NORTHWEST GERIATRIC EDUCATION CENTER

Helping older adults live healthier, happier lives since 1985.

Spring 2013 Geriatric Health Lecture Series on Alzheimer's Disease and Related Issues

Bipolar Disorder in the Elderly

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Learning Objectives

By the end of this lecture, you should be able to:

- Describe the criteria for diagnosis of bipolar disorder and differential diagnosis.
- Discuss the longitudinal course of bipolar disorder and its unique aspects in the elderly.
- List the major pharmacologic treatment options for mania and for bipolar depression.

A non-508-compliant streaming video of this lecture and related self-test is available on the NWGEC website (Bipolar Online Lecture, http://nwgec.org/educational-opportunities/lectures/online-videos/bipolar-disorder).

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Bipolar Disorder in the Elderly

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May 21, 2013

Overview

- Context and Epidemiology
- Diagnosis and Subtypes
- Association with Dementia
- Treatment
- Summary

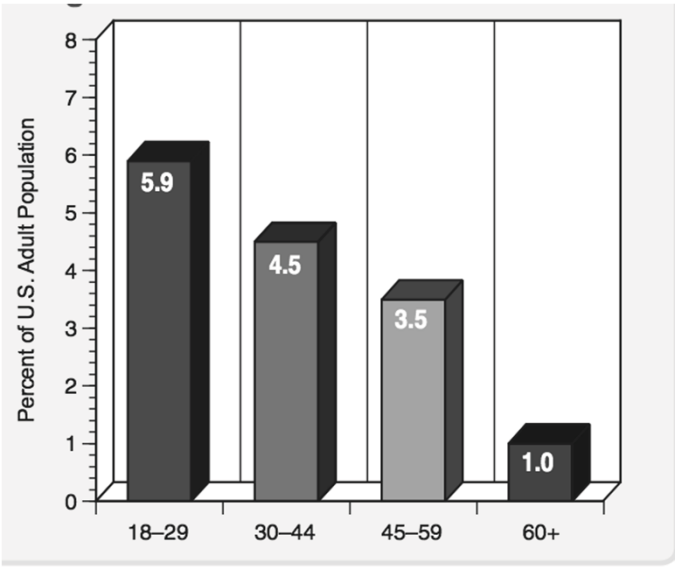
Significance and Context

- Bipolar disorder w/significant disability
- Elders: treatment complex
  - Medical comorbidity
  - Increased risk for adverse drug side-effects
- Few studies in elderly
  - Most guidelines based on mixed-age studies

EPIDEMIOLOGY

- Lifetime prevalence 4%
- Equal prevalence males and females
- Less common in the elderly
- Geriatric Bipolar Disorder
  - 0.1-1.0% Community
  - 10% in hospitals, Long term care
    - » RC Kessler et al, Arch Gen Psych 2005
    - » J Unutzer et al, Psychiatr Serv 1998
    - » RN Hirshfiek J Clin Psych 2003
    - » A Vasudev Maturitas 2010

Bipolar Disorder Prevalence



Kessler et al., Arch Gen Psych 2005 62(6) 593

Definition of Bipolar Disorder

- Mood disorder with alternating mood states of depression or mania
- Depression: criteria for Major Depression
- Mania: at least 4-7 days
- Mixed state: both depressed and manic
  - depressed, SI, energized, agitated

Bipolar-Depressed State

- Depressed mood, fatigue, guilt
- Sleep and appetite increased
- More episodes of depression than mania
- Earlier onset than unipolar depression
- Severe: psychotic or catatonic

Bipolar-Manic State

- Mood: Expansive, euphoric, irritable
- Other symptoms: require 3-4

  Energized

  Decreased sleep

  Talkative, Racing thoughts, distractible

  Grandiose,

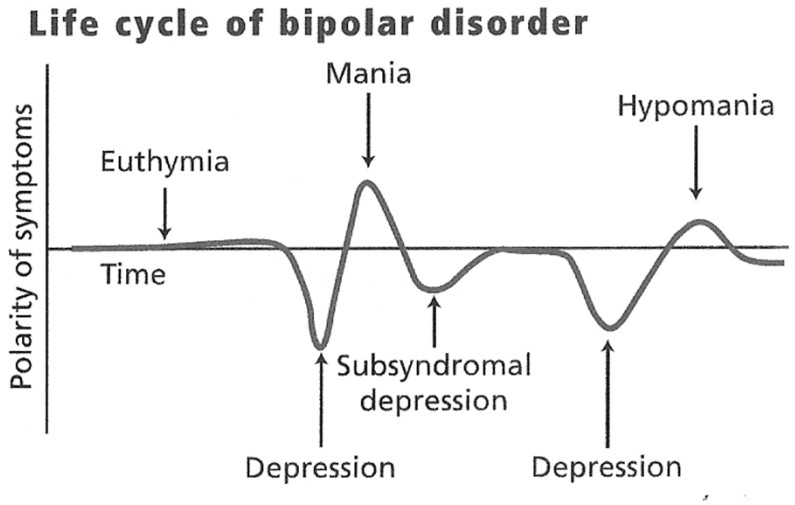
  Increased activities

  Impulsive with money, sexual, travel

  Psychotic if severe–religious delusions, grandiose delusions, paranoia

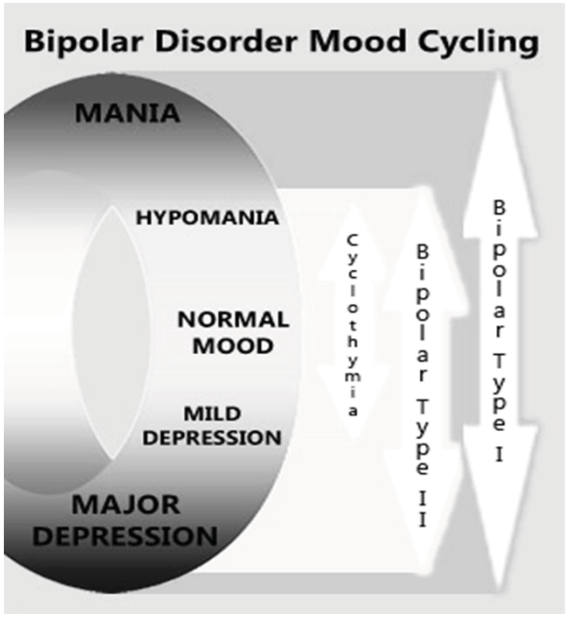
  :

From Muzina DJ et al. Clevel Clin J Med, 2007 72(2):89-99



Bipolar Types

- Bipolar I
  - Severe mania and depression
- Bipolar II
  - Mild mania, Hypomania and depression
- Rapid cycling: >=4 episodes/yr
- Late onset: Onset age >= 50



Clues that Suggest Bipolar Disorder

- Early age onset of depression
- Family history of bipolar disorder
- More functional impairment, less well
- Refractory, repeated depression with ↑sleep, appetite, fatigue, SAD
- Switch to mania with antidepressants
  - » Muzina 2007

Bipolar subtype by onset

- Late onset (>50 yrs old)
  - Often presents with mania
  - ↑neurologic illness, white matter lesions
  - Risk for stroke and dementia
- Early onset (<50 yrs)
  - Stronger family history of bipolar disorder
  - More substance use 40% young ~ 15% elders

A. Vasudev Maturitas, 2010

Case: Early onset bipolar disorder

- Dr M retired professional, now disabled
- Alcohol dependence for many years
- Noncompliant with medication for first 30 yrs
- Numerous episodes of mania and depression
- Refractory mania with persistent psychosis and dementia
- Homeless, hoped to be institutionalized

Case: Late onset bipolar disorder

- Ms M was a retired teacher 66 yo woman
- History of depression, anxiety, no mania
- Developed pressured speech, numerous projects, insomnia, increased spending
- Refused treatment
- Committed as gravely disabled-released
- Travelled to Southwest
- Incarcerated and recommitted

Medical Causes of Manic States

Focal: Right side CNS lesion

Frontotemporal Dementia

Seizures: temporal lobe

Neurosyphillis, HIV encephalopathy

Multiple sclerosis

Hyperthyroid

Pheochromocytoma

Lupus

Medications that may cause Mania

Steroids

Cholinesterase Inhibitor

Bronchodilators, theophyline

Amphetamines, cocaine

Dopamine agonists, L-DOPA

Stimulants, Caffeine, Pseudophed

Antidepressants

Case

- Mr A was 61 yo man
- Admitted for chemotherapy for brain CA
- Received high dose steroids
- Increased irritability, pressured speech, insomnia, paranoia, grandiosity
- Threatened staff and AMA discharge
- Responded to DC of steroids and rx with antipsychotics

Medical Illness in Elderly with Bipolar Disorder

- Average 3-4 medical conditions
- Diabetes II (33%),
- Respiratory
- Cardiovascular
- Cognitive disorders 4-19%

SV Lala J Geriatr Psych Neruol 2012 25:20

Mood Episodes Increase Risk for Dementia

- Severe mood episodes and dementia risk
- All hospitalizations 1970-1999 in Denmark
- Approx 23,000 pts, ~ 4000 bipolar pts
- 60-68% female, ages 52-58
- Mania: 6% increase dementia/episode
- Depression: 13% increase dementia/episode

J Neurol Neurosurg Psychiatry 2004;75:1662–1666.

Cognition and Bipolar Disorder

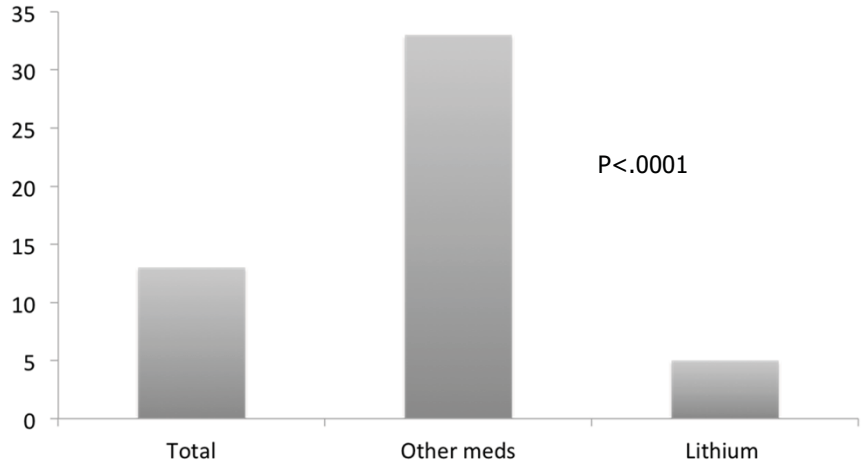
Variables	Bipolar Disorder (N = 59), N (%)	Comparison Group (N = 59), N (%)	χ^2	p
Cognitive functioning				
Abnormal education-adjusted MMSE scores	19 (32.2)	2 (3.4)	16.74	<0.0001
Medical comorbidity				
Hypertension	26 (44.1)	41 (69.5)	7.50	0.006
Previous diagnosis or awareness of hypertension	14 (23.7)	30 (50.9)	7.26	0.007
Diabetes mellitus	16 (27.1)	8 (13.6)	2.50	0.113
Atopic diseases	12 (20.3)	2 (3.4)	5.79	0.019

Tsai, Am J Gerait Psych 2009

Dementia and Lithium

- Does lithium affect cognitive function
- Bipolar ds, mean duration>25 years
- 60+, current euthymic and treated
- Prevalent Alzheimer's 13%
- Lithium compared to other treatment
- Mean lithium treatment 6 yrs

Alzheimers Disease and Lithium Treatment



Nunes et al, BJp 2007; 190:359

Lithium Associated with Decreased Risk of Dementia

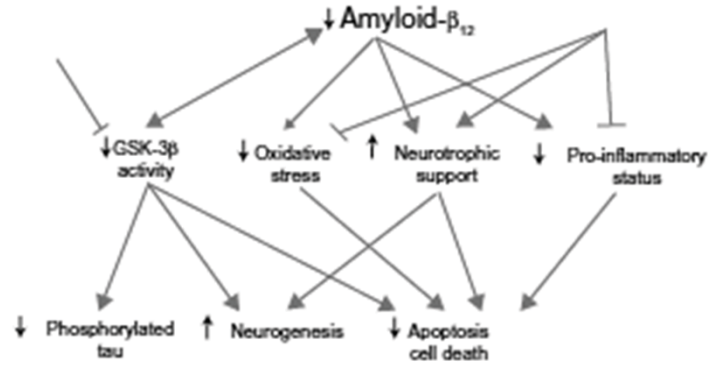
Number of prescriptions	Lithium RR (95% CI)	Anticonvulsants RR (95% CI)
1	1	1
2–4	0.46 (0.21–1.01)	1.49 (0.53–4.19)
5–9	0.38 (0.16–0.86)	1.81 (0.66–5.01)
10–19	0.39 (0.19–0.81)	2.24 (0.86–5.81)
≥ 20	0.44 (0.23–0.85)	1.05 (0.38–2.93)

- 10 yrs of data Danish medical registry 1995-2005
- Hospital dx bipolar disorder
- Approximately 5000 pts, age 52, 60% female
- Lithium-50% Mood stabilizers-37%

Kessing et al, Bipolar ds 2010 12:87

Lithium Neuroprotective Effects

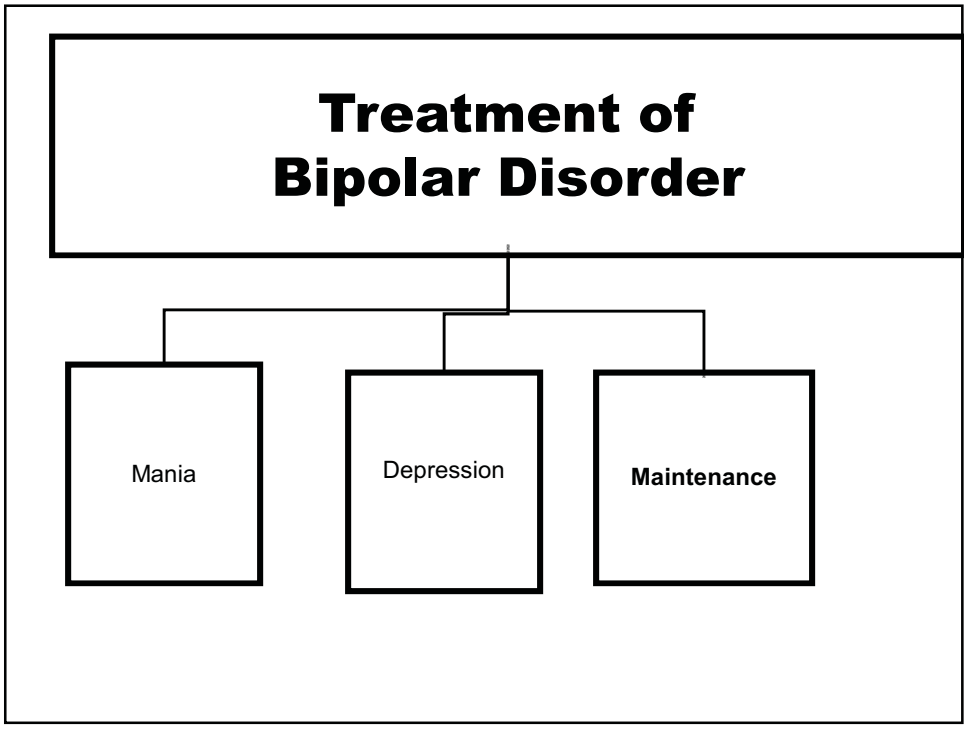
Potential targets of lithium neuroprotective effects

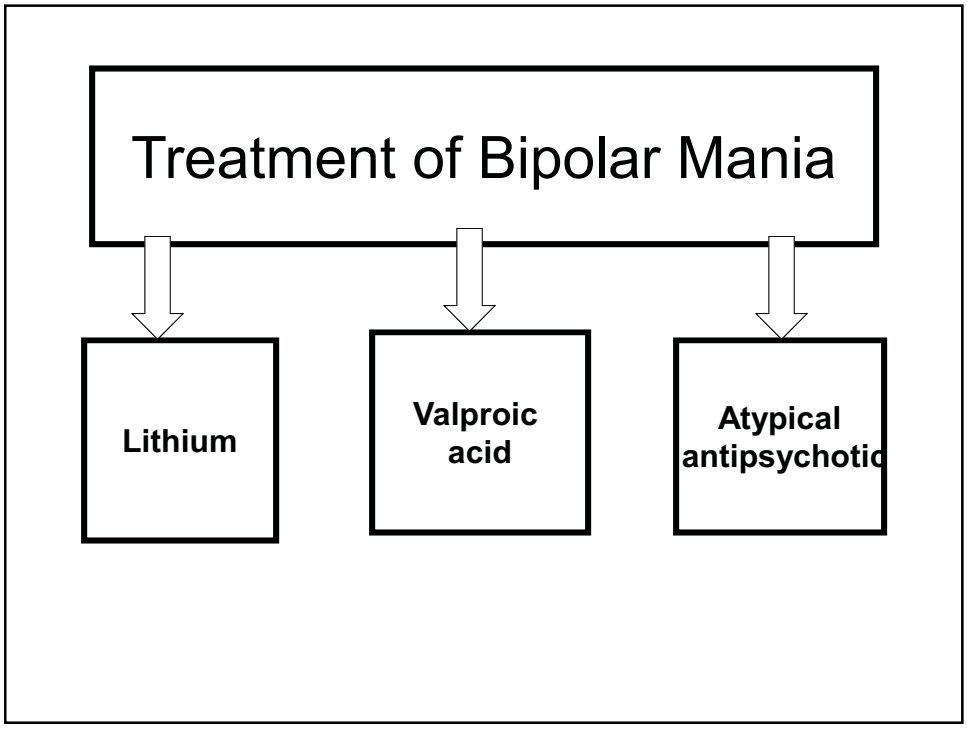


BS Diniz 2013, Neuropsych Dx and Treatment

General Treatment Issues

- Collaborative Model
- Educate-compliance
  - More episodes→ severe, refractory disorder
- Monitor: early signs of relapse/communicate
- Regular schedule
  - Insomnia→mania
- Collateral information from family
  - (SI, substance, function)





Treatment of Mania in the Elderly

- Valproic acid
  - Less neurotoxicity
  - Mixed episode, rapid cycling
- Consider lithium if prior use of it
- Atypical antipsychotic: if psychotic
  - Or need rapid response
- Neurologic illness: worse response
- Ensure Sleep

Lithium

- Indications: Mania or depression
- Benefits: Decr Suicide
- Side-effects:
  - GI, diarrhea, tremor, EPS acne, bradycardia
  - Renal and thyroid

Lithium Clearance

- Renally excreted
- Increased Lithium/ Toxicity levels with:
  - NSAIDS
  - Diuretics: HCTZ
  - ACE inhibitors
  - Low sodium diet
  - Age: increased brain/sera levels

Lithium Toxicity

- NARROW therapeutic index
- Symptoms of toxicity:
  slurred speech, ataxia, tremor, diarrhea, delirium

**Toxicity may occur at therapeutic levels
Levels young 1.0-1.5
Levels Elderly 0.4-0.8

Valproic Acid

- Indications: Mania
- More effective than Lithium for mixed mania and rapid cycling
- Side-effects: sedation, ↑weight, hair loss, liver, intention tremor, ↓plts ↑ ammonia
- Less discontinuation than lithium

Valproic Acid Use in the Elderly

- Well tolerated in elderly
- No controlled studies for mania in elderly
- Extrapolated from mixed age studies
- Mania: start 250 BID
- Mania with dementia:
  - 125 BID, increase slowly by 125 qd

Valproic Acid Metabolism

- Metabolism: hepatic
- ↓Clearance in the elderly by 40%
- Valproic acid drug interactions
  - ↓ dilantin levels
  - ↑ lamotrigine levels
- Adjust level to therapeutic response,
- In mania level ~ 65-90 (same as young)

Caution: Valproic Acid

- Encephalopathy,ammonia levels
- Free serum valporaite
- Proteint binidng
- Asa, warfarin, dig, dilantin

Adverse Events with Lithium and Divalproex in Elderly NH Patients

Morbidity	Lithium Carbonate (n = 28)	Divalproex Sodium (n = 44)
Toxicity and/or dehydration*	19	3
MICU hospitalizations	6	0
Leukocytosis†	7	0
Thrombocytopenia†	0	4
Hepatotoxicity†	0	3
Total occurrences	32	10

MICU = medical intensive care unit.
*As evidenced by an increased serum level over therapeutic levels (lithium, 0.6 to 1.2 mEq/L; divalproex, 50 to 120 µg/mL) and/or clinical signs or symptoms.
†Indicated by abnormal values on serum test results. Conney Am J Managed Care 1999, 197

Cost Component	Lithium Carbonate (US$; n = 28)	Divalproex Sodium (US$; n = 44)
MICU (1-week admission)	12,299*	0
ECG monitoring	240	0
Intravenous fluid rehydration	31†	0
Laboratory tests	327‡	0
Emergency measures for toxicity	13§	0
Cost per patient	12,910‖	0
Total costs	77,462¶	0

*MICU hospitalization for 1 week at $1171 per day plus overhead costs of $586 per day, for a total cost of $1757 per patient per day.
†Intravenous fluid rehydration with 23 bags of normal saline plus 20-mEq potassium chloride per week.
‡Lithium level on average 6 times per week; complete blood cell count with differential on average 9 times per week; Panel 7, on average 14 times per week; urinalysis, on average 4 times per week.
§Gastric lavage and activated charcoal intervention.
‖Per 1 MICU hospitalization.
¶Total for all 6 MICU hospitalizations.

Case Lithium toxicity

- Mr. G treated with lithium
- Rxed ibruprofen after dental produre
- Developed N&V, tremor, diarrhea
- Presented to ED and discharged
- Presented to another ED next day
- Severe lithium toxicity
- Residual
  - Extended hopsitalization and rehab
  - Dysphagia, ataxia, memory loss

Atypical Antipsychotics

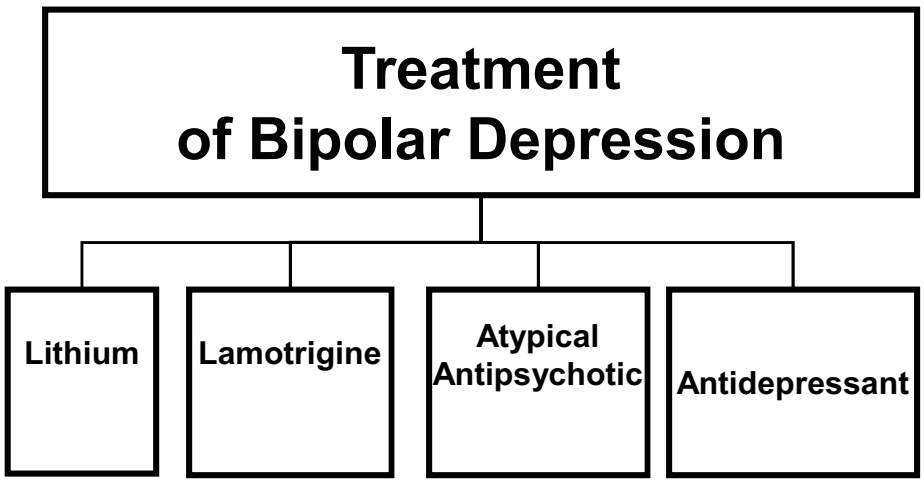
- FDA approved for mania
  - Olanzapine (zyprexa)
  - Risperidone (Risperidol)
  - Aripiprazole (Abilify)
  - Quetiapine (Seroquel)
  - Ziprasidone (Geodon)
- Europe: first line for mania, US -mood stabilizers first line

Atypical Antipsychotics

	Benefits	**Adverse**	**Dose mg**
Quetiapine (Seroquel)	Least EPS Sedating	Postural BP	12.5-200
Risperidone (Risperidol)	More potent ~Metabolic	EPS Postural BP	0.5-2.0
Olanzapine (Zyprexa)	Low EPS Low Postural BP	Metabolic Weight	5-10
Aripiprazole (Abilify)	Low sedation Low metabolic	Akathisia Anxiety	10-15
Ziprasidone (Geodon)	Low sedation Low metabolic	Qtc 20 msec	20 BID

Antipsychotics and Mortality

- ↑Mortality and stroke in dementia pts
  - FDA advisory 2005
- Review 17 placebo studies with atypicals
  - Mortality:HR 1.6, absolute risk 1- 2%
  - CVA, absolute risk 1%
- Recent studies: Increased mortality risk with typical antipsychotics

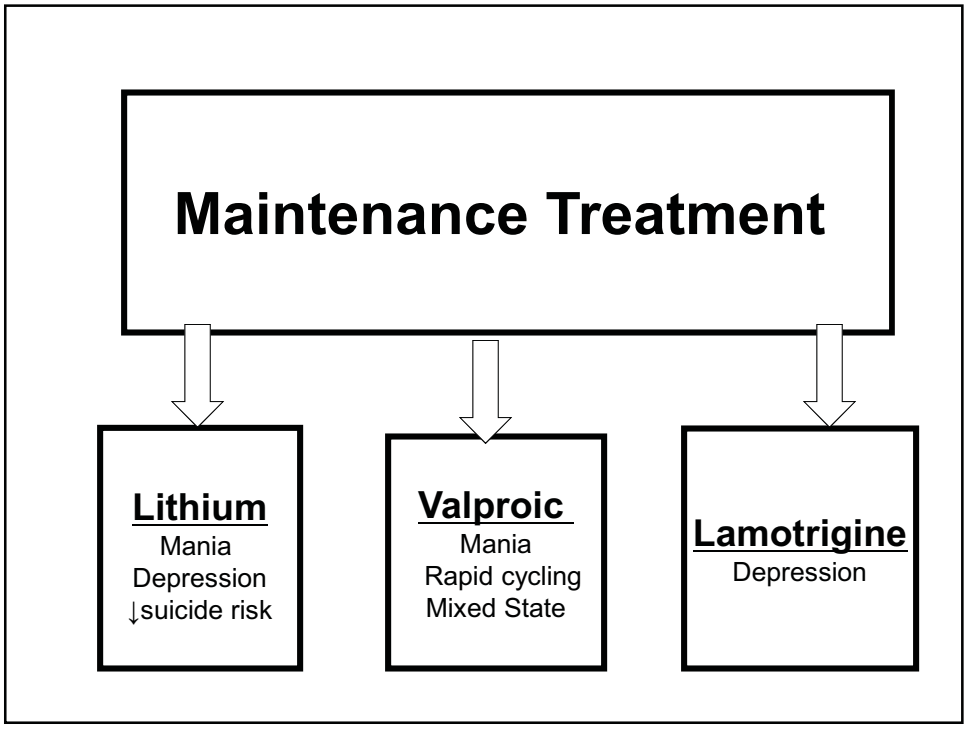


Bipolar depression and antidepressants

- Depression is more common, refractory
- Mood stabilizers: if severe symptoms
  - Lamotrigine: slow titration upward
  - Lithium: hx of lithium rx, suicide prevention
- Antipsychotics: olanzapine, quetiapine
- Antidepressants → switch but risk less in elderly

Lamotrigine

- Indications: Bipolar depression
- Side effects: headache, nausea, rash,
- Lamotrigine: Start 25 mg increase slowly
  - (12.5 mg q/wk)
  - Target dose in Elderly 75-200 mg qd
  - COMPLIANT PT OR TOO RISKY
- Stevens Johnson syndrome
  - 1% of patients: ↑ high and rapid dose
  - Halve dose if given with valproic acid



Maintenance Treatment

- Continue mood-stabilizers indefinitely
- Decrease relapse and severity
- Prevent depression: Lamictal and Lithium
- Prevent mania: Lithium and Valproic acid
- Combination rx if needed
- Taper after stable for 6-12 months

Treatment Summary

- Bipolar depression
  - Lamictal or lithium
  - Lamictal or lithium or VPA + antidepressant
  - If hypomania → stop antidepressant
- Mania in elderly, r/o neurologic disease
  - Valproic acid-better tolerated in elderly
  - Lithium-prior lithium and normal renal function
  - Antipsychotic- if psychotic symptoms, rapid rx

Resources for Education and Support

- An Unquiet Mind, by Kay Jamison, PhD
- Depression and Bipolar Support Alliance www.dbsalliance.org
- NAMI: National Alliance for Mental Illness www.nami.org

Conclusions

- Bipolar ds less common in elderly
- Late onset associated with neurologic illness
- Bipolar disorder associated with dementia
- Recommend chronic treatment- need to consider phase of illness