

An Overview of Medications Commonly Used in I/DD Nursing

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Treatment of Seizure Disorder

Medications



Developmental Disabilities

- Differs from elderly patients with epilepsy in:
 - etiology
 - severity
 - chronicity
 - comorbid conditions

Medication Usage

- Seizure Disorder
- Aggression
- SIB
- Anxiety
- Depression
- Psychosis
- Sleep
- Dementia
- GERD
- Osteoporosis
- Arthritis
- Spasticity
- Urinary Incontinence
- Constipation

Developmental Disabilities

- Etiology: genetic; fetal or birth insult
- Severity: often medically intractable
 - Multiple AEDs
 - AED side effects
 - Chronic effects of seizures
- Chronicity: usually life-long illness

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. 7

Comorbidities in Individuals With Epilepsy and MR/DD

- Behavioral disturbances: 50% to 60%
- Affective disorders: up to 29%
- Medical conditions
 - Pulmonary (aspiration)
 - Neuromuscular (hypotonia)
 - Gastrointestinal (oral motor dysfunction, drooling, constipation)
 - Nutritional deficiencies

Kerr MP. *Epilepsy Behav.* 2002;3:S14-S17.
Epile CA, et al. *J Neurol Neurosurg Psychiatry.* 2003;74:1485-1492.
Persad V, et al. *J Dev Disabil.* 2003;10:123-151.

Features of Epilepsy in Individuals With MR/DD

- Multiple seizure types
- Higher rates of:
 - Seizure recurrence after first seizure
 - Medically intractable epilepsy
 - Sudden unexplained death after adolescence (and possible childhood)
- Lower rates of:
 - Staying seizure-free without medication after control of seizures with AEDs
- Frequent cognitive and behavioral disorders
 - Complicate several aspects of care

Devinsky O. *Epilepsia.* 2002;43(suppl 3):71-79.

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

Possible Aggravation of Seizures or Epilepsy Syndromes

	CBZ	PHT	LTG	GBP	VGB	TGB	BDZ
Absence	+	+		+	+	+	+
Myoclonic	+	+	+	+	+	+	+
Juvenile myoclonic epilepsy	+	+	+				
Lennox-Gastaut syndrome	+	+	+	+	+	+	+
Benign epilepsy of childhood with centro-temporal spikes	+	+					
Severe myoclonic epilepsy in infancy	+		+		+		
Landau-Kieffner syndrome/ electrical status epilepticus during slow sleep	+	+					

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

Bourgeois BF. *Epilepsy Res.* 2002;52:53-60.

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

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Challenges of Drugs

- Absorption changes with age
- Total serum proteins decreases with age
- Metabolism and elimination slows with age
- The elderly are often on multiple medications that can change drug metabolism

Seizure Types: Established vs New AEDs

	Partial	Secondary Generalized	Tonic-Clonic	Absence	Myoclonic
Established					
Carbamazepine	+	+	+	-	-
Phenytoin	0	0	0	-	0
Phenobarbital	+	+	+	0	?+
Valproic acid	-	-	-	-	-
Primidone	+	+	+	0	?
New					
Gabapentin	+	+	?+	0	?
Lamotrigine	-	-	-	-	-
Levetiracetam	+	?	?	?	?+
Oxcarbazepine	-	-	-	-	-
Tiagabine	+	+	?	?	?
Topiramate	-	-	+	+	-
Vigabatrin	+	+	?+	-	-
Zonisamide	-	-	-	-	-

++ = efficacy; ?+ = probably efficacy; 0 = ineffective; ?- = may worsen; - = worsen; ? = unknown
Brodie MJ, et al. Lancet. 2000;356:323-329.

Anticonvulsants

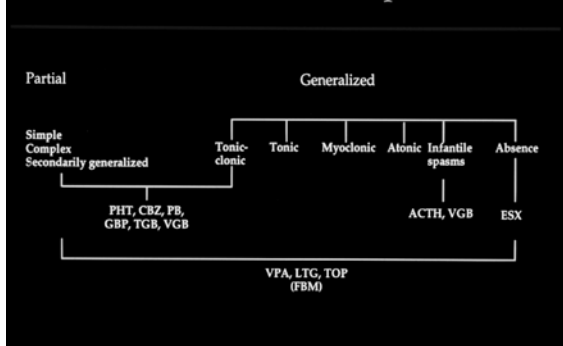
- Standard AEDs
 - Phenytoin
 - Carbamazepine
 - Divalproex Sodium
- New AEDs
 - Gabapentin (Neurontin)
 - Lamotrigine (Lamictal)
 - Levetiracetam (Keppra)
 - Oxcarbazepine (Trileptil)
 - Tiagabine (Gabatril)
 - Topiramate (Topamax)
 - Zonisamide (Zonegran)
 - Felbamate (Felbatol)
 - Pregabalin (Lyrica)
 - Vigabatrin (Sabril)
 - Lacosamide (Vimpat)

Established vs New AEDs

	Linear PK	Renal Elimination	Affects Drug Metabolizing Enzymes	Associated With AED Interactions
Established				
Carbamazepine	-	-	+	+
Phenytoin	-	-	+	+
Phenobarbital	+	+	+	+
Primidone	-	-	-	-
Valproic acid	+	+	+	+
New				
Lacosamide	-	-	-	-
Gabapentin	-	+	-	-
Lamotrigine	-	-	-	-
Levetiracetam	+	-	-	-
Pregabalin	-	-	-	-
Tiagabine	+	-	-	+
Vigabatrin	+	+	-	+
Zonisamide	-	-	-	-

Patsalos P, et al. Epilepsia. 2002;43:365-385.

Current Treatment Options



Agitation, Aggression, SIB

Historical Perspective: Increasing Options, Simplifying Regimens

	Tablet/ Capsule	IV	IM	Sprinkle Capsule	Chewable	Suspension/ Syrup/Elixir	Extended-Release
Phenobarbital	+	1912	+				
Primidone	1954						
Carbamazepine	1974				2000	2000	1997
Felbamate	1993					1993	
Lamotrigine	1994				1998 (Dispersible)		
Ethosuximide	1960	1960					
Topiramate	1996			1999			
Rufinamide	1997						
Levetiracetam	1999						
Oxcarbazepine	2000						
Zonisamide	2000						

Other AEs: Established vs New AEDs

	Alopecia	Hirsutism	Hyponatremia	Hypersensitivity	Kidney Stones	Induces Cyt450
Established						
Carbamazepine			+	+		+
Phenobarbital				+		+
Primidone				+		+
Vigabatrin	+					
New						
Felbamate						+
Gabapentin						
Lamotrigine						
Levetiracetam						
Oxcarbazepine						
Tiagabine						
Vigabatrin						
Zonisamide						

Chapman DP, et al. *South Med J.* 1997;90:L171-L180.

Adverse Effects (AE) of AEDs

- AEs frequently lead to stopping medications
- 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

Carbamazepine

- Dose – 4-6 mg/kg/day
- 75 - 85% protein bound
- Metabolized in liver
- Side effects are caused by active metabolite
- Inducer of Hepatic enzymes
- Elimination may be decreased in the elderly
- Sodium is often decreased

CNS AEs: Established vs New AEDs

	Ataxia	Blurred Vision	Cognitive Effects	Dizziness	Drowsiness	Fatigue	Headache
Established							
Carbamazepine	+	+	+	+			+
Ethosuximide							
Phenobarbital	+	+	+	+	+		+
Phenytoin							
Primidone	+	+	+	+	+		+
New							
Felbamate							
Gabapentin	+				+	+	+
Lamotrigine							
Levetiracetam				+	+	+	
Oxcarbazepine							
Tiagabine			+	+		+	+
Topiramate							
Vigabatrin	+	+			+	+	+
Zonisamide							

Chapman DP, et al. *South Med J.* 1997;90:L171-L180.

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
- 80 - 90% protein bound
- Metabolized in the liver
- Reduced protein stores may significantly affect free levels
- Metabolism is decreased in the elderly

Phenomenology of Agitation

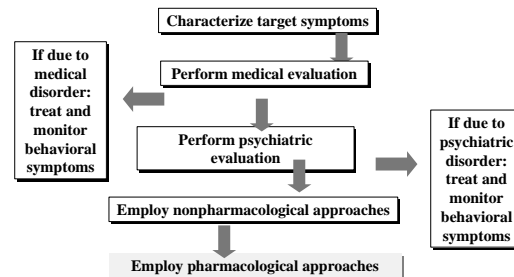
- Physically non-aggressive
 - Hyperactivity
 - Headbanging
 - Temper tantrum
- Physically aggressive
 - Self-injury
 - Hitting/Pushing
 - Kicking
 - Biting/Scratching
- Verbally non-aggressive
 - Complaining
 - Attention seeking
 - Screaming
- Verbally aggressive
 - Threats
 - Obscenities

J. Am. Acad. Child Adolesc. Psychiatry, 38: 12 Supplement, Dec. 1999.

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

General Approach to Treating Behavioral Complications



Madrid et al., Psychopharmacology, 9: 225-243, 2000.

Agitation

- Any inappropriate verbal, vocal, or motor activity that is not an obvious expression of need or confusion
- Physical or verbal
- Aggressive or nonaggressive
- It is not a diagnostic term but a group of signs and symptoms that can result from a variety of medical or psychiatric conditions

Cohen-Mansfield J, Deutsch LH. *Semin Clin Neuropsychiatry*, 1996;1:325-339.

Pharmacotherapy

General Principles

- Identify most salient symptoms
- and**
- Identify medication class with at least some evidence of efficacy
- and**
- Select medication with best tolerability and fewest side effects

J. Am. Acad. Child Adolesc. Psychiatry, 38: 12 Supplement, Dec. 1999.
Madrid et al., Psychopharmacology, 9: 225-243, 2000

Target Symptoms

- Self-injurious behavior (SIB)
- Physical aggression to people or property
- Nonaggressive agitation

Treatment of Psychiatric Problems in Mental Retardation

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

Postgraduate Medicine. Consensus Guideline Series. 105(3), 2000.

Target Systems

- Opiate
- Dopamine
- Serotonin
- Androgen
- Glutamate

Anticonvulsants/Mood Stabilizers

- Lithium
- Divalproex (Depakote®)
- Carbamazepine (Tegretol®)
- Lamotrigine (Lamictal®)
- Oxcarbazepine (Trileptal®)

King. J Autism and Dev Disorders. 30(5): 439-445, 2000.

Commonly Prescribed Medication Classes

- Antipsychotics
- Anxiolytics
- Antidepressants
- Anticonvulsants/Mood stabilizers
- Stimulants
- Opiate Receptor-Blocking Agents
- Beta-blockers

Madrid et al., Psychopharmacology, 9: 225-243, 2000

Treatment of Psychiatric Problems in Mental Retardation

<u>Condition</u>	<u>Preferred Mood stabilizer/opiate or beta blocker</u>
Self-injurious behavior	Divalproex/valproic acid Carbamazepine Naltrexone (ReVia) or propranolol etc.
For aggressive or destructive behavior	Divalproex/valproic acid Carbamazepine Also consider Lithium

Postgraduate Medicine. Consensus Guideline Series. 105(3), 2000.

**Treatment of Psychiatric Problems in
Mental Retardation**

<u>Condition</u>	<u>Preferred Antipsychotics</u>
Self-injurious behavior	Choice based on comorbid conditions and ease of dosing and potential side effects
For aggressive or destructive behavior	Choice based on co-morbid conditions and ease of dosing and potential side effects

Postgraduate Medicine. Consensus Guideline Series. 105(3), 2000.

- ### Symptoms
- Worrying
 - Increased blood pressure
 - Increased heart rate
 - Sweating
 - Dilated pupils
 - Insomnia

Treatment of Anxiety

- ### What does this look like?
- Fidgeting, hand wringing
 - Inability to sit still, pacing
 - Facial expression of tension
 - Stomach complaints
 - Headache
 - Skin picking

- ### 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 (chloazepate)

Drug Interactions

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

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

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

Side Effects

- Skeletal muscle relaxation
- Dizziness
- Drowsiness
- Amnesia
- Increase in falls

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

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

Treatment of Depression

Definitions

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



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

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 calmativ 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

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

Tricyclic Side Effects

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



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

Tricyclics

- | | |
|-----------------------------|-----------|
| • Anafranil (chlomipramine) | 75-300mg |
| • Ascendin (amoxapine) | 150-600mg |
| • Elavil (amitriptyline) | 75-300mg |
| • Ludiomil (maprotiline) | 75-225mg |
| • Norpramin (desipramine) | 75-300mg |
| • Pamelor (nortriptyline) | 50-150mg |
| • Sinequan (doxepin) | 150-300mg |
| • Surmontil (trimipramine) | 75-300mg |
| • Tofranil (imipramine) | 75-300mg |
| • Vivactil (protriptyline) | 15-60mg |

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

SSRIs

- Luvox (fluoxetine) 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

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

- 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

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

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 (nafazodone) 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

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

Noradrenergic / specific Serotonergic antidepressant (NaSSA)

- Enhances the release of norepinephrine and serotonin while blocking certain serotonin receptors
- Remeron (mirtazapine) usual dosage 15-45mg help when insomnia is a problem, may cause weight gain

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

Norepinephrine / Dopamine Reuptake Inhibitor (NDRI)

- Welbutrin (bupropion) 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)

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

Diseases

- Psychosis
- Schizophrenia
- Schizoaffective disorder

Antipsychotics

- Abilify (aripiprazole) 5-10mg, start at 2mg and increase to 5mg then 10mg, then 15 or 20mg as needed
- 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

Antipsychotics

- Positive symptoms
 - Hostility
 - Excitability
 - Delusions
 - Suspiciousness/persecution
 - Hallucinatory behavior
 - Conceptual disorganization
 - Grandiosity

Treatment of Psychosis

Antipsychotics

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

What does this look like?

- Bizarre behavior
- Talking to object or person that does not exist (watch appropriate mental age self talk or imaginary friend)
- Seeing things that do not exist
- Saying that God / devil is telling them to do something
- Feeling that you are poisoning them
- Suspicious of people

Antipsychotics

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

Pharmacology

- Dopamine Receptor Antagonists
 - Block dopamine receptors on post synaptic neurons
 - Effectively decrease the functional levels of dopamine
 - Most often used to treat psychotic patients whose psychosis is related to a hyperdopaminergic state

Typical Antipsychotics

- Absorbed erratically
- Very lipid soluble
- Highly protein bound
- Distributed throughout the tissues and concentrated in the brain

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

Side Effects of Typical Agents

- High, mid, low potency
- High potency = greater affinity for D2 receptor and greatest EPS
- Low potency = less EPS, more postural hypotension, sedation and anticholinergic effects

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

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

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

Clozapine

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

Side Effect Considerations of Atypical Antipsychotics

- Sedation
- Orthostasis, esp upon arising
- EPS and TD
- Anticholinergic
- Gait disturbance
- Metabolic abnormalities
- Cerebrovascular adverse events: stroke, TIA
- QT prolongation

Clozapine

- Interactions:
 - cigarette smoking
 - grapefruit juice

avoid carbamazepine (Tegretol), ciprofloxin (Cipro)

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

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

Risperidone

Side effects:

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

Olanzapine

Side effects (cont):

- Headache, dizziness, insomnia, agitation
- Weight gain!!!
- Hyperlipidemia
- Increased glucose levels, risk for diabetes mellitus
- Lowers seizure threshold

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

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

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
- 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

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

Aripiprazole

- Side effects:
 - Sedation or activation
 - 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

Ziprasidone

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

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)

Monitoring

- Many potential side effects
 - Evaluation of short term
 - Evaluation of long term (AIMS / DISCUS)
 - Evaluate and rank potential harmful vs troublesome
- Lab work:
 - Blood levels questionable and not needed
 - Metabolic effects (diabetes, hyperlipidemia, abdominal girth)

Medications

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

Treatment of Sleep Disorders

Medications

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

Sleep Disorders

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

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

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

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

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

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

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

Treatment of GERD

H2 Blockers

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

GERD presentation

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

Proton pump inhibitors

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

Treatment

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

Treatment of Osteoporosis

