Psychopharmacology in Primary Care

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Disclosures

The speaker has no disclosures to make regarding grants or research support, consultations, speakers' bureaus, stocks, or other financial or material support.

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Disclaimer

- Medication indications, doses, and recommendations change rapidly
- Purpose of this presentation is to provide
  - Overview of topic
  - Resources that may be helpful
  - FDA indications
- Do NOT use these slides as final authority on prescribing
- Best practice
  - Use published guidelines from reputable sources
  - Peer-reviewed
  - Current
  - Information in talks and informal documents should always be verified for prescription information

3

FDA Approved Indications

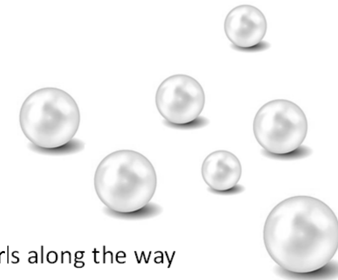
- Result from drug companies spending money on development and testing of drug for specific populations with specific disorders
- Not real-life situations, since comorbidities are often excluded
- Psychotropic drugs for the elderly, children/adolescents, and intellectually disabled persons are difficult to test, therefore have fewer FDA indications
- Therefore, in psychiatry off-label prescribing is often necessary

However, ***this workshop is an overview and will focus on FDA indications only***. References cited may refer to off-label prescribing. It is the responsibility of the provider to make an informed practice decision.

4

Today's Topics

- The Crisis
- The Brain
- The Patient
- The Agents
- Strategy
- Monitoring
- Optimization



. . . and a few pearls along the way

5

A Shared Fear
A Shared Responsibility
A Shared Privilege

THE CRISIS: MENTAL HEALTH IN PRIMARY CARE

6

A Shared Fear: The Global Mental Health Crisis

- National Institute for Mental Health (NIMH.gov)
- Substance Abuse and Mental Health Services Administration (SAMHSA.gov)
- National Alliance for Mental Health (NAMI.org)

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A Shared Responsibility: Mental Illness in Primary Care

- Primary care point of entry for most mental health care
  - Even in integrated care models, primary care providers must often diagnose, treat, prescribe, and prioritize
  - 70% of primary care visits related to psychosocial problems (Robinson & Reiter)
- Less perceived stigma associated with primary care
- Allows trusted provider to deliver holistic care
- An acute shortage of psychiatric prescribers
- Triages: Keeps less acute problems out of specialty care
- Some primary care providers express lack of confidence in the treatment of mental health problems in primary care.

Robinson, P. & Reiter, J. (2007). Behavioral consultation and primary care: A guide to integrating services.

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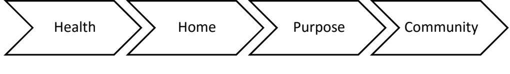
A Shared Privilege: The Journey to Recovery

Definition

"A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach full potential."

SAMHSA working definition (http://www.samhsa.gov/recovery)

4 Dimensions



9

Recovery Principles

- Hope
- Person-driven
- Many pathways
- Holistic
- Peer support
- Relational
- Culture
- Addresses trauma
- Strengths/reponsibility
- Respect

www.SAMHSA.gov

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Neuroanatomy

Pathophysiology

THE BRAIN

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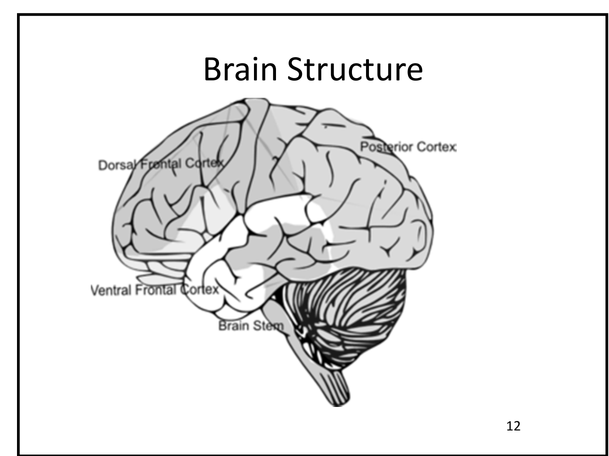
Brain Structure



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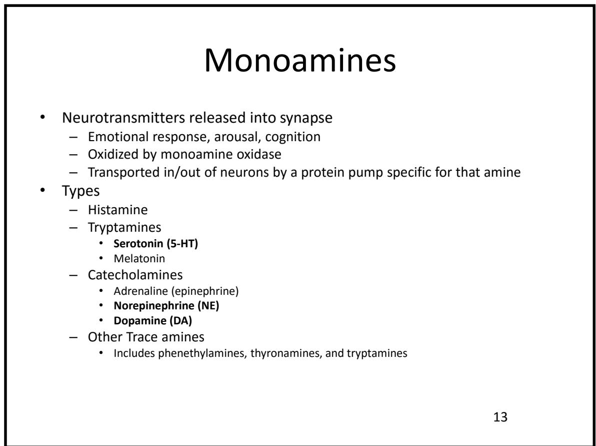
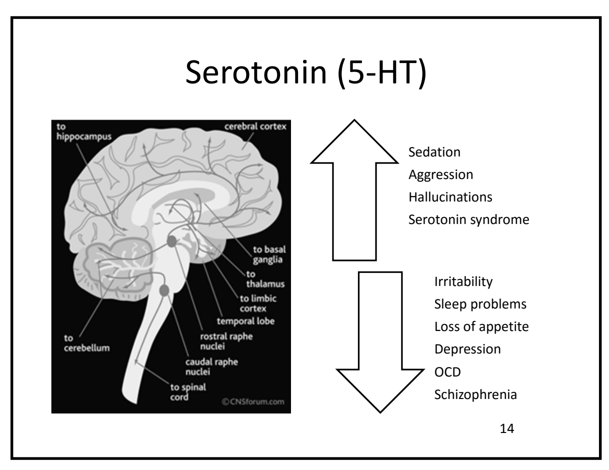

Monoamines
• Neurotransmitters released into synapse
– Emotional response, arousal, cognition
– Oxidized by monoamine oxidase
– Transported in/out of neurons by a protein pump specific for that amine
• Types
– Histamine
– Tryptamines
• Serotonin (5-HT)
• Melatonin
– Catecholamines
• Adrenaline (epinephrine)
• Norepinephrine (NE)
• Dopamine (DA)
– Other Trace amines
• Includes phenethylamines, thyronamines, and tryptamines
13


Serotonin (5-HT)
to hippocampus
cerebral cortex
to basal ganglia
to thalamus
to limbic cortex
temporal lobe
rostral raphe nuclei
caudal raphe nuclei
to cerebellum
to spinal cord
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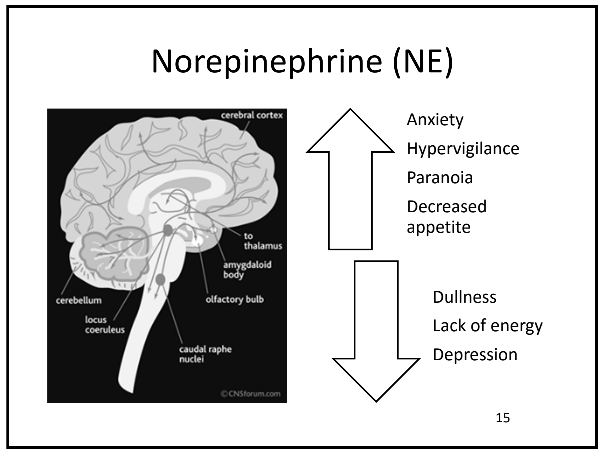
Sedation
Aggression
Hallucinations
Serotonin syndrome
Irritability
Sleep problems
Loss of appetite
Depression
OCD
Schizophrenia
14


Norepinephrine (NE)
cerebral cortex
to thalamus
amygdaloid body
olfactory bulb
cerebellum
locus coeruleus
caudal raphe nuclei
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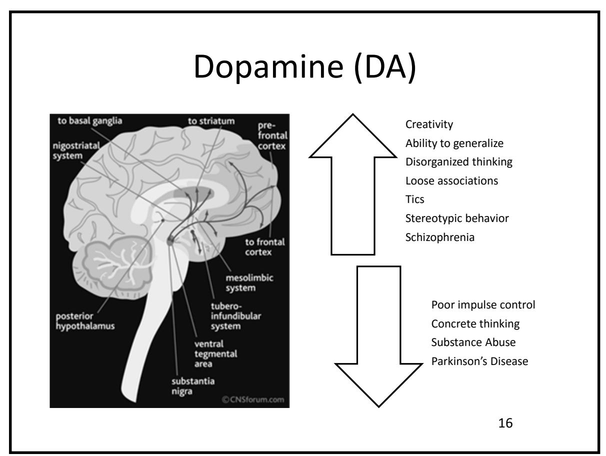
Anxiety
Hypervigilance
Paranoia
Decreased appetite
Dullness
Lack of energy
Depression
15


Dopamine (DA)
to basal ganglia
to striatum
pre-frontal cortex
nigostriatal system
to frontal cortex
mesolimbic system
tubero-infundibular system
posterior hypothalamus
ventral tegmental area
substantia nigra
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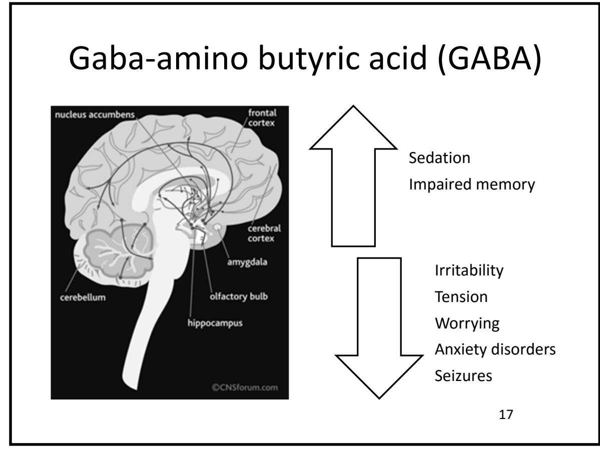
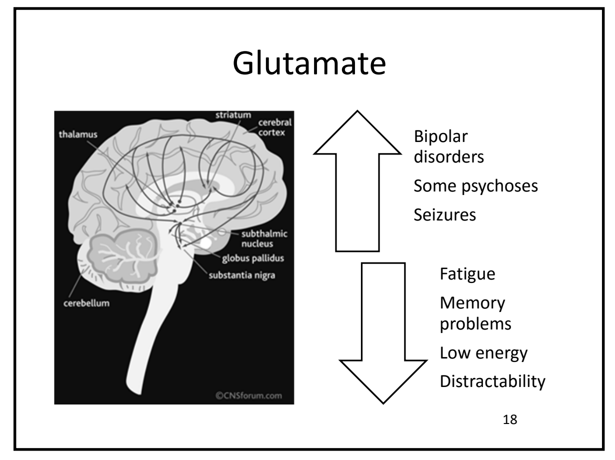
Creativity
Ability to generalize
Disorganized thinking
Loose associations
Tics
Stereotypic behavior
Schizophrenia
Poor impulse control
Concrete thinking
Substance Abuse
Parkinson's Disease
16


Gaba-amino butyric acid (GABA)
nucleus accumbens
frontal cortex
cerebral cortex
amygdala
cerebellum
olfactory bulb
hippocampus
©CNSforum.com
Sedation
Impaired memory
Irritability
Tension
Worrying
Anxiety disorders
Seizures
17


Glutamate
striatum
thalamus
cerebral cortex
subthalmic nucleus
globus pallidus
substantia nigra
cerebellum
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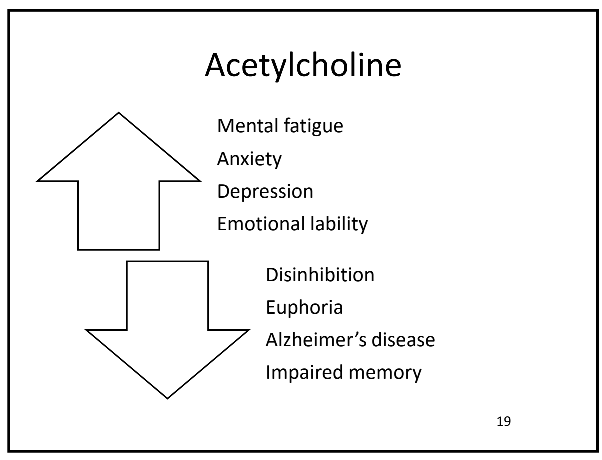
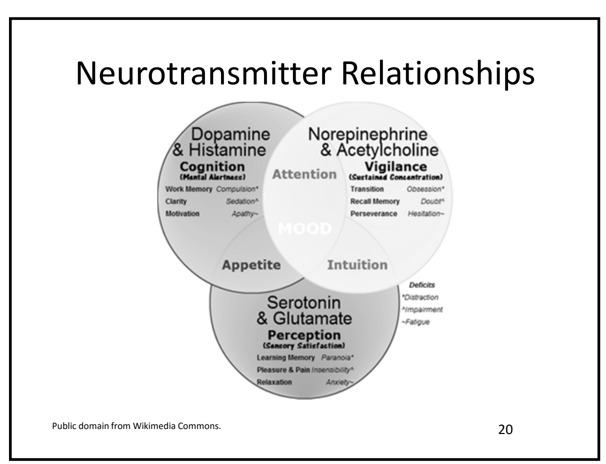
Bipolar disorders
Some psychoses
Seizures
Fatigue
Memory problems
Low energy
Distractability
18


Acetylcholine
Mental fatigue
Anxiety
Depression
Emotional lability
Disinhibition
Euphoria
Alzheimer's disease
Impaired memory
19


Neurotransmitter Relationships
Dopamine & Histamine
Cognition
Norepinephrine & Acetylcholine
Vigilance
Attention
MOOD
Appetite
Intuition
Serotonin & Glutamate
Perception
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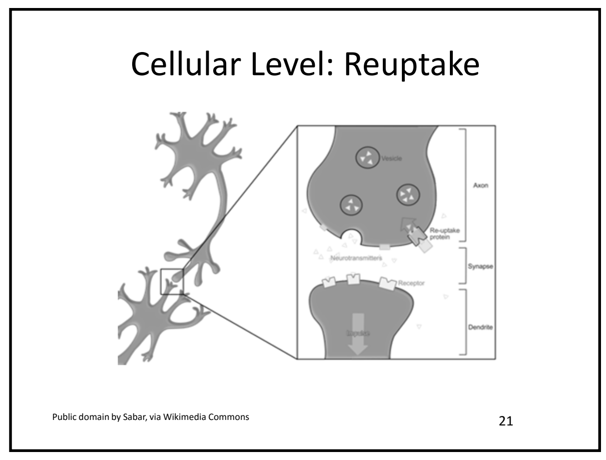
Cellular Level: Reuptake
Axon
Synapse
Dendrite
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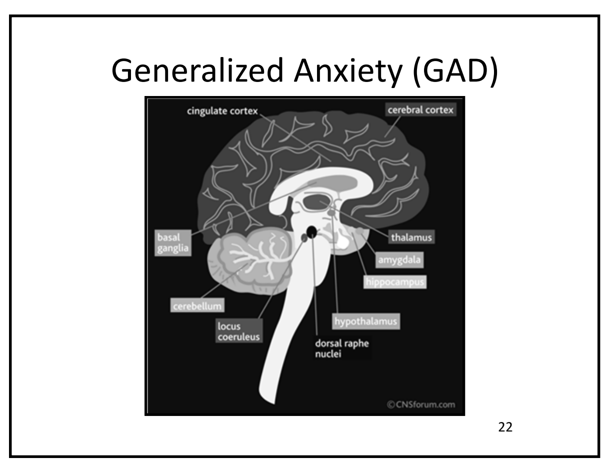
Generalized Anxiety (GAD)
cingulate cortex
cerebral cortex
basal ganglia
thalamus
amygdala
hippocampus
cerebellum
hypothalamus
locus coeruleus
dorsal raphe nuclei
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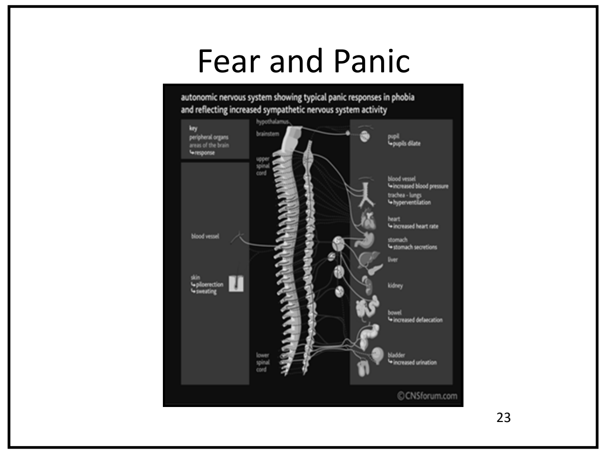
Fear and Panic
autonomic nervous system showing typical panic responses in phobia and reflecting increased sympathetic nervous system activity
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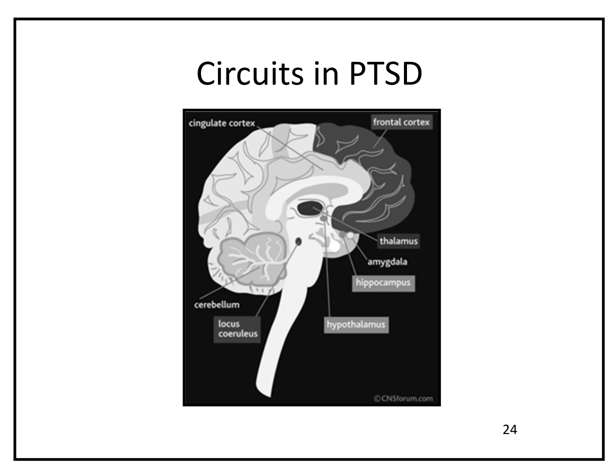
Circuits in PTSD
cingulate cortex
frontal cortex
thalamus
amygdala
hippocampus
cerebellum
locus coeruleus
hypothalamus
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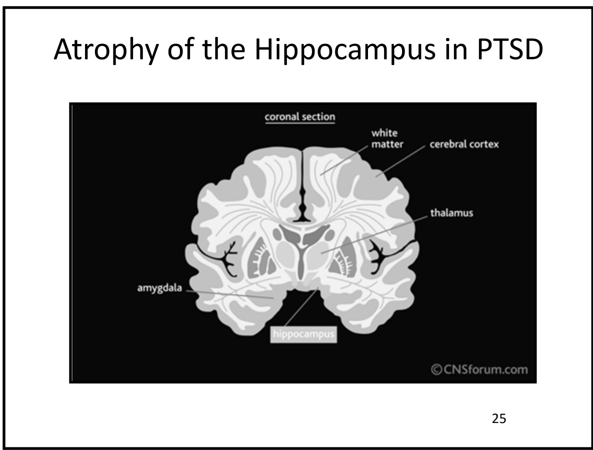
Atrophy of the Hippocampus in PTSD



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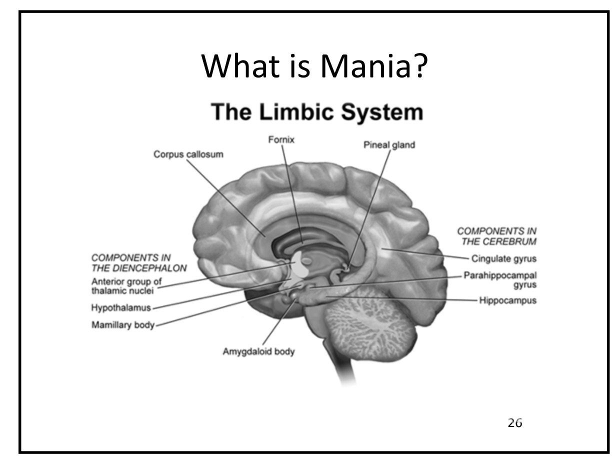
What is Mania?



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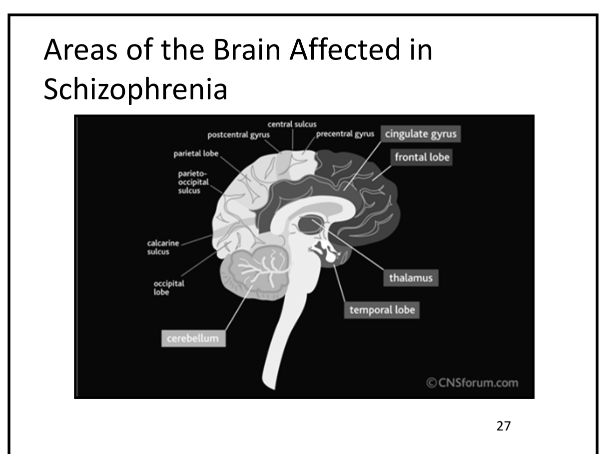
Areas of the Brain Affected in Schizophrenia



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A Life With Potential

A Person Entrusted to Your Care

THE PATIENT

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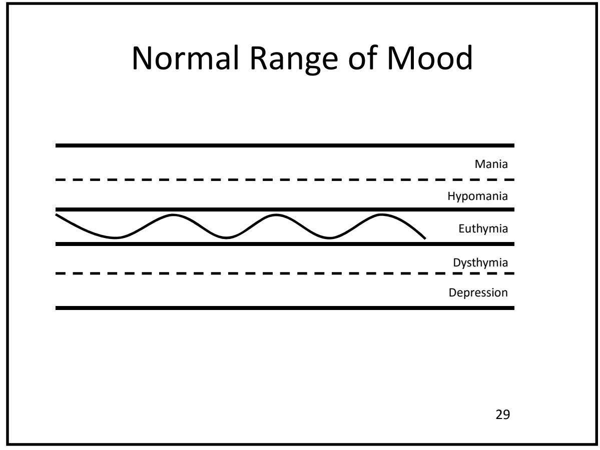
Normal Range of Mood



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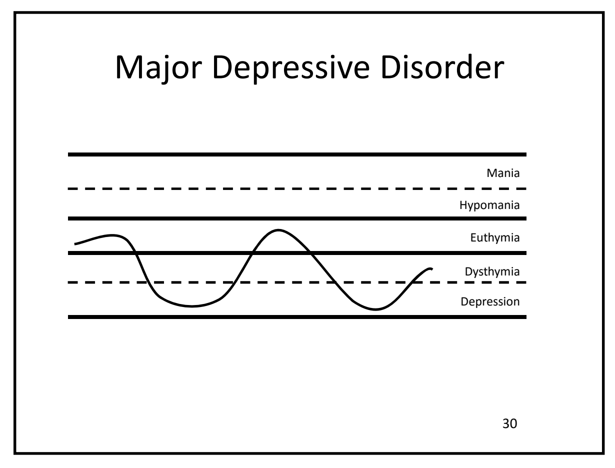
Major Depressive Disorder



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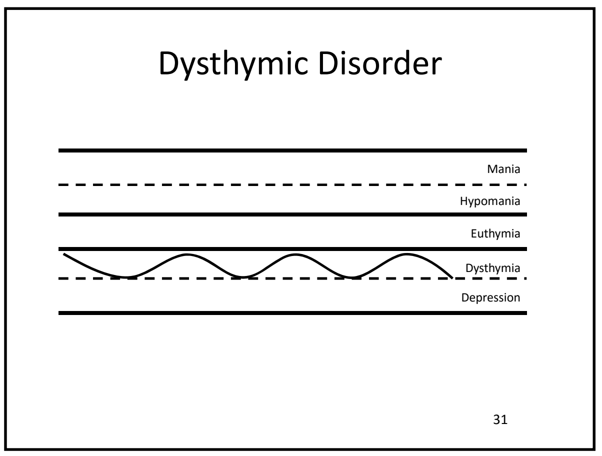
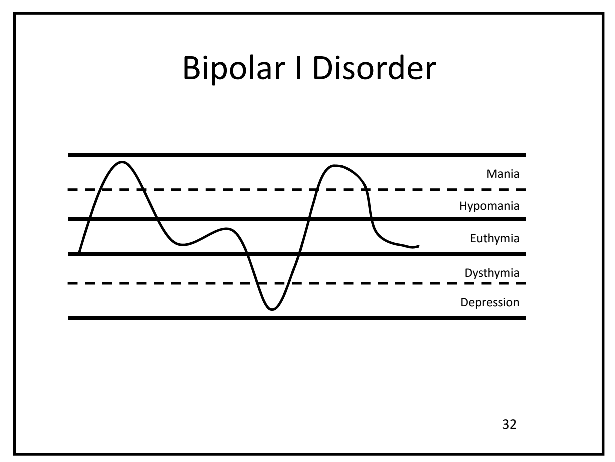
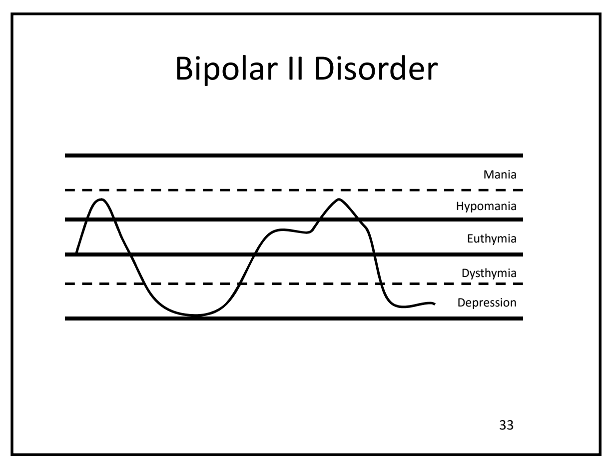
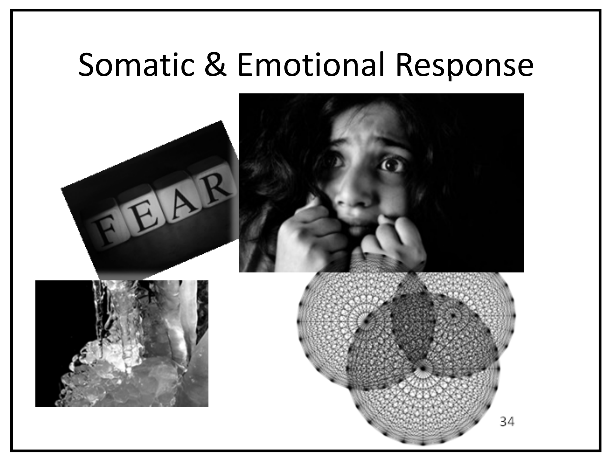
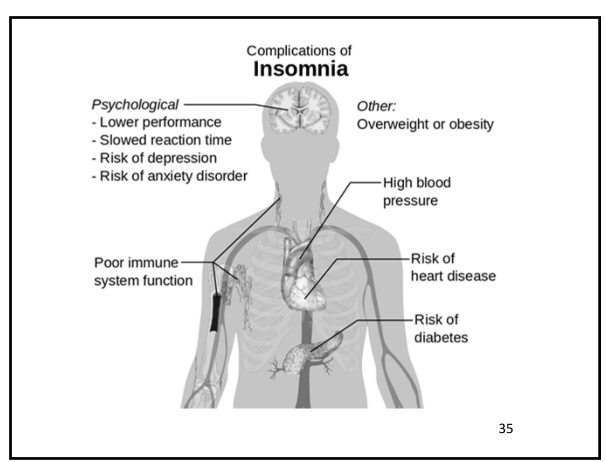
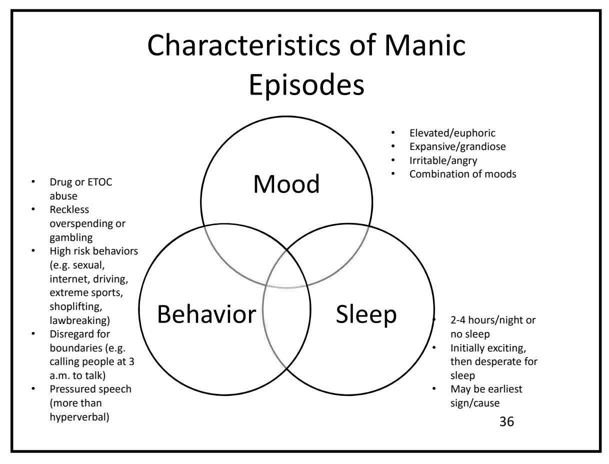

Dysthymic Disorder
Mania
Hypomania
Euthymia
Dysthymia
Depression
31


Bipolar I Disorder
Mania
Hypomania
Euthymia
Dysthymia
Depression
32


Bipolar II Disorder
Mania
Hypomania
Euthymia
Dysthymia
Depression
33


Somatic & Emotional Response
FEAR
34


Complications of
Insomnia
Psychological
- Lower performance
- Slowed reaction time
- Risk of depression
- Risk of anxiety disorder
Other:
Overweight or obesity
High blood pressure
Poor immune system function
Risk of heart disease
Risk of diabetes
35


Characteristics of Manic Episodes
Mood
Behavior
Sleep
Elevated/euphoric
Expansive/grandiose
Irritable/angry
Combination of moods
Drug or ETOC abuse
Reckless overspending or gambling
High risk behaviors (e.g. sexual, internet, driving, extreme sports, shoplifting, lawbreaking)
Disregard for boundaries (e.g. calling people at 3 a.m. to talk)
Pressured speech (more than hyperverbal)
2-4 hours/night or no sleep
Initially exciting, then desperate for sleep
May be earliest sign/cause
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Antidepressants

THE AGENTS

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Antidepressant Classification

SSRI (selective serotonin reuptake inhibitor)
- Blocks 5-HT reuptake
- As effective as TCAs and better tolerated

SNRI (selective serotonin and norepinephrine reuptake inhibitor)
- Blocks 5-HT & NE reuptake
- NE may make SNRIs poorly tolerated for some patients, more energizing for others

TCA (tricyclic antidepressant)
- Blocks 5-HT & NE reuptake
- Efficacious and cost-effective, but poorly tolerated
- Potentially lethal in overdose

MAOI (monoamine oxidase inhibitor)
- Stops the oxidation of any monoamine
- Effective, but very dangerous, so reserved for refractory, atypical depression (rare use)
- Requires prolonged wash-out period when stopping/starting other antidepressants
- May cause significant and life-threatening interactions with food and other drugs

Atypical Antidepressants
- Bupropion blocks DA reuptake
- Others act in various ways to increase effective 5-HT and NE

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Black Box Warning

Antidepressants
- Increased risk compared to placebo of suicidal thinking and behavior
  - Children
  - Adolescents
  - Young adults <=24 yrs
- Reduced risk >= 65 yrs
- No difference in risk 24-64 yrs

What to Do
- Discuss with patient and parents
  - Depressive disorders also have risk of suicide
- Monitor closely
  - Worsening condition
  - Suicidality
  - Unusual changes in behavior
- Weigh risks and clinical need (potential benefits of treatment)

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SSRIs

Generic	Brand Name(s)	FDA Indications	Adult Daily Dose (mg)
Citalopram	Celexa	depression	20-40*
Escitalopram	Lexapro	MDD > 12 yrs, GAD	10-20
Fluoxetine	Prozac	MDD > 8 yrs, OCD > 7 yrs, PMDD, bulimia nervosa, panic DO, bipolar depression or treatment-resistant depression w/olanzapine (Symbyax)	20-80 depression/anxiety; 60-80 bulimia
Fluvoxamine	Luvox, Luvox CR	OCD > 8 yrs, social anxiety DO (CR)	100-300 (OCD), 100-200 (dep), 100-300 (SAD)
Paroxetine	Paxil, Paxil CR	MDD, OCD, panic DO, SAD, PTSD, GAD, PMDD	20-50, 25-62.5 (CR)
Sertraline	Zoloft	MDD, PMDD, panic DO, PTSD, SAD, OCD > 6 rys	50-200

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press

*Revision to citalopram due to current practice guidelines.

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SSRIs

Advantages
- Good efficacy
- Well tolerated, few side effects
- Not usually lethal in overdose
- Expect dose to vary depending on dx
- Always start here

Considerations
- Fluoxetine (Prozac)—very activating. Begin in a.m.
- Paroxetine (Paxil)—watch for weight gain
- Citalopram (Celexa)—qTc elevation risk at > = 60 mg

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SNRIs

Generic	Brand Name(s)	FDA Indications	Adult Dose (mg)
Duloxetine	Cymbalta	MDD, GAD	40-60
Venlafaxine	Effexor	depression, GAD, SAD, panic DO	75-225 (dep), 150-225 (GAD)
Desvenlafaxine	Pristiq	MDD	50

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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SNRIs

Advantages

- Good efficacy
- Good tolerability
- Most algorithms include as second tier after SSRIs have received adequate trial

Considerations

- Venlafaxine (Effexor)—difficult to discontinue
- Duloxetine (Cymbalta)—patients with comorbid fibromyalgia often report relief in higher doses
- Norepinephrine effects may be difficult for some patients to tolerate
  - Can exacerbate anxiety in some patients
  - Relieves anxiety in others

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Atypical Antidepressants

Generic	Brand Name(s)	Class	FDA Indications	Adult Daily Dose (mg)
Bupropion	Wellbutrin, Wellbutrin SR, Wellbutrin XL	NDRI	MDD, SAD (XL), nicotine addiction (SR)	225-450 (IR--div 3 doses), 200-450 (SR-div 2 doses), 150-450 (XL)
Mirtazapine	Remeron	Atypical (SN)	MDD	15-45
Nefazodone		SARI	depression, relapse prevention in MDD	300-600
Trazodone	Desyrel	SARI	depression	150-600, 150-375 (ER)

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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TCAs

Generic	Brand Name(s)	FDA Indications	Adult Daily Dose (mg)
Amitriptyline	(generic only)	depression*	50-150
Amoxapine	Asendin	depression*	200-300
Doxepin	Sinequan	depression*, anxiety*, manic-depressive DO*, insomnia	75-150
Imipramine	Tofranil	depression	50-150
Nortriptyline	Pamelor	MDD	75-150
Protriptyline	Vivactil	depression*	15-40
Trimipramine	Surmontil	depression	50-150
Desipramine	Norpramin	depression	100-200

*Indication not a current DSM diagnosis

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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TCAs

Potentially lethal
- Overdose of 1-week's meds may be lethal
- TCAs with MAOIs may be lethal

Good efficacy

Poor tolerability
- Antihistaminic effects—sedation, weight gain, memory problems
- Antiadrenergic effects—orthostatic hypotension
- Anticholinergic effects—dry mouth, blurred vision, constipation, urinary retention
- EKG changes, dysrhythmia
- Hypomania (like SSRIs, SNRIs)
- Increased seizures in seizure disorders
- Sexual side effects

No longer considered first-line treatment for depression

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MAOIs

Generic	Brand Name(s)	FDA Indications	Adult Daily Dose (mg)
Isocarboxazid	Marplan	depression	40-60
Phenelzine	Nardil	depression*	45-75
Selegiline	EMSAM	MDD (transdermal)	6 mg/24 hrs – 12 mg/24 hrs
Tranylcypromine	Parnate	major depressive episode without melancholia*	30

*Indication not a current DSM diagnosis

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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MAOIs

Good efficacy

Dangerous to use
- Potentially lethal hypertensive crisis from food or drug interactions
- TCAs with MAOIs may be lethal
- Dangerous in overdose

Poor tolerability
- Insomnia
- Anticholinergic side effects
  - Dry mouth
  - Blurred vision
  - Constipation
  - Memory problems
- Dizziness
- Sexual side effects

Never first-line drugs

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Black Box Warning

Stimulants

- Increased risk cardiac complications or sudden death, especially in patients with pre-existing cardiac problems
- These drugs also have potential for abuse and diversion

What to Do

- Discuss with patient and parents
  - EKG and cardiology clearance (in writing) if history or problems
- Monitor closely
  - Cardiovascular symptoms
  - Unusual changes in behavior
- Weigh risks and clinical need (potential benefits of treatment)

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Anxiolytics

THE AGENTS

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Anti-Anxiety Agents

Generic	Brand Name(s)	Class	FDA Indications	Adult Daily Dose (mg)
Alprazolam	Xanax, Xanax XR	BDZ	GAD (IR), Panic DO (IR, XR)	1-4 (Anx), 5-6 (Panic), 3-6 (XR, Panic)
Chlordiazepoxide	Librium, Librax	BDZ	Anxiety DO	15-40 mild-mod, 60-100 severe
Clonazepam	Klonopin	BDZ	Panic DO w/wo agoraphobia	0.5-2
Diazepam	Valium	BDZ	Anxiety DO	4--40
Lorazepam	Ativan	BDZ	Anxiety DO, Anxiety with depressive symptoms	1--2
Hydroxyzine	Atarax, Vistaril	Antihistamine	Anxiety	50-100
Buspirone	BuSpar	Anxiolytic (5-HT1A partial agonist)	Anxiety DO	20-30

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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Benzodiazepines

- Potential for dependence and addiction
- Duration of action and "roller coaster" effect
- Potential for abuse with all BDZ
- Contraindicated with ETOH
- Withdrawal can include seizures and be life-threatening
- Know or look up equivalents

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Benzodiazepine Equivalents

	Approximately Equivalent Oral Doses, mg	Time to Peak Level, hours	Half-life, hours
Alprazolam (Xanax)	0.5	1-2	12
Bromazepam (Lexotan)	3	1-4	20
Chlordiazepoxide (Librium)	25	1-4	100
Clonazepam (Klonopin)	0.25	1-4	34
Clorazepate (Tranxene)	10	0.5-2	100
Diazepam (Valium)	5	1-2	100
Flurazepam (Dalmane)	15	0.5-1	100
Lorazepam (Ativan)	1	1-4	15
Nitrazepam (Mogadon)	2.5	0.5-2	30
Oxazepam (Serax)	15	1-4	8
Quazepam (Doral)	10	1.5	25-41
Temazepam (Restoril)	10	2-3	11
Triazolam (Halcion)	0.25	1-2	2

http://emedicine.medscape.com/article/2172250-overview

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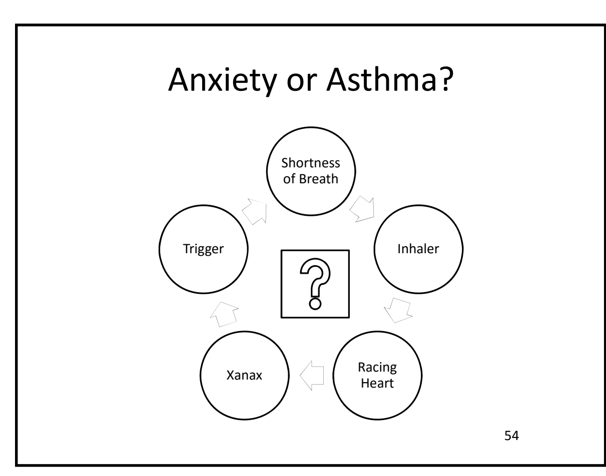

Mood Stabilizers

THE AGENTS

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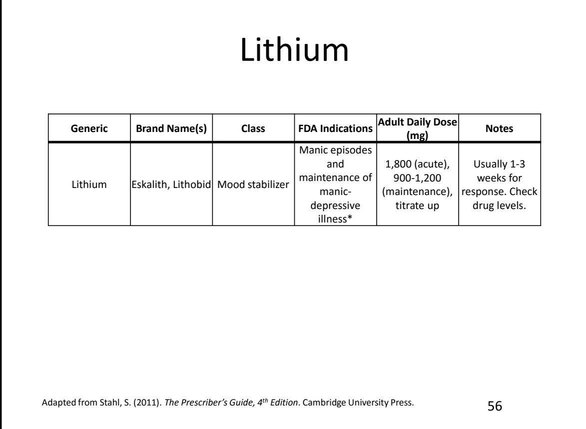
Lithium



Generic	Brand Name(s)	Class	FDA Indications	Adult Daily Dose (mg)	Notes
Lithium	Eskalith, Lithobid	Mood stabilizer	Manic episodes and maintenance of manic-depressive illness*	1,800 (acute), 900-1,200 (maintenance), titrate up	Usually 1-3 weeks for response. Check drug levels.

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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Lithium

- Mechanism of action: Unknown
- Affect
  - Alters sodium transport across cell membranes
  - Alters metabolism of neurotransmitters
  - Increases cytoprotective protein
- Problems
  - Must maintain consistent fluid & electrolyte balance—diet and hydration difficult to regulate with environmental , activity, infection
  - Many patients refuse lithium due to stigma
  - Narrow therapeutic window
    - Affected by other drugs—especially NSAIDs, diuretics (thiazide), calcium channel blockers, SSRIs
  - Overdose or toxic level may cause renal failure or death
- Contraindicated
  - Kidney disease
  - Cardiovascular disease
  - Dehydration
  - Sodium depletion
  - Allergy to lithium
- Signs & symptoms of toxicity
  - Tremor
  - Ataxia
  - Diarrhea
  - Vomiting
  - Sedation
  - Renal compromise
- Overdose
  - Signs of toxicity (above)
  - Seizures
  - Delirium
  - Coma

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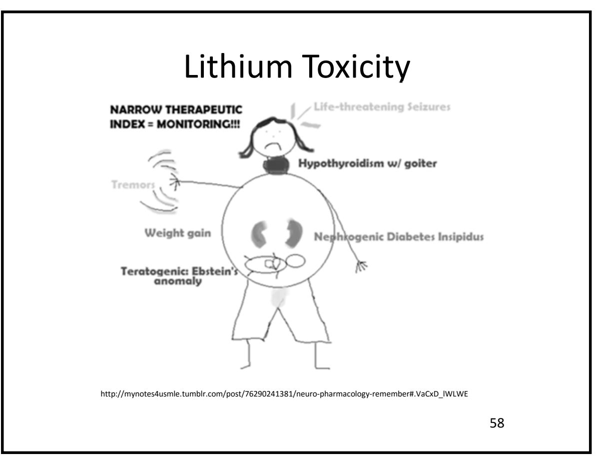
Lithium Toxicity



http://mynotes4usmle.tumblr.com/post/76290241381/neuro-pharmacology-remember#.VaCxD_IWLWE

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Antiepileptic Drugs

Generic	Brand Name(s)	Class	FDA Indications	Adult Daily Dose (mg)	Notes
Valproate	Depakote, Depakote ER	AED, mood stabilizer	Acute mania or mixed episodes	1,200-1,500	Titrate. Rare hepatotoxicity. Monitor drug levels.
Carbamazepine	Tegretol	AED	Acute mania or mixed mania	400-1,200	Titrate. Overdose can be fatal. Monitor for agranulocytosis. Monitor drug levels.
Lamotrigine	Lamictal	AED, mood stabilizer	Maintenance Bipolar I	100-200 (monotherapy), 100 (w/ valproate), 400 (w/carbamazepine or other drugs)	Slow titration: 2+ weeks at each level (25 mg, 50 mg, 100 mg, 150 mg, 200 mg. Risk of SJS

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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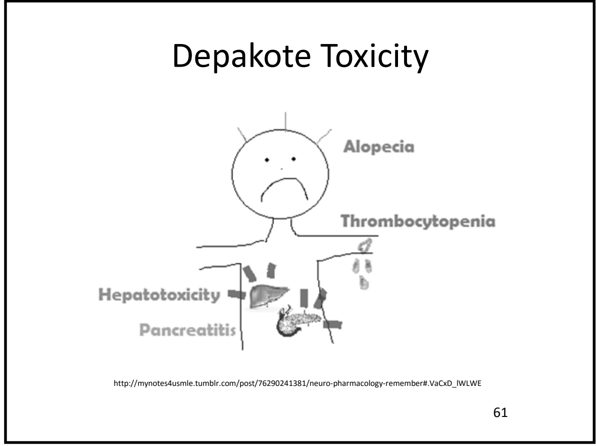
Antiepileptic Drugs

- Valproate (Depakote)
- Carbamazepine (Tegretol)
- Lamotrigine (Lamictal)
- Off label or adjuncts
  - Oxcarbazepine (Trileptal)
  - Topirimate (Topamax)
  - Gabapentin (Neurontin)
  - Benzodiazepines are not adequate monotherapy for Bipolar DO!

60

Depakote Toxicity



http://mynotes4usmle.tumblr.com/post/76290241381/neuro-pharmacology-remember#.VaCxD_IWLWE

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Antipsychotics

THE AGENTS

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Black Box Warning

Antipsychotics

- Increased risk of death in elderly patients treated with antipsychotic drugs
- Not approved for dementia-related psychosis
- Children, adolescents, and young adults taking antipsychotics that are also antidepressants may be at increased risk for suicidal thinking and behavior

What to Do

- Discuss with patient and parents
  - Psychosis associated with dementia affects quality of life
- Monitor closely
  - Worsening condition
  - Suicidality
  - Unusual changes in behavior
- Weigh risks and clinical need (potential benefits of treatment)

63

Second Generation Antipsychotics

Generic	Brand Name(s)	Class	FDA Indications	Adult Daily Dose (mg)
Aripiprozole	Abilify	SGA	SCZ > 13 yr, SCZ maintenance, acute mania/mixed > 10, bipolar maintenance, adjunct depression, autism-related irritability (6-17 yr)	15-30
Asenapine	Saphris	SGA	SCZ, (acute & maintenance), acute mania/mixed (monotherapy or adjunt to lithium or valproate)	10--20
Iloperidone	Fanapt	SGA, MS	SCZ	12--24
Lurasidone	Latuda	SGA	SCZ	40-80
Olanzapine	Zyprexa	SGA	SCZ > 13 yr, SCZ maintenance, acute agitation in SCZ or bipolar I mania, acute mania/mixed (monotherapy & adjunct to Li or VPA) > 13, bipolar maintenance, bipolar depression and tx-resistant depression (combination with fluoxetine--Symbyax)	10--20
Olanzapine + Fluoxetine	Symbyax	SGA	bipolar depression, treatment-resistant depression	6--12 olanzapine/25-50 fluoxetine

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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Second Generation Antipsychotics

Generic	Brand Name(s)	Class	FDA Indications	Adult Daily Dose (mg)
Paliperidone	Invega, Invega Sustenna	SGA, MS	SCZ, (acute & maintenance), schizoaffective DO	6 mg/day (oral), 39-234 mg/month (IM)
Quetiapine	Seroquel, Seroquel XR	SGA	SCZ (acute & maintenance), acute mania > 10 yr, bipolar maintenance, bipolar depression, depression (adjunct)	400-800 1 dose XR or 2 doses IR for SCZ or bipolar mania, 300 for bipolar depression
Risperidone	Risperdal, Consta (depot)	SGA	SCZ > 13 yr, delaying relapse SCZ, other psychotic DO, acute mania/mixed mania > 10, autism-related irritability 5-16 yr, bipolar maintenance (monotherapy & adjunct)	2-8 (oral) acute psychosis/bipolar DO, 0.5-2.0 (oral) children and elderly, 25-50 mg/2weeks (IM)
Ziprasidone	Geodon	SGA	SCZ, delaying relapse in SCZ, acute agitation SCZ, acute mania/mixed mania, bipolar maintenance	40-200 (SCZ), 80-160 (oral--bipolar DO), 10-20 mg (IM)

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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SGA Metabolic Effects

	Weight Gain	Risk for Diabetes	Worsening Lipid Profile
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	D	D
Quetiapine	++	D	D
Aripiprazole*	+/-	-	-
Ziprasidone*	+/-	-	-

+ = increased effect; - = no effect; D = discrepant results; *Newer drugs with limited long-term data

American Diabetes Association (2004). Consensus development conference on antipsychotic drugs and obesity and diabetes.

66

First Generation Antipsychotics

Generic	Brand Name(s)	Class	FDA Indications	Adult Daily Dose (mg)
Chlorpromazine	Thorazine	FGA	SCZ, psychosis, mania, explosive hyperexcitable behavior (children), hyperactivity with conduct disorders (children)	200-800
Clozapine	Clozaril	FGA	treatment-resistant SCZ, recurrent suicidal behavior in SCZ or schizoaffective DO	300-450
Haloperidol	Haldol, Haldol decanoate	FGA	psychotic DO, SCZ (decanoate)	1-40 (oral), 2-5 (IR IM), 10-20 times previous daily dose of oral
Loxapine	Loxitane	FGA	SCZ	60-100
Perphenazine	Trilafon	FGA	SCZ	12--24
Thioridazine	Mellaril	FGA	SCZ failing other drugs	200-800

Representative sample: other drugs in this class are not commonly seen in primary care.

Adapted from Stahl, S. (2011). *The Prescriber's Guide, 4th Edition*. Cambridge University Press.

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First Generation Antipsychotics (FGA)

- Haloperidol
  - First choice emergencies (delerium, agitation, acute psychosis)
  - Inexpensive
  - Extra pyramidal symptoms (EPS)—benztropine or diphenhydramine concurrently as needed or scheduled
  - Cognitive dulling
  - Prolactinemia
- Other FGAs more uncommon, especially in primary care

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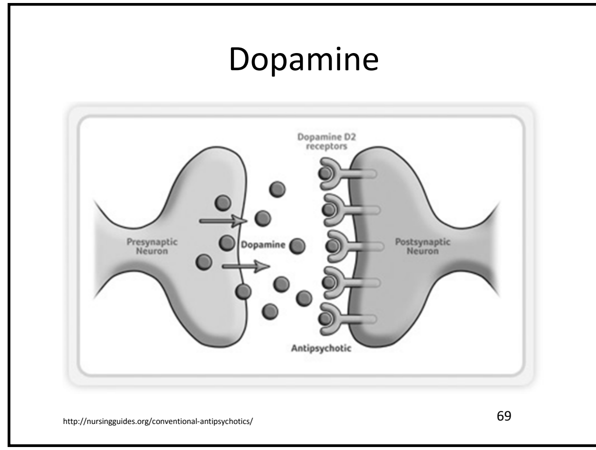
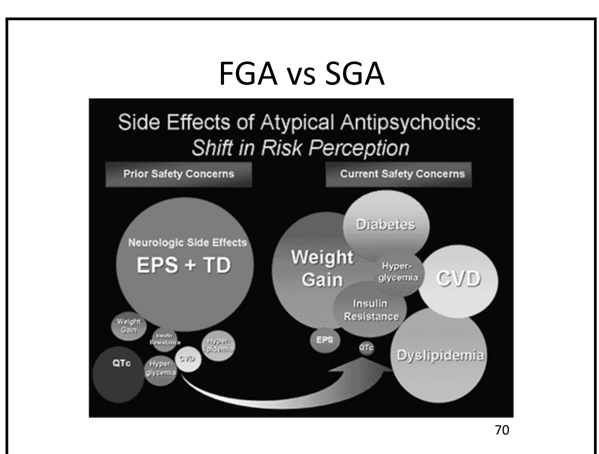
Dopamine



http://nursingguides.org/conventional-antipsychotics/

69

FGA vs SGA



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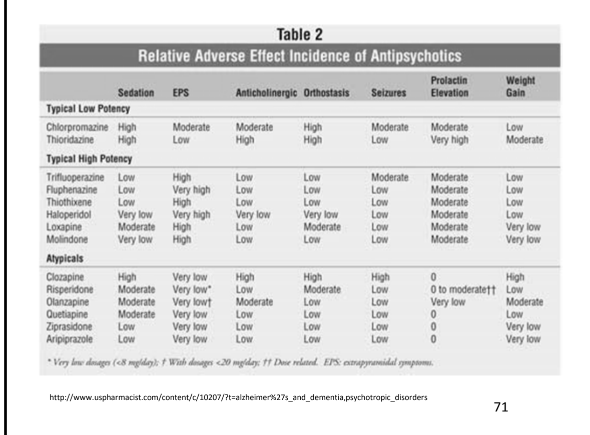

Table 2

Relative Adverse Effect Incidence of Antipsychotics

	Sedation	EPS	Anticholinergic	Orthostasis	Seizures	Prolactin Elevation	Weight Gain
Typical Low Potency							
Chlorpromazine	High	Moderate	Moderate	High	Moderate	Moderate	Low
Thioridazine	High	Low	High	High	Low	Very high	Moderate
Typical High Potency							
Trifluoperazine	Low	High	Low	Low	Moderate	Moderate	Low
Fluphenazine	Low	Very high	Low	Low	Low	Moderate	Low
Thiothixene	Low	High	Low	Low	Low	Moderate	Low
Haloperidol	Very low	Very high	Very low	Very low	Low	Moderate	Low
Loxapine	Moderate	High	Low	Moderate	Low	Moderate	Very low
Molindone	Very low	High	Low	Low	Low	Moderate	Very low
Atypicals							
Clozapine	High	Very low	High	High	High	0	High
Risperidone	Moderate	Very low*	Low	Moderate	Low	0 to moderate††	Low
Olanzapine	Moderate	Very low†	Moderate	Low	Low	Very low	Moderate
Quetiapine	Moderate	Very low	Low	Low	Low	0	Low
Ziprasidone	Low	Very low	Low	Low	Low	0	Very low
Aripiprazole	Low	Very low	Low	Low	Low	0	Very low

** Very low dosages (<8 mg/day); † With dosages <20 mg/day; †† Dose related. EPS: extrapyramidal symptoms.*

http://www.uspharmacist.com/content/c/10207/?t=alzheimer%27s_and_dementia,psychotropic_disorders

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Priorities
Decisions
Treatment

STRATEGY

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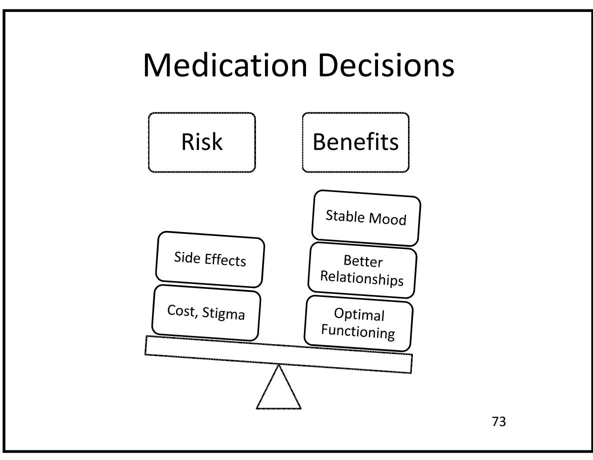
Medication Decisions



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Prioritize Treatment

1. Mania & Psychosis
2. Sleep
3. Depression
4. Anxiety
5. Don't consider treatment of ADHD until mood, sleep, depression, and anxiety are well controlled
   - Then re-evaluate diagnosis
   - Understand that stimulants can upset everything else

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Treating Mania

- Use a mood stabilizer first
  - Lithium
  - Anti-epileptic drugs
  - Second-generation antipsychotics
- Treat concurrently for sleep
- Monitor closely
- For more severe symptoms use rapid acting drugs
  - AEDs or SGAs
- For less severe symptoms of hypomania, may be able to start with Lamictal

75

Treating Psychotic Disorders

Treat with antipsychotic

- Second Generation (atypical) antipsychotics (SGAs) are usually first line (and often second and third line)
  - Effective, but more expensive
  - Well tolerated
  - Metabolic side effects
- First Generation antipsychotics (FGAs) are used less commonly
  - Effective and inexpensive
  - Poorly tolerated
    - Extrapyramidal symptoms/side effects (EPS)
    - Tardive dyskinesia
  - Clozapine requires special skills and vigilance

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Treating Bipolar Depression

- Antidepressants are NEVER monotherapy for bipolar disorder
- When to avoid antidepressants
  - Bipolar I
    - Never give antidepressants as monotherapy
    - Never give antidepressants as adjunct therapy if more than 2 symptoms of mania, rapid cycling, or psychomotor agitation
  - Bipolar II
    - Never give antidepressants as monotherapy if more than 2 symptoms of mania are present
    - Never give as adjunct therapy if more than 2 symptoms of mania
  - Mixed features
- Consider antidepressants
  - Adjunct in bipolar I or II depression with history of good antidepressant response
  - Adjunct when relapse occurs after stopping antidepressant

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Treating Depression

- Start with SSRI (safety, efficacy)
- Educate patient
  - Strict adherence to daily dosing
  - Do not stop prematurely—cessation must be managed with down-titration
- Begin at low end of dose range
- Allow 4-6 weeks to assess efficacy
  - Transient side effects—wait
- If suboptimal effect, but tolerated sufficiently, increase one dosage step and allow another 4-6 weeks to assess efficacy
- Rule out for non-response only after maximum dose attained for 4-6 weeks
- Alert patient that process may be long, progress slow, and commitment needed for at least 9-12 months for first episode MDD

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Treating Depression

- After full trial of first drug given and failed, change to another drug in the same class (SSRI)
- Titrate dose until symptoms remit
- If second drug fails, switch to another class (SNRI or Atypical), per algorithm or protocol
- For multiple failed trials, consider augmentation
- Always wait out less serious side effects—many resolve after a few weeks or months
- Considerations
  - Past medication responses (need careful inquiry)
  - Side effect profile
  - Cost

79

Treating Anxiety

- Related to serotonin deficiency
- Frequently comorbid with depression
- Long-term stabilization—antidepressants
- Symptomatic treatment with anxiolytics
- Augment with psychotherapy

80

Informed Practice Decisions

Information about "off label" prescribing, common in psychiatry

- Drug must be covered under practice law
  - Not investigational or unapproved drug
- Consistent with facility/practice protocols and procedures
- Consistent with prescriptive authority agreement with delegating physician
- FDA-approved drug used for other purpose
  - Similar indication (e.g. use of another SSRI when fluoxetine fails in a child/adolescent)
  - Indication for different population with appropriate dose adjustments (e.g. use of Intuniv for treating ADHD in college students)
- Supported by research
  - Documented in medical literature, including algorithms, protocols, guidelines, or recommendations from reputable authorities
- Evidence based practice
  - Standard practice by providers in same field or similar training and experience

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Algorithms

"A systematic process consisting of an ordered sequence of steps, each step depending on the outcome of the previous one. In clinical medicine, a step-by-step protocol for management of a health care problem"

(http://*www.medilexicon.com/medicaldictionary.php?t=2189*)

Forms of Algorithms

- Decision-tree
- Flowchart
- Table
- Narrative or other expression of policy

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Algorithms

Pros

- Standardizes approach to care
- Allows uniform guidelines within a clinic or system
- Smoother transition between providers
- Patient and provider know what to expect
- Better outcomes than treatment as usual (Trivedi et al)
- Improved patient satisfaction (Trivedi et al)

Cons

- Sometimes developed based on studies that are not "real world"
- Take a long time to develop, therefore quickly out of date
- Not all patients fit into algorithm
- Can't address all complications
- Algorithms differ

Trivedi, M., Fava, M., Marangell, L., Osser, D. & Shelton, R. (2006). Use of treatment algorithms for depression. *Primary Care Companion Journal of Clinical Psychiatry, 8*(5), 291-298.

83

mhGAP Guide (Algorithm)

mhGAP Intervention Guide for Mental, Neurological and Substance Use Disorders in Non-specialized Health Settings

- Mental, neurological, and substance use disorders
- 14% of global burden of disease attributable to mental, neurological and substance use disorders
- 75% occurs in low- and middle-income countries with few resources
- Majority of countries allocate less than 2% of their health budgets to mental health
- Treatment gap > 75% in many of these countries

This free resource is a helpful tool for decision-making in diagnosis. Less helpful for medications in United States.

World Health Organization Mental Health Gap Action Programme. (2010). *www.who.int/mental_health/mhgap*

84

VA / DoD Publications for Mental Health Problems

Algorithms and Guidelines
- Major Depressive Disorder (MDD)
- Post Traumatic Stress Disorder (PTSD)
- Bipolar Disorder in Adults (BD)
- Substance Abuse Disorder (SUD)
- Tobacco Use
- Assessment and Management of Patients at Risk for Suicide

http://www.healthquality.va.gov/

85

Texas Medication Algorithm Project

Suehs BT, Argo TR, Bendele SD, Crismon ML, Trivedi MH, Kurian B. *Texas Medication Algorithm Project Procedural Manual: Major Depressive Disorder Algorithms.* The Texas Department of State Health Services. 2008.
- Algorithms
- Discussions
- Process Measures
- Medication charts

Considerations
- May not be used or adapted without written permission
- Difficult to locate
- Once a standard for other algorithms
- Some concern over role of pharmaceutical companies

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Sequenced Treatment Alternatives to Relieve Depression (Star*D) Algorithm

- Largest prospective, randomized treatment study to date of outpatients
- Real world psychiatric and primary care patients
- More information at *www.nimh.nih.gov*

Trivedi, M., Fava, M., Marangell, L., Osser, D. & Shelton, R. (2006). Use of treatment algorithms for depression. *Primary Care Companion Journal of Clinical Psychiatry, 8*(5), 291-298.

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AGS Beers Criteria

American Gerontological Society (AGS) Beers Criteria
Goals
- Reduce exposure to Potentially Inappropriate Medications (PIMs)
  - Guide to identify medications with risks that may outweigh benefits
  - Not intended to be punitive
  - Does not supersede clinical judgment, values, or needs
  - Individualize care
  - Shared decision-making
- Use collaborative approach
- Complementary to other guides or algorithms

Drugs to Avoid—Pocket Reference
- Find the pocket card at: *http://www.americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/2012*

88

Alosa Foundation

- Independent non-profit providing drug detailing for education and cost containment in prescribing
- Partners
  - Pharmaceutical Assistance Contract for the Elderly (PACE) of the Pennsylvania Department of Aging
  - District of Columbia Department of Health from 2009 to 2014
  - Massachusetts Department of Public Health
  - Washington D.C. Department of Health's HIV/AIDS, Hepatitis, STD and TB Administration (HAHSTA)
- Algorithms
  - Behavioral symptoms of dementia
  - Managing behavioral problems in older patients with dementia
  - Pharmacologic management of depression

Alosa Foundation (2014). Antipsychotic medications in nursing homes. http://www.alosafoundation.org/modules/antipsychotic-medications-nursing-homes/

89

Measures : What is Going Right?
Emergencies: What is Going Wrong?
Teaching the Patient to Monitor

MONITORING

90

Measures

- Assessment tool
  - Does not replace the interview, but can determine the target
- Outcome measure for treatment
  - Standardized evaluation response to medications
- Patient participation
  - Teaches them to self-assess

- Saundra's Corner: a great resource for measures: http://www.psychcongress.com/saundras-corner/scales-screeners

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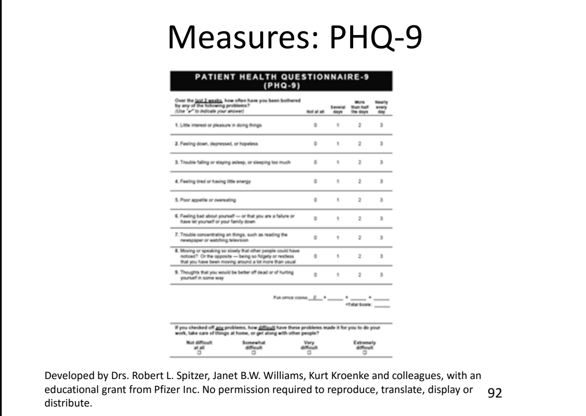
Measures: PHQ-9



PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use "✔" to indicate your answer)	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + ___ + ___ + ___
=Total Score: ___

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult ☐

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

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Management of Side Effects

- Minor side effects
  - Nausea, headache, gastrointestinal symptoms
  - "Wait, Wait, Wait" (Stahl)—minor side effects often resolve
- Sexual side effects
- Take seriously
  - Patients often do not mention them until after they have decided to stop their medication
- Extrapyramidal Side Effects
  - Treat promptly
  - Benztropine (Cogentin)—commonly prescribed with FGAs
  - Diphenhydramine (Benadryl)—more sedating
  - Amantadine

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SGA Monitoring Protocol

	Baseline	4 wks	8 wks	12 wks	Quarterly	Annually	Every 5 yrs
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X

+ = increased effect
– = no effect
D = discrepant results
***** = Newer drugs with limited long-term data

American Diabetes Association (2004). Consensus development conference on antipsychotic drugs and obesity and diabetes.

94

Discontinuation Syndrome

Causes
- Abrupt discontinuation of antidepressant or irregular use
- Higher doses
- Long treatment duration

Prevention
- Taper down to discontinue at same rate or slower as taper up
- Cross-titrate when changing medications

Symptoms
- Anxiety, irritability, crying
- Dizziness
- Myalgia, fatigue (flu-like)
- Difficulty with concentration and focus
- Shock sensations or "brain zaps"
- TCAs—cholinergic rebound syndrome (GI/nausea, diaphoresis, myalgia)

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Serotonin Syndrome

Potentially life threatening

Cause
- Excess serotonin, usually from two (or more) drugs taken together
  - Migraine medicines: triptans
  - SSRIs and MAOIs
  - Pain meds: meperidine, tramadol
  - Dextromethorphan
  - Illicit drugs: ecstasy (MDMA), LSD
  - SSRIs and St. John's Wort
- More likely when medicine is started or increased

Symptoms
- Rapid onset—minutes to hours
- Agitation or restlessness
- Tachycardia
- High/labile blood pressure
- Fever, shivering
- Nausea, vomiting, diarrhea
- Hyperreflexia
- Diaphoresis
- Confusion, hypomania, or hallucinations
- Myoclonus, tremor, ataxia

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Serotonin Syndrome

Differentials
- Can mimic symptoms of overdoses (cocaine, lithium, or MAOI)
- May initially present like neuroleptic malignant syndrome

Treatment
- Medical emergency requiring close observation for 24 hours
- Stop medication(s) that precipitated syndrome
- Benzodiazepines to decrease agitation, seizure-like movements, and muscle stiffness
- Cyproheptadine (Periactin) to block serotonin production
- IV Fluids
- Intubation may be needed

Prognosis
- Good if promptly treated
- Poor if not treated
- Complications may include renal failure

U.S. National Library of Medicine, National Institute for Health (2014). *http://www.nlm.nih.gov/medlineplus/ency/article/007272.htm*

97

Hypertensive Crisis

Cause
- Occurs when MAOI is taken with foods containing tyramine
  - Severe hypertension
  - Abrupt, severe onset of headache
  - Facial flushing
  - Diaphoresis
  - Fever
  - Palpitations

Life threatening

Treatment
- Stop MAOI
- Administer phentolamine (Regitine) or chlorpromazine (Thorazine) to inhibit norepinephrine
- Treatment is rapid, but condition is irreversible until MAO (monoamine oxidase) is replenished
- Treat fever
- Determine cause
- If spontaneous (not related to tyramine) do not restart an MAOI

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Neuroleptic Malignant Syndrome

Life-threatening neurological disorder

Adverse reaction to neuroleptic or antipsychotic drugs
- Usually within first 2 weeks of treatment, but can occur at any time

Symptoms
- High fever
- Sweating
- Unstable blood pressure
- Stupor
- Muscular rigidity
- Autonomic dysfunction

Treatment
- Medical emergency
- Usually intensive care
- Discontinue neuroleptic or antipsychotic medication
- Aggressive symptomatic treatment
- Once stable,
  - Reintroduce drug gradually or give different class of drug
  - Educate to inform provider before receiving anesthesia

National Institute of Neurological Diseases and Stroke (2014).

99

Adherence
Collaboration
Outcomes

OPTIMIZATION

100

Optimizing Treatment Adherence

- Therapeutic Relationship
- Educate Family/friends
  - Prevent splitting
  - Encourage early recognition of problems
  - Affirm assistance with meds and treatment
- Medication reminders
  - Charts at home
  - Phone apps
  - Pill sorters
- Normalize Reporting
  - "Many people find that they forget some of their doses. Out of the last 30 days, how many days would you say you missed your medication?"
  - "How do you feel when you miss it."
  - "Thank you for being honest about missing your medications. It's important for me to know this."
- Emphasize Consequences
  - No medication works if it stays in the bottle
- Long-acting Injectibles

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Negative Outcomes

- Serious mental illness causes changes to the brain
- Non-adherence exacerbates symptoms
- More manic episodes lead to more manic episodes
- More major depressive episodes lead to more major depressive episodes
- Over time disorders tend to become
  - More severe
  - Treatment resistant

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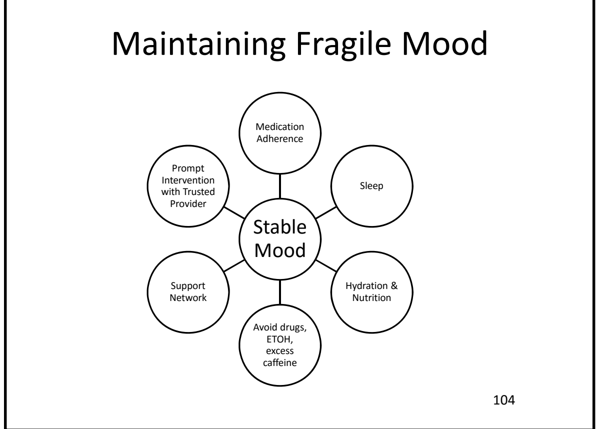
Positive Outcomes

- Goals
  - Optimize function
  - Maintain stability
  - Adherence to medication regimen
  - Instill hope
  - Self-advocacy
- Recovery Journey
  - Accepting set backs
  - Becoming one's best self
  - Changing the world

103

Maintaining Fragile Mood



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Adjunct: Sleep

- Critical in stabilizing psychiatric disorders
- Sleep goals
  - Adult: 8-9 hours/night
  - Teen: 9-10 hours/night
  - Child: 10+ hours/night
- Sleep hygiene
  - Example of handout: WebMD Medical Reference in collaboration with *http://www.webmd.com/content/Article/105/107668.htm*
- Should be restful and restorative
- Resources
  - American Sleep Association
  - American Academy of Sleep Medicine
  - National Center on Sleep Disorders Research

105

Adjunct: Hydration & Caffeine

Water

- Extremely important—goal at least 64 ounces/day
- Make it appealing—add mint or citrus slice

Caffeine

- Highly addictive—most patients unwilling to give it up
- Mixed effects—increases anxiety but perks up depressed mood
- Too much can destabilize bipolar disorder or psychotic disorder
- Disrupts sleep late in day—even if patient thinks they slept well
- Rule of thumb: "1 or 2 finished by 2" (1-2 caffeinated drinks, finished by 2 p.m. to avoid sleep disruption; energy drinks = 2)
- Taper slowly for success
  - Drop latest serving (8 oz) of caffeinated drink
  - Maintain that for 4-5 days
  - Replace caffeinated drink with a glass of water (until 64 oz/day)
  - Continue doing that until off caffeine or at "1-2 finished by 2"
  - Used successfully by patients tapering from up to 17 servings per day
  - Abrupt caffeine withdrawal can cause headache and agitation

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Adjunct: Exercise

- 30 minutes a day, 4-5 days/week
- Walking
  - In a safe place
  - Preferably with family members
  - Early morning or late afternoon on warm days
- Swimming
- Start small and work up
  - Some patients will only be able to walk to the mailbox
  - Celebrate gains
  - Accountability
  - Stay safe—important consideration for many psychiatric patients

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Optimizing Prescribing

Problem: Inundated with literature (Bastian, Glsziou & Chambers)

- 75 reports of trials published per day
- 11 systematic reviews of trials per day

Solution: Find and use reliable resources

- Government sites (NIMH, SAMHSA, CDC, FDA)
- International organizations (WHO)
- Systematic reviews (Cochrane)
- Algorithms (TX Algorithm Project, VA/DoD)
- Patient education (Mayo Clinic, Drugs.com)
- Psychopharmacology (Stahl, Lexi-Comp, Epocrates)

Bastian, H., Glasziou, P., Chalmers, I (2010). Seventy-five trials and eleven systematic reviews a day: How will we ever keep up? PLoS Medicine 7(9): e1000326.doi:10.1371/journal/pmed.1000326

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Referring for Medication Management

Refer for psychiatric medication management when

- The patient's psychotropic medication management is beyond
  - Scope of practice
  - Competence
  - Confidence
- Policies or procedures of your practice/facility specify
- Patient will need extensive education about medications or disorder that cannot be accomplished in primary care

Consider referring when

- Polypharmacy is required
- Patient has atypical presentation
- Failed drug trials with condition unstable or worsening
- Patient requests psychiatric specialist

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RESOURCES

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Resources

- APA (2013). *Diagnostic and statistical manual of mental disorders, fifth ed*. Arlington, VA: American Psychiatric Association.
- Guess, K. (2008). *Psychiatric-mental health nurse practitioner review and resource manual, second ed.* Silver Spring, MD: American Nurses Credentialing Center.
- Pedersen, D. (2005). *Psych notes: Clinical pocket guide.* Philadelphia: F.A. Davis Company.
- Sadock, B. & Sadock, V. *Kaplan & Sadock's synopsis of psychitary, tenth ed.* Philadelphia: Lippincott Williams & Wilkins.
- Stahl, S. (2008). *Stahl's essential psychopharmacology: Neuroscientific basis and practical applications, third ed.* New York: Cambridge University Press.
- Stahl, S. (2011). *The prescriber's guide: Stahl's essential psychopharmacology, fourth ed.* New York: Cambridge University Press.

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