Pharmacology Refresher for Home Health Therapists & Nurses

Session 3:
Medications used for Selected Psychiatric and Neurologic Conditions

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Learning Objectives

- At the end of this presentation the participant should be able to:

1. Given a patient case with medications that affect the central nervous system identify the class of medication.
2. Identify basic therapeutic effects, adverse effects and common indications for medications used in the treatment of anxiety, insomnia, psychosis, depression, seizures, and Parkinson's disease, and multiple sclerosis.
3. Describe the outcome of using two or more medications with the same clinical effect or similar adverse effects.
4. Describe common anticholinergic effects and explain why medications with these characteristics should be used carefully in elderly patients.

Drugs in CNS

- Disease pathophysiology and drug mechanisms not always well understood.
- Drugs actions most commonly involve modulation of neurotransmitters by affecting:
  - Synthesis, storage or release
  - Metabolism
- Agonist or antagonist action at receptors

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Central Neurotransmitters

- Acetylcholine
  In CNS involved in memory, cognitive functions
- Dopamine
  Important in treatment of psychosis and Parkinson's disease
- Norepinephrine
  Involved in attention and arousal in addition to CV effects
- Serotonin
  Pathway involved in treatment of major depression
- GABA
  Inhibitory neurotransmitter in brain and spinal cord

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Sedative-Hypnotic Agents

- Anxiolytic effects
- Hypnotic effects
- Effect can be dose related
  - At higher doses can cause more drowsiness or even general anesthesia
  - All effects occur at expense of alertness
- 3 major categories
  - Barbiturates
  - Benzodiazepines
  - Miscellaneous

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Example Sedative Hypnotic Agents

Barbiturates	**Benzodiazepines**	**Miscellaneous**
Amobarbital (Amytal)	Alprazolam (Xanax)	Antihistamines
Pentobarbital	Clonazepam (Klonopin)	Eszopiclone (Lunesta)
Phenobarbital	Diazepam (Valium)	Zaleplon (Sonata)
Secobarbital (Seconal)	Lorazepam (Ativan)	Zolpidem (Ambien)
	Oxazepam (Serax)	Ramelteon (Rozerem)
	Triazolam (Halcion)	

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Antihistamines as Hypnotics

- Sedation and drowsiness due to anticholinergic effects
- Concerns:
  - Found in OTC combo meds
    - PM
    - Nighttime preparations
  - May worsen dementia
  - Amnestic effects
  - Increasing risk of falls

- Example OTC Agents:
  - Diphenhydramine (Benadryl)
    - Often in combo products like "Tylenol PM"
  - Doxlyamine (Unisom)

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Sedative Hypnotic Actions

- Increase effects of GABA in CNS
- Therapeutic effects:
  - Anxiolytic
  - Hypnosis
  - Anesthesia
  - Anticonvulsant
  - Muscle relaxant

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Sedative Hypnotic Adverse Effects

- Effects on:
  - Respiration
  - CV function
  - Psychomotor dysfunction
- Residual sedation
- Tolerance
- Dependence
- Rebound Insomnia

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Sedative Hypnotic Summary

- Cause sedation to promote relaxation and sleep
- Impact on therapy:
  - Residual sedation
  - Risk of tolerance/ dependence
  - Risk of falls
  - Anticholinergic effects (watch OTC agents, especially in older patients)
  - Additive CNS depression

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Antiepileptic Drugs (AEDs)

- Seizures result from excessive excitation of cortical neurons.
  - Spontaneous or abnormal firing of neurons
  - Propagation of excitation
- AEDs act to:
  - Increase the threshold for neuronal firing
  - Slow propagation of seizure transmission

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Seizure Type	First-Line Drugs	Alternatives
Partial Seizures	Carbemazepine (Tegretol) Phenytion (Dilantin) Lamotrigine (Lamictal) Valproic Acid (Depakote) Oxcarbazepine (Tripletal)	Gabapentin (Neurontin) Topiramate (Topamax) Zonisamide (Zonegran) Tiagabine (Gabitril) Phenobarbital Felbamate (Felbatol)
Generalized Seizures		
Absence	Valproic Acid (Depakote) Ethosuximide (Zarontin)	Lamotrigine (Lamictal)
Myoclonic	Valproic Acid (Depakote) Clonazepam (Klonopin)	Lamotrigine (Lamictal) Topiramate (Topamax) Felbamate (Felbatol)
Tonic-Clonic	Carbemazepine (Tegretol) Phenytion (Dilantin) Valproic Acid (Depakote)	Lamotrigine (Lamictal) Topiramate (Topamax) Oxcarbazepine (Tripletal) Primodone (Mysoline) Phenobarbital

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Antiepileptic Drugs

- Selection depends on seizure type, patient characteristics, expected ADR and drug profile.
- Many AEDs have 'target' drug levels, but this is only a tool to help guide treatment, not an endpoint itself
- Notable ADRs of AEDs
  - Blood dyscrasias (usually decreases in RBC, WBC or platelets possible)
  - Ataxia, sedation and/or cognitive dysfunction
  - Organ toxicity (liver, kidney)
  - Various rashes/ skin toxicity
  - Weight changes
  - Changes in EKG pattern
  - May increase risk of other types of seizures

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Antiepileptic Drugs Summary

- Patients may need to balance efficacy with adverse effects and may need to accept higher risk of seizures in order to tolerate ADRs.
- Role of drug levels
- Monitor for occurrence of seizure or changes in behavioral or functional status.
- Encourage adherence to prescribed regimen

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Anti-Depressants

- Generally work to increase levels of brain neurotransmitters to affect mood
  - Tricyclic Antidepressants (TCAs)
  - Second generation agents
  - MAOIs
  - SSRIs
- Most take 4-6 weeks to exert antidepressant effects

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Tricyclic Antidepressants (TCAs)

- Clinical Use:
  - depression
  - sleep (in low doses, usually amitriptyline used)
  - neuropathic pain
- ADRs:
  - Anticholinergic effects
  - Sedation
  - Sympathomimetic
  - Muscle weakness possible
  - Orthostatic Hypotension
  - Can decrease seizure threshold

- Example Agents
  - Amitriptyline
  - Clomipramine
  - Desipramine
  - Doxepin
  - Imipramine
  - Nortriptyline
- Note: 'amine' ending

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MAO inhibitors

- Inhibit breakdown of neurotransmitters
- Used rarely due to drug and food interactions
  - hypertensive crisis
  - avoid tyramine-containing foods
- ADRs – Orthostatic hypotension, some sedation

- Example Agents
  - Isocarboxazid
  - Tranylcypramine
  - Phenylzine

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Second Generation Agents and SNRIs

- Similarly effective to TCAs for depression
- Better tolerated overall

- Example Agents
  - Amoxapine
  - Bupropion (Wellbutrin)
  - Desvenlafaxine (Pristiq)
  - Duloxetine (Cymbalta)
  - Mirtazepine (Remeron)
  - Trazodone
  - Venlafaxine (Effexor)

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Selective Serotonin Reuptake Inhibitors (SSRIs)

- Effective, fewer ADRs
  - May be activating or sedating
  - Fewer anticholinergic effects
    - Preferred in elderly
  - Other ADRs possible, but generally better tolerated than TCAs

- Example Agents
  - Fluoxetine (Prozac)
  - Citalopram (Celexa)
  - Excitalopram (Lexapro)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)

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Summary – Affective Medications

- TCAs and SSRIs also used as adjunct treatment in chronic pain syndromes
- Impact on rehabilitation:
  - ADR risk : sedation, lethargy, muscle weakness, orthostatic hypotension, difficulty concentrating
    - Monitor BP
    - Fall risk
  - Treatment may take 4-6 weeks to onset
    - Monitor for increased depression during this time

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Antipsychotic (Neuroleptic) Agents

- Used to treat various psychiatric disorders
  - Targeted to neurotransmitters in brain
  - Many reduce activity of dopamine
- Historically used for agitation, but not recommended
- May also be used for nausea and vomiting
- Generally classified as 'typical' or newer 'atypical' agents

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Traditional Antipsychotics

Potential ADRs:

- Extrapyramidal Symptoms (EPS)- abnormal movement disorders
- Sedation
- Anticholinergic effects
- Orthostatic hypotension
- Weight gain

- Example Agents
  - Chlorpromazine
  - Haloperidol (Haldol)
  - Thioridazine
  - Trifluoperazine

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Atypical Antipsychotics

- May be more effective to treat some symptoms of psychosis
- Generally better ADR profile
- Less risk of EPS and anticholinergic ADRs
- Sedating
- Can cause metabolic ADRs
  - Diabetes
  - Weight gain
  - Hyperlipidemia

- Example Agents
  - Aripiprazole (Abilify)
  - Clozapine (Clozaril)
  - Olanzapine (Zyprexa)
  - Quetiapine (Seroquel)
  - Risperidone (Risperidal)
  - Ziprasidone (Geodon)

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Lithium (and Lithium Salts)

- Used for mood stabilization and to prevent mania associated with bipolar disorder
- Requires precise dosing and monitoring via blood levels
- ADRs associated with blood levels
  - Mild: fine resting tremor, weakness, fatigue, lack of concentration
  - Moderate: confusion, lethargy, ataxia, nystagmus, increased tremor and deep tendon reflexes
  - Severe: seizures, coma, possible death

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Summary- Antipsychotics and Lithium

- Drugs tend to normalize behavior, enhance cooperation
- Impact on therapy:
  - Risk of ADRs:
    - Sedation
    - Orthostatic hypotension risk of falls
    - Abnormal movement disorders
    - Impact of metabolic ADRs

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Medications for Parkinson's Disease (PD)

- Pathology related to destruction of dopamine neurons
  - Leads to relative excess of acetylcholine
- Strategies to treat include:
  1. Replace dopamine
  2. Dopamine receptor agonists
  3. Give drugs that slow dopamine breakdown
  4. Give anticholinergics to balance relative amounts of dopamine

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Levodopa/ Carbidopa (Sinemet)

- Levodopa is converted to dopamine in the body
- Levodopa is rapidly broken down before it can get into the brain, so is administered with carbidopa to inhibit metabolism
- Typically used in older patients or those with significant disability
  - Used in almost all PD patients at some point.

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Levodopa/ Carbidopa

- Doses written as levodopa/ carbidopa
  - CR and regular release available
- ADRs/ complications include:
  - Nausea, hallucinations, dyskinesias
  - Loss of efficacy or "wearing off effects" common with long term therapy
  - Important to distinguish "wearing off" from disease related motor fluctuations ("on / off" effects)

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Dopamine Agonists

- Stimulate dopamine receptors
- Often used in younger patients
- Can delay need to take levodopa 4-5 yrs
- May take 4-8 weeks for full effect

Example Agents:
- Bromocriptine
- Pramipexole (Mirapex)
- Ropinirole (Requip)
- Rotigotine (Neupro Patch)

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Dopamine metabolism blockers

- Inhibits dopamine breakdown by MAO type B enzymes or by COMT
- Allows for delay to levodopa treatment or lower doses

COMT inhibitors:
- Tolcapone (Tasmar)
- Entacapone (Comtan)

MAO- B Inhibitors:
- Selegiline (Eldepryl)
- Rasagiline (Azilect)

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Anticholinergics

- Can help with tremor
- Used in younger patients with preserved cognition
- Anti-cholinergic ADRs possible

Example agents:
- Benzotropine
- Procyclidine
- Trihexyphenidyl

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Medications for Multiple Sclerosis (MS)

- General treatment includes:

1. Management of acute exacerbations or relapses
   Decrease edema and inflammation in areas of nerve breakdown:
2. Disease Modifying Drugs
   Try to reduce frequency and severity of relapses
3. Symptom Management
   fatigue, depression, spasticity, neuropathic pain

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Disease Modifying Drugs for MS

- Interferon-β1a (Avonex, Rebif)
- Interferon-β1b (Betaseron)
- Glatiramer acetate (Copaxone)
- Natalizumab (Tysabri)
- Mitoxantrone (Novantrone)
- Fingolimod (Gilenya)

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Interferon-β products

- Reduce pro-inflammatory cytokines and reduce number of exacerbations
- Differences lie in dosing and frequency of administration
- Common ADRs:
  - Influenza-like symptoms
  - Injection site reactions
  - Possible increased spasticity
  - Possible depression

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Glatiramer acetate (Copaxone)

- Reduces inflammatory activity of T cells
- Common ADRs:
  - Injection site reactions
  - 10-15% of people will experience "Post-injection reaction"
    - Chest pain, palpitations, trouble breathing
    - Resolves within 30 minutes without treatment

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Fingolimod (Gilenya)

- Acts to prevent some WBCs from entering CNS and causing neuronal damage
- First oral agent (others are injectable)
- Possibly less effective than Avonex
- Associated with serious ADRs:
  - Decreased HR, Heart block
  - Bronchitis, pneumonia
- Cost about $4000 / month

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Teriflunomide (Aubagio)

- Acts to reduce numbers of activated T and B lymphocytes in CNS to reduce demyelination of neurons
- Administered PO once daily
- Generally as effective as fingolimod
- ADRs: general immunosuppression, increase risk of infection, diarrhea

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Mitoxantrone (Novantrone)

- Administered intermittently, used in conjunction with interferon-β products
- Not first line due to ADRs
- ADRs:
  - Cardiotoxic, so lifetime exposure limited
  - Bone marrow suppression
  - Increased risk of infection
  - Hair loss
  - Mouth sores

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Natalizumab (Tysabri)

- Used as monotherapy for patients who cannot tolerate or don't respond to other agents.
- Associated with:
  - Increase risk of PML (viral brain infection)
  - Infusion reactions
  - Headache, Fatigue, Depression
  - Joint pain

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Symptom Management in MS

Pain Management (typically neuropathic)

- Occurs in ~80% of patients
- Traditional pain meds usually not effective
- Effective agents:
  - Gabapentin (Neurontin)
  - Pregabalin (Lyrica)
  - Duloxetine (Cymbalta)
  - Venlafaxine (Effexor XR)
  - TCAs

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Symptom Management in MS

- Spasticity
  - Baclofen is first line treatment
  - Tizanadine
  - Benzodiazepines (diazepam, clonazepam)
  - Dantrolene
  - Botulinum injections

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Questions?

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