects and report as needed
• Use all other possible therapies prior to initiation of hypnotics
  – Investigate reason for lack of sleep (noise, roommate, GERD)
  – Quiet music, sound machine, warm bath, warm milk
  – Develop sleep patterns and hygiene
• Medications used for Alzheimer’s Disease
Hypothesis of Alzheimer’s Disease

- Role of acetylcholine
  - Stimulate muscle tissue, involved in thinking, judgment, attention, reasoning, learning, recording and storing memories
  - In AD, neurons that use Ach are damaged/destroyed
• Cholinergic neurons diminished in critical areas of the brain in those with Alzheimer’s Disease (AD)
• Neurotransmitter changes result in decrease in acetylcholine (AC)
• Pre-synaptic cholinergic neurons release AC
• Cholinesterase inhibitors inhibit the degradation of AC
• Effectively increase the amount of AC available for neurotransmission
Cholinesterase Inhibitors

- Emerging evidence suggests that long term treatment with cholinesterase inhibitors not only preserves cognition and behavior, but also influences neuronal function and survival
Cholinesterase Inhibitors

- There are four FDA approved cholinesterase inhibitors for the treatment of AD:
  - Tacrine (1st showed improved cognition, but associated with hepatotoxicity and clinically significant drug interactions)
  - Donepezil (Aricept)
  - Rivastigmine (Exalon)
  - Galantamine (Remenyl)
- The three above = better side effect profiles and fewer drug interactions
Cholinesterase Inhibitors

- All have clinically meaningful responses in individuals with AD
- Outcome measures: increase in cognition, clinician global impression, ADL, disability, quality of life, and delay in nursing home placement
- Magnitude of response: stabilization or slowing of disease equal to 6 months of cognitive decline
- Improvement in behavior
Donepazil (Aricept)

- MOA specificity for acetylcholinesterase
- Delayed progression of AD for 6-9 months longer than if untreated
- Initiate at 5mg at bedtime (single daily dose)
- Increase in 4-6 weeks to 10mg at bedtime if tolerated
- Potential CYP450 and 2D6/3A4 drug interactions
- Side effects: anxiety, GI (increase in acetylcholine increases stomach acid production), increase in bowel frequency, nausea and vomiting, potential cardiac and pulmonary problems
- No lab monitoring needed
Rivastigmine (Exalon and Exalon Patch)

- **MOA:** inhibits acetylcholinesterase and butylcholinesterase centrally
- Dosed twice daily
- Start at 1.5mg twice daily. Increase by increments of 1.5mg/dose until 6mg/day, max of 8mg twice daily
- Take with food, although absorption is delayed
- Liquid preparation available
Rivastigmine (Exalon)

- Greater cholinesterase inhibition at the highest dose, but greater frequency of SE
- Side effects similar to donepezil with somewhat higher incidence of GI side effects. Minimize SE by advancing dosing schedule slowly (2-4 week basis)
- Delayed progression of AD for 6-9 months longer than if untreated
Galatamine (Reminyl/Razadyme)

- MOA: inhibition of acetylcholinesterase and nicotinic receptor agonism
- By modulating activity at nicotinic receptors, it may increase release of acetylcholine from surviving presynaptic nerve terminals
- Combination action may diminish cholinesterase supersensitivity from developing, prolonging the benefit.
- May provide greatest delay of illness progression
- May require increase of dose after patient declines below initial baseline, to maintain benefit for longer term.
Galatamine (Reminyl/Razadyne)

- Delayed progression of AD for 9 months longer than if untreated
- Initiate at 4mg twice daily with meals
- Increase dose by 8mg/day at 4 week intervals (no sooner)
- Recommended dosing range is 24-36mg/day in divided dosages initially morning and night then morning and mid afternoon snack to avoid late night cholinergic activation
- Potential CYP450 2D6/3A4 drug interactions
- Side effects: nausea, vomiting, anorexia, weight loss which are mild to moderate and transient
Hypothesis of Alzheimer’s Disease

• Additional factors to consider:

Normal levels of glutamate as well as acetylcholine play a role in learning and memory
– Increased glutamate (major excitatory chemical) and NMDA receptor activity as well as accumulation of plaques and tangles causes cell damage and loss leading to dementia
– Inflammation and oxidation on the cellular level may also be involved
– After cell damage and death, cholinergic deficit occurs
Memantine (Namenda)

- First and only medication approved for the treatment of moderate to severe AD
- Approved by FDA: October 2003
- MOA: a low to moderate affinity NMDA (N-methyl-D-Aspartane) receptor antagonist
- Thought that the overstimulation of NMDA receptors by the neurotransmitter glutamate may play role in AD since glutamate plays role in the neural pathways associated with learning and memory
Memantine (Namenda)

- MOA: the excitotoxicity produced by abnormal levels of glutamate is thought to be responsible for the neuronal cell dysfunction observed in AD.
- Namenda is thought to selectively block the excitotoxic effects of glutamate, while allowing the physiological transmission associated with normal cell functioning.
Memantine (Namenda)

- It’s efficacy and safety (similar to placebo and less GI side effects) has been proven when used alone or with other treatments, so multiple agents with different MOAs should be tried
- Namenda dosepak over one month
- Essentially no drug interactions
- Should continue on treatment throughout course of disease
Combination Therapy

- Combinations of therapies have additive or even synergistic effects in the treatment of AD
- Addition of memantine to donepezil has been studied
- Combination therapy improved GI side effect profile
Stimulants

• Useful in the treatment of ADHD
• Alleviation of neurobehavioral symptoms of depression
Signs and Symptoms of ADHD

- Moderate to severe distractibility
- Short attention span
- Hyperactivity
- Emotional lability
- Impulsivity
What does this look like?

- Client difficulties at home in interpersonal relationships, attention to tasks and completion of chores
- Workshop production worsens or is poor
- Physically appears to be “wound up”, with difficulty relaxing, tense, bothersome and annoying physical activity
- Emotionally appears to be manic and irritable
- Depression many times accompanies this diagnosis
Medications

- Adderall (amphetamine and dextroamphetamine)
- Cylert (Pemoline)
- Ritalin (methylphenydate)
Amphetamine and dextroamphetamine

- Dosage in ADHD: 5-80mg/day in 1-2 doses
- Pharmacology: blocks reuptake and increases release of norepinephrine and dopamine, may activate the brain stem arousal system
- Side effects: HTN, aggressive behavior, strokes, Tourette’s syndrome with increased tics, growth suppression, nervousness, insomnia, headache, dizziness, loss of appetite, abdominal pain
- Adderall XR: dosage 20mg every morning
methylphenidate

- Concerta (18-72mg ER/day)
- Metadate CD (20-60mg ER/day)
- Metadate ER (10-20mg 1 to 2x/day)
- Metylin (5-15mg 2-3x/day)
- Methlin ER (10-20mg 1-2x/day)
- Ritalin (5-15mg 2-3x/day)
- Ritalin LA (20-40mg q am)
- Ritalin SR (20mg 1-2x/day)
Monitoring

- Blood levels not needed
- Evaluate side effects like weight loss. Insomnia (timing important) and headache over time
- Watch individuals with cardiac symptoms especially carefully
- Report troublesome side effects to clinician
Antidepressants

• Antidepressants with stimulant properties also used
  – Welbutrin
  – Norpramin
• Treatment of GERD
GERD presentation

- GI symptoms: heartburn, difficulty/pain of swallowing, vomiting
- Respiratory: chronic cough, wheezing, asthma
- Behavioral: screaming, aggression, depression, SIB
Treatment

• Lifestyle changes
• Antacids
• Eradication of H pylori
• H2 blockers
• Proton pump inhibitors
H2 Blockers

- Nizatidine (Axid)
- Famotidine (Pepcid)
- Cimetidine (Tagamet)
- Ranitidine (Zantac)

- Side Effects: usually mild GI and CNS
- Many drug interactions
Proton pump inhibitors

- Esomeprazole (Nexium)
- Lansoprazole (Prevacid)
- Omeprazole (Prilosec)
- Pantoprazole (Protonix)
- Rabeprazole (Aciphex)

- Side effects: gastric atrophy, polyps, dizziness, bone fractures, continued cough in supine position
- Drug interactions: clopidogrel (Plavix)-decreases effectiveness of Plavix
Others

• Metochlopramide (Reglan)-short term treatment of 4-12 weeks, do AIMS/DISCUS
• Sulcrafate (Carafate)-lines stomach, many drug interactions and should be dosed 1-2 hours prior to other drugs
Treatment of Osteoporosis
Calcium supplements

- Many products
- Should be dosed with meals
- Should avoid concurrent dosing with many other medications
Biphosphonates

• Inhibit bone breakdown, preserve bone mass, increase bone density

• SE: nausea, abdominal pain/ulcers
  – Alendrenate (Fosamax)
  – Ibandronate (Boniva)
  – Risendronate (Actonel)
  – Zolendronic acid (Reclast)-IV infusion once/yr
Selective Estrogen Receptive Modulators

• Mimics estrogen’s beneficial effects on postmenopausal women without the estrogen harmful effects
  – Raloxifene (Evista)
Calcitonin

• Hormone produced by thyroid gland. Reduces bone reabsorption
• Provides pain relief, may prevent spine fractures
• Nasal spray
Teriparatide (Forteo)

- Analog of parathyroid hormone
- Treats both men and women at high risk for fractures
- Once daily sq
• Treatment of Urinary Incontinence
Urinary Incontinence

• Urge: urge to urinate frequently
• Stress: urine leakage (cough/sneeze/laugh)
• Mixed: combination of urge and stress
• Overflow: overfilling of the bladder
• Functional: unrelated to storage or output (dementia)
Antispasmodotics

• Oral agents
  – Oxybutynin (Ditropan and Ditropan XL)
  – Solifenacin (Vesicare)
  – Tolterodine (Detrol and Detrol LA)
  – Trospium (Sanctura)
  – Darifenacin (Enablex)

• Patch therapy
  – Oxybutynin TDS (Oxytrol)
Side Effects of Antisposmotics

• Each has anticholinergic side effects to a greater or lesser degree

• Anticholinergic:
  – Dry mouth, urinary retention, constipation, glaucoma, dementia
• Treatment of Constipation
Laxatives

- Bulk (metamucil, citracel)
- Muscle contraction (dulcolax, senokot)
- Stool softener (colace, surfak)
- Lubricant (mineral oil)
- Saline (MOM, Citrate of magnesia)
- Chloride channel activator (Amitiza)
• Treatment of Arthritis
Medications for Arthritis

- NSAIDs
- COX-2 Inhibitors
- Disease Modifying Agents
- Corticosteroids
- Analgesics
NSAIDS

• Common medications
  – Sulindac (Clinoril), ibuprofen (Motrin), indomethacin (Indocin), naproxin (Naprosyn), etc

• Side effects
  – GI, sodium retention

• Drug interactions
  – Cardiac drugs, lithium
Cox -2 Inhibitors

- Celecoxib (Celebrex)
- Side effects
  - GI
  - Cardiac concerns
DMARDs

• Sulfasalazine (Azulfidine), cyclosporin (Sandimmune), azothiaprine (Imuran), hydroxychloroquine (Plaquenil), etc
• Stop disease aggression and halt joint pain
• Take weeks or months to work
• Many potential serious side effects
Corticosteroids

- Dexamethasone (Decadron), hydrocortisone (Cortef), methylprednisolone (Medrol) etc
- Potential for serious side effects at high doses, or prolonged usage
Analgesics

- Codeine, propoxyphene (Darvon), tramadol (Ultram), hydrocodone/tylenol (Vicodin), etc
- GI side effects, dizziness, drowsiness
• Medications for Spasticity
Spasticity Treatment

• Oral
  – Dantrolene-effects fast more than slow muscle
  – Benzodiazepines-no indication, used off label
  – Imidazolines-clonidine (Catapes and Catapres patch), tizanidine (Zanaflex)-watch hypotension
  – Baclofen (Lioresal)-decreases rate of muscle twitch

• Injectable
  – Baclofen intrathecal/pump-much smaller dose
Questions?
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  I have been a member and attending DDNA conferences for 20 years, so DDNA national has my contact information as well