MOOD FLIPS and BAD TRIPS : WAYS OUT OF THE MAZE

Co-Occurring Disorder Conference

October 1, 2007

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“Face it Fred, you’re lost.”

WAYS OUT OF THE MAZE

- Me
- Me and my patient
- Me and my patient and his/her spouse/SO and his/her/their family and/or friends

WAYS OUT OF THE MAZE

- You (other treatment providers)
- You and your patient
- You and your patient and his/her spouse/SO and his/her/their family and/or friends

WAYS OUT OF THE MAZE

- Our patients' treatment team:
  - CDC (inpatient or outpatient CD treatment)
  - Therapists
  - Primary care providers
  - Specialists, inc. psychiatrist, PhD, ARNP, etc.
  - Agencies
    - – Community Mental Health Centers
    - – DSHS, ADATSA, etc.
  - Other

WAYS OUT OF THE MAZE

- "There are things I can't force. I must adjust. There are times when the greatest change needed is a change in my attitude." C. M. Ward

- "There is nothing about a caterpillar which suggests that it will one day become a butterfly."

  Buckminster Fuller

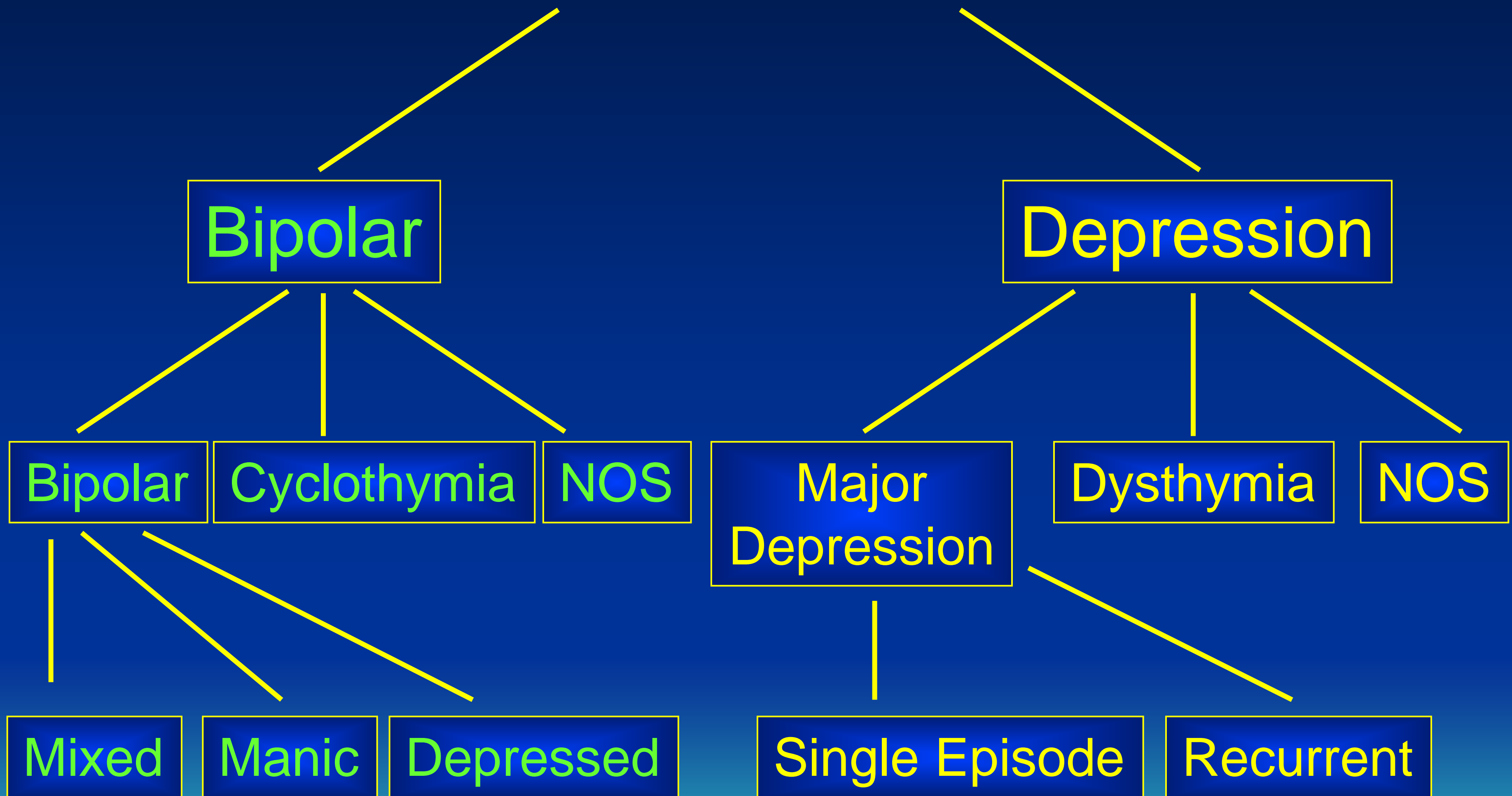
WAYS OUT OF THE MAZE

- Old way of helping these patients:
  - "When you are sober and clean for 3 months, then we'll prescribe psychotropic meds"
  - "When you are stable psychiatrically, then we'll treat your SUD"

WAYS OUT OF THE MAZE

- Preferred way for most people with CODs:
  - Concurrent treatment
    - Preferably staff that are dually-trained
    - Ideally under the same roof

MOOD DISORDERS



American Psychiatric Association. *DSM-IV*. Washington, DC: APP;1994.

BIPOLAR TYPES

- Bipolar type I
  - At least one mania
- Bipolar type II
  - At least one hypomania
- Bipolar NOS
  - At least one mania or hypomania but insufficient duration for I or II

SCREENING TOOLS

- History from others who know pt well
- Studies to R/O organic cause
- Mood Disorder Questionnaire

MANIC EPISODE

- Elevated, expansive, or irritable mood for ≥1 wk, *plus* ≥3 of the following:
  - Inflated self-esteem or grandiosity
  - Decreased need for sleep
  - Pressured speech
  - Racing thoughts/flight of ideas
  - Distractibility
  - Psychomotor agitation/increase goal-directed activity
  - Excessive involvement in high-risk activities

American Psychiatric Association. *DSM-IV.* Washington, DC: APP;1994.

MANIA: DIGFAST

- Distractibility -- poorly focused
- Insomnia -- decreased need for sleep
- Grandiosity -- inflated self-esteem
- Flight of ideas -- racing thoughts
- Activities -- inc'd goal-directed activities
- Speech -- pressured or more talkative
- Thoughtlessness -- risk-taking behaviors

www.medscape.com **(Mood change plus 3+ for 1 wk +)**

HYPOMANIA

- Elevated, expansive, or irritable mood, lasting ≥ 4 days, *plus*
- ≥ 3 symptoms of mania that
  - Are *not* severe enough to impair functioning markedly
  - Do *not* necessitate hospitalization
  - Are *not* accompanied by psychotic features
- Produces enough change to be noticed by others

American Psychiatric Association. *DSM-IV.* Washington, DC: APP;1994.

HYPOMANIA < 4 DAYS

- Duration criteria is ≥ 4 days
- Many people have hypomanic symptoms of sufficient severity but insufficient duration….such as 2 to 3 days
- Bipolar Disorder, Not Otherwise Specified

BIPOLAR DISORDER, DEPRESSED

- Distinct mood change **OR** loss of interest in things that used to give interest or pleasure PLUS
- Daily or near daily for at least 2 weeks PLUS
- A change in at least 4 out of these 7 baseline features:
  - Sleep; Appetite; Concentration; Energy; Guilt; (feelings of H/H/W); Suicidal thoughts; Psychomotor

BIPOLAR DISORDER, DEPRESSED

- AND causes significant distress or impairment in function at work or home or school
- AND is not due to another medical disorder (drug/alcohol, thyroid, meds, etc)
- AND episodes of hypomania or mania
  - Bipolar type I: mania; type II: hypomania
  - Major Depression: Neither mania nor hypomania

BIPOLAR DEPRESSION WHY IS IT HARD TO DX ?

- Hypomanic and manic episode may go unnoticed by the patient
    - > 50 % have depression as 1st episode
- Hypomania or mania may be difficult to recognize or recall for patients
    - Most enjoy the hypomania, great productivity so hard to see it as a “problem”
- Studies show ~ 75% of mood states are depressed

BIPOLAR DISORDER, MIXED

- Criteria met for both manic episode + major depressive episode for ≥1 week
- Symptoms
  - Are sufficient to impair functioning ***OR***
  - Necessitate hospitalization ***OR***
  - Are accompanied by psychotic features

American Psychiatric Association. *DSM-IV.* Washington, DC: APP;1994.

RAPID CYCLING

- 4 or more episodes of depression, mania or hypomania in previous 12 months

- Episodes are demarcated by a switch to the opposite polarity or by a period of remission

- Often triggered by antidepressants (esp. TCA though any antidepressant can do it)

American Psychiatric Association. *DSM-IV*. Washington, DC: APP;1994.

RAPID CYCLING

- 13 - 20% of all bipolar patients
- Initial onset 20%, later onset 80%
- Predominantly in females
- Associated with increased thyroid dysfunction

WHAT TO ASK

- Precipitant ?
  - (loss / threat of loss)
- Duration of episode
  - Longest ever
  - Shortest ever
  - Average
- Frequency/intensity
  - Tends to increase

WHAT TO ASK

- Do you have days of energy or ideas that come and go *abruptly*
- Do others notice the change in your mood or energy level ?
- During these “up times” do you do things that you later regret ?

Mood Disorder Questionnaire

Has there ever been a period of time when you were not your usual self and…

… you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?

… you were so irritable that you shouted at people or started fights or arguments?

… you felt much more self-confident than usual?

… you got much less sleep than usual and found you didn't really miss it?

… you were much more talkative or spoke much faster than usual?

… thoughts raced through your head or you couldn't slow your mind down?

Mood Disorder Questionnaire

… you were so easily distracted by things around you that you had trouble concentrating or staying on track?

… you had much more energy than usual?

… you were much more active or did many more things than usual?

… you were much more social or outgoing than usual; for example, you telephoned friends in the middle of the night?

… you were much more interested in sex than usual?

… you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?

… spending money got you or your family into trouble?

Mood Disorder Questionnaire

If you checked YES to more than one of the above, have several of these ever happened during the same period of time?

How much of a problem did any of these cause you – like being unable to work; having family, money, or legal troubles; getting into arguments or fights? (Please circle one response only)

No problem **Minor problem** **Moderate problem** **Serious problem**

MDQ Case Descriptions

- MDQ Positive Cases
  - 7 or more symptoms and
  - Co-occurrence and
  - Moderate to severe impairment

- MDQ Negative Cases
  - Less than 5 symptoms or
  - 5 or more symptoms without both co-occurrence and moderate to severe impairment

MDQ NEGATIVE
(not Bipolar Disorder, type I)

- May represent :
  – Bipolar Disorder, type II or NOS
  – Cyclothymic Disorder
  – Other causes of mood swings
    - Metabolic; Structural lesions in brain; Infectious; medications (esp. Prednisone > 40 to 60 mg/d)
  - Substance-Induced Mood Disorder, cyclic

Manic Episode: Differential Diagnoses

Differential diagnosis	Consider if . . .
Mood disorder due to a general medical condition	• **Major medical condition present** • **First episode at >50 years of age**
Substance-induced mood disorder	• **Symptoms in context of intoxication or withdrawal** • **H/O treatment for depression**
Hypomanic episode	• **Mood disturbance not severe enough to require hospitalization or impair functioning**
Mixed episode	• **Manic episode and major depressive episode in 1 wk**

American Psychiatric Association. *DSM-IV.* Washington, DC: APP;1994.

Manic Episode: Differential Diagnoses

Differential diagnosis	Consider if . . .
ADHD	• **Early childhood mood disturbance onset** • **Chronic rather than episodic course** • **No clear onsets and offsets** • **No abnormally elevated mood** • **No psychotic features**

American Psychiatric Association. *DSM-IV.* Washington, DC: APP;1994.

I've gotta cut back on the caffeine

- www.dbsalliance.org

COMMONLY ABUSED DRUGS

- Alcohol
- Marijuana
- Opiates
- Cocaine, meth and other stimulants, including caffeine
- Cigarettes / Nicotine
- Benzodiazepines and barbiturates
- Hallucinogens
- Inhalants
- Rave drugs
- _______________

WHAT IS ONE DRINK ?

- 12 grams of pure alcohol

= one 12 oz beer

= one wine cooler

= one 5 oz glass wine

= 1.5 ounces of distilled spirits
(a jigger, vs. shot = 1 oz)

ALCOHOL / DRUG HISTORY

- Age 1st drink / use
  - Amount consumed / used
- Last intoxication w alcohol; last drug use
  - Amount able to "hold" w/o gross impairment
  - ? Increased tolerance
- Episodes of loss of control and what was done to contain or reduce future episodes
  - ? Success of control efforts ?

ALCOHOL / DRUG HISTORY

- Consequences
    - Self
    - Relationships
    - Employment
    - Financial
    - Legal
        - DUI, DIP, how many should have had ?
- Is your alcohol / drug use helping you ?

QUESTIONS TO ASK

- Have you, or people who care about you, been concerned about your alcohol and/or drug use ?
- What is it about your use or your behavior when you use that concerns you / them ?
- Alcohol/drugs to prolong the “ups” or to reduce the “downs”

DRUGS AND ALCOHOL

- Anything that causes a problem, is a problem
  - If your alcohol or drug use causes you problems, then you have an alcohol and/or drug problem **PLUS** whatever problems the alcohol and/or drugs caused you

CHEMICAL DEPENDENCE

- 3 C ' s :
  - C ompulsive Use
  - Loss of C ontrol
  - C ontinued use despite adverse consequences

SUBSTANCE-INDUCED MOOD DISORDER

- Mood changes due to direct or indirect effects of drugs and/or alcohol in the brain
- Different from mood variability seen in the first several weeks to months of recovery from SUD
- Often requires medication and concurrent mental health tx and usual SUD tx

ABSTINENCE

- Staying “clean and sober” is no guarantee that problematic mood disruptions will go away
- Untreated problematic mood disruptions will undermine effective treatment of the SUD
- Cannot get full benefit of treatment of mood disorder if person continues to drink or use

(IDEAL) OBJECTIVE

- Differentiate:

  - Bipolar Disorder

    from

  - Substance-induced mood disorder, cyclic

    from

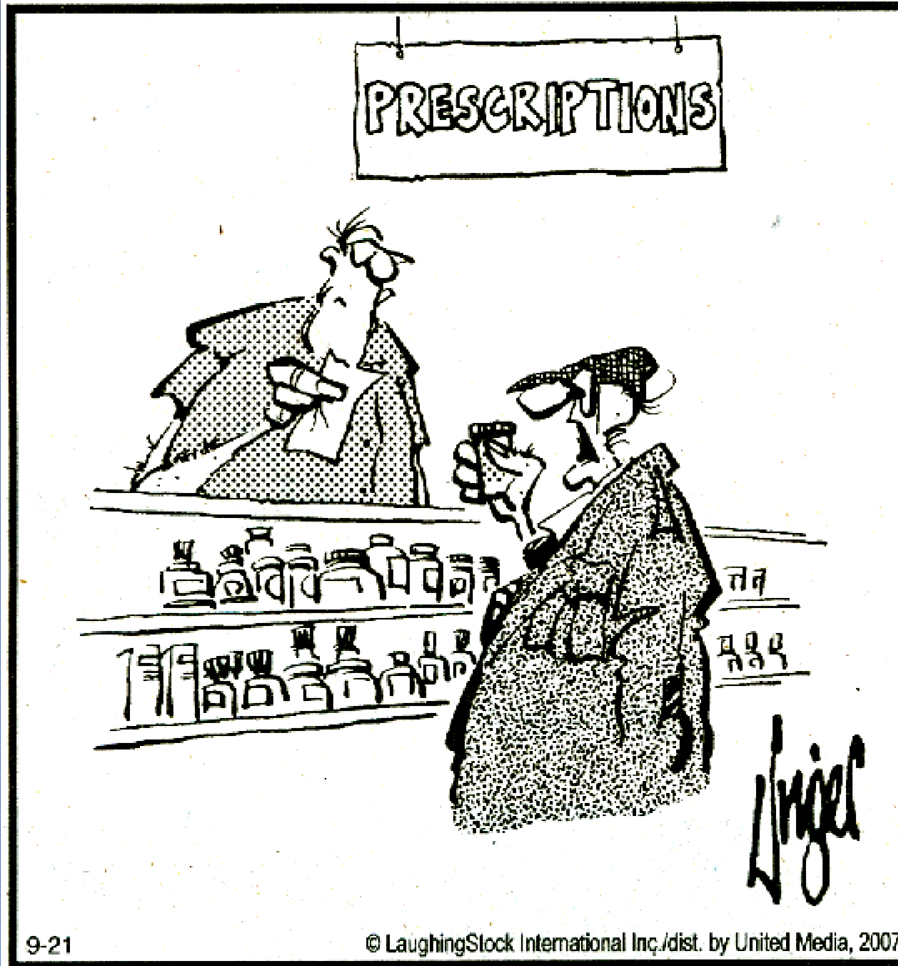
  - Mood swings of other etiologies

HAS BD AND SUD: NOW WHAT ?

- Is patient Safe ?
  - Assess risks:
    - Suicide; homicide; self-care; shelter; support
- Is patient Sane ?
    - Any impairing psychotic symptoms
- Is patient "Sober and clean ?"
    - Encourage / motivate ideal of abstinence
- Is patient Stable ?

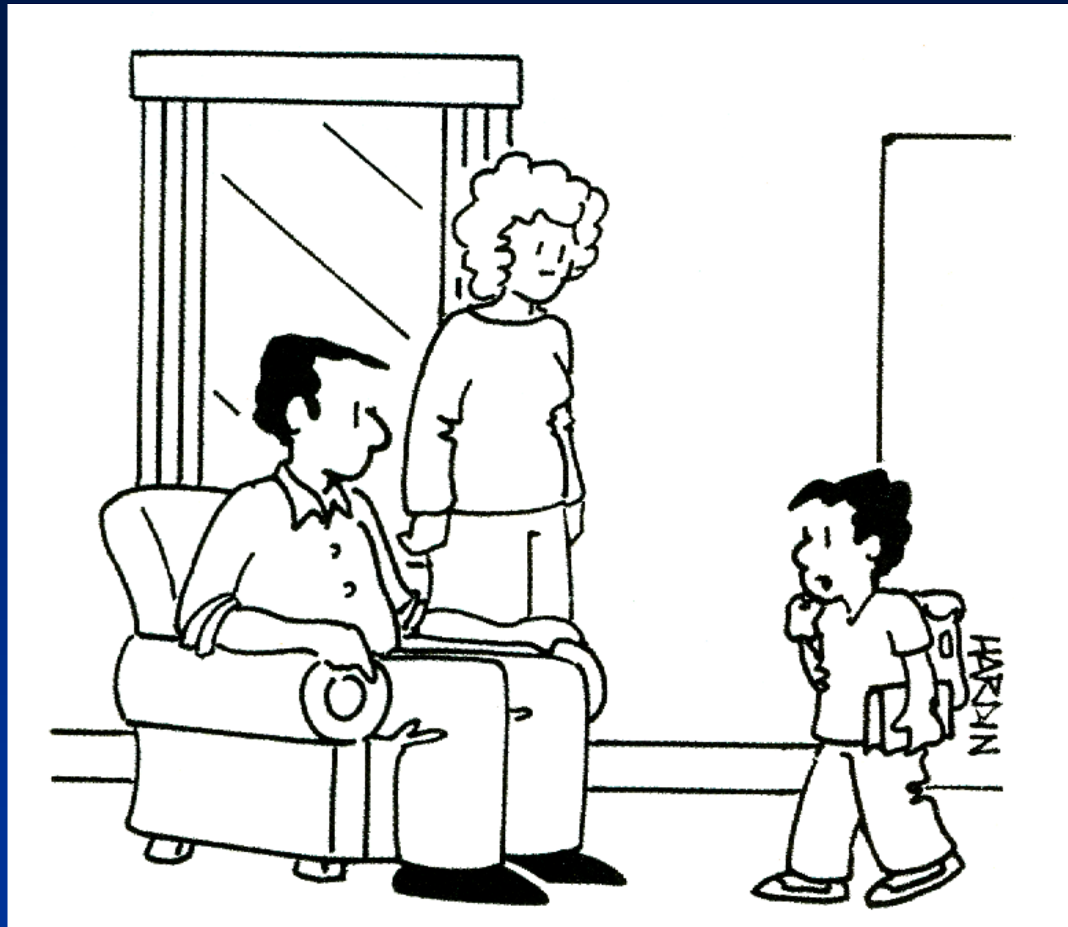
TREAT IMPAIRING SYMPTOMS

- Mood stabilizing medication
- Antipsychotic medication
  - Atypical vs. Conventional
- Combination



"Are there any side-effects to these besides bankruptcy ?"

“I only smoke now so that I can sue someone for it later.”



“Boy, what a depressing day. We studied hereditary.”

SPECIAL TREATMENT CONSIDERATIONS

- Psychiatric features
  - psychotic; catatonic; suicide, homicide, and violence; SUDs,
- Demographic & psychosocial factors
  - Gender, cross-cultural issues, geriatric patients
- Concurrent general medical conditions
  - HIV infection, other medical

Hirschfeld RMA et al. Am Journal of Psychiatry 2002;159(4):1-50.

TREATMENT GOALS

- Establish + maintain therapeutic alliance
- Monitor psychiatric and SUD status
- Provide patient and family education
- Anticipate stressors
- Enhance patient engagement in tx
- Promote patterns of regular sleep
- Identify new episodes early as possible
- Minimize functional impairments

Hirschfeld RMA et al. Am Journal of Psychiatry 2002;159(4):1-50

MOOD STABILIZERS

- Lithium *
- Divalproex *
- Lamotrigine *
- Equetro *
  (Carbamazepine ER)

* FDA-approved for use in Mania for Bipolar Disorder

(why this is important: Liability risk and “off-label” term used more and more by HIPs to deny coverage)

MOOD STABILIZERS

- Lithium carbonate
  - Eskalith, Lithobid, Lithium
- Divalproex
  - Depakote ER, Valproic acid
- Carbamazepine
  - Tegretol, Carbatrol ER
  - Equetra
- Oxcarbazepine
  - Trileptal

MOOD STABILIZERS

- Neurontin
  - Gabapentin
- Lamotrigine
  - Lamictal
- Topiramate
  - Topamax
- Tiagibine
  - Gabatril

MOOD STABILIZERS

- Keppra
  - Levetiracetam
- Zonegran
  - Zonisamide
- Newer ones

ATYPICAL ANTIPSYCHOTICS

- Clozaril (Clozapine)
- Risperidone (Risperdal)
- Quetiapine (Seroquel)
- Olanzapine (Zyprexa)
- Ziprasidone (Geodon)
- Aripiprazole (Abilify)
- Invega (Paliperidone)

CONVENTIONAL ANTIPSYCHOTICS

- Haldol (Haloperidol)
- Stelazine (Trifluoperazine)
- Thorazine (Chlorpromazine)
- Mellaril (Thioridazine)
- Trilafon (Perphenazine)
- Navane (Thiothixene)
- Prolixin (   )

ACUTE MANIA

- With or without psychosis: Meds of choice:

Lithium OR Divalproex

+

Risperidone OR Olanzapine

ARE BETTER THAN ANY ONE ALONE

MEDICATION COMBINATIONS

- Combinations often needed to achieve symptom control, if not remission, and to prevent future episodes

- Each additional medication increases risk of side - effects and/or med interactions

Hirschfeld RMA et al. Am Journal of Psychiatry 2002;159(4):1-50

LITHIUM

- Substantial clinical confidence by leading experts as first-line treatment for long-term management of mania.[1]
- Maintenance therapy with lithium can prevent or diminish the severity and intensity of subsequent episodes.

1. American Psychiatric Association. *Practice Guideline for Treatment of Patients with Bipolar Disorder* (Revision). April 2002;159(4):2-50.

LITHIUM

- Lithium still considered an effective agent even after 50+ years of clinical use
- In two 18-month, double-blind clinical trials, lithium was shown to be superior to placebo in the prevention of manic episodes.

Fieve R, Adler L, Allen M, et al. Lithium as a mood stabilizer: 50+ years later. Poster presented at: Annual Meeting of the American Psychiatric Association; May 18-23; Philadelphia, Pa.

LITHIUM FOR ACUTE MANIA

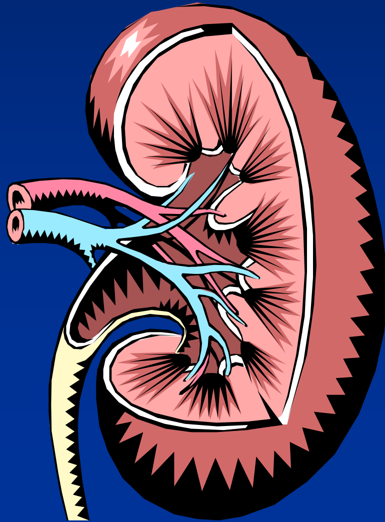
- Ability to tolerate Lithium is greater during acute mania and then decreases
- Start dose: 300 mg TID or once daily
- Serum lithium level:
  - 10 to 14 hours post-last dose
  - Q 4 - 7 days until level and clinical condition stable or until side-effects preclude higher dose

ESKALITH CR® (Lithium carbonate)

- Formulated to reduce variability of serum lithium levels
- Lower mean peak plasma lithium concentrations than other forms lithium
- Slows the rise to mean peak serum lithium levels
- Permits twice-daily dosing (about 12-hr intervals)

1. Kirkwood CK, Wilson SK, Hayes PE, Barr WH, Sarkar MA, Ettigi PG. Single-dose bioavailability of two extended-release lithium carbonate products. *Am J Hosp Pharm.* 1994;51:486-489. ; 2. Caldwell HC, Westlake WJ, Schriver RC, Bumbier EE. Steady-state lithium blood level fluctuations in man following administration of a lithium carbonate conventional and controlled-release dosage form. *J Clin Pharmacol.* 1981;21(2/3):106-109.

LITHIUM SIDE-EFFECTS



- Relative Contraindications:
  - Heart or kidney dis.
  - Diuretic use
  - NSAID use
    - Inc. Lithium levels 40 + %
  - Chronic diarrhea
    - Li caps vs. tabs
  - Psoriasis / acne

LITHIUM SIDE-EFFECTS

- Hand tremors
- Urinary frequency
- GI (nausea, diarrhea)
- Metallic taste
- Weight gain
  - 20 to 25 % gain weight, often > 10 to 15 lbs

LITHIUM DOSES LONG-TERM

- Varies from one person to another
- Often 900 - 1200 mg/day in divided doses
- Serum levels Q 2 - 6 mos. in uncomplicated cases during remission

ANTICONVULSANTS

- Except Lithium, all other mood stabilizing medications are anticonvulsants with shared side-effect risks:
  - Sedation, fatigue
  - Blurred / double vision
  - Balance problems, clumsy, falls
  - Cognition fuzziness, forgetfulness
- These can occur in therapeutic doses, too

DIVAPROEX (Valproic acid)

- Loading dose for middle aged folks:
  - 30 mg/kg body wt for 2 days, then
  - 20 mg/kg body wt
- Effective serum Depakene levels achieved in 3 days and well-tolerated

Keck, Allen et al. *Safety and Efficacy of Rapid-Loading Divalproex Sodium in Acutely Manic Bipolar Patients.* 1999, Poster Session 152nd Meeting APA

DIVAPROEX (Valproic acid)

- Alternate strategy:

  Take patient's weight in lbs, add "zero," and it converts to oral dose mg/day in divided doses (gives in-between dose relative to the mg/kg approach)

DIVALPROEX

- Baseline labs:
  - CBC with plts
  - AST (SGOT)
  - ? UDS
- Risk to liver and bone marrow, esp. 1st 3 m
- Lab monthly for 3 m, then Q6m
- Serum Depakene level 50 to 100
- Beware of med interactions

DIVALPROEX

- Divalproex
  - Peak onset 2 hours, half-life 10 hours
  - TID, sometimes BID dosing
- Depakote ER
  - Peak onset 5 hours; HL 9 to 16 hours but slow release is over 18 to 24 hours, so once daily dosing, AM or HS; steady state 3 days
  - More consistent efficacy through the day
  - Less side-effects (less peak and trough)

DIVALPROEX

- Oral BCPs:
  - – Best BCP with Divalproex is Tri-cyclen
  - – Best BCP with Lamotrigine is Ovral
    - Reference: Neurologist at Harborview Hospital

DIVALPROEX

- Divalproex may ↑ blood levels of:
  - Demerol (Meperidine; increases metabolites)
  - Within 10 days of adding Divalproex, may ↑ levels of:
    - Amitriptyline (Elavil)
    - Nortriptyline (Pamelor)
    - Possibly other tricyclic AD
      - Doxepin (Sinequan)
      - Imipramine (Tofranil)
      - Desipramine (Norpramin)
- Check med interaction lists (ePocrates), etc.

EQUETRO (CARBAMAZEPINE ER)

- Acute mania: 200 mg BID for 3 to 7 days, then 400 mg BID
  - Serum Tegretol levels not recommended
- Average effective dose 700 mg daily
- 100, 200, and 300 mg caps
  - Can be pulled apart and sprinkled on food
- Pre-treatment CBC w plts, AST
- Many med interactions

LAMOTRIGINE

- Dosing to minimize risk of skin rash
  - Weeks 1 - 2 25 mg QD
  - Weeks 3 - 4 50 mg QD
  - Week 5 100 mg QD
  - After week 5: increase by 100 mg/wk, up to 300 mg/day if clinically indicated
- Not for acute mania

Calabrese JR, et al. J Clin Psychiatry 2000; 61: 841-50.

LAMOTRIGINE

- FDA-approved June 2003 Bipolar Disorder
- Bioavailability not affected by food
- Half-life 24 hours, steady state 4 – 5 days
- No reports of weight gain

LAMOTRIGINE

- Metabolized mostly by glucuronic acid conjugaton, so: medication interactions:
  - Doubles Lamotrigine levels by ↓ clearance:
    - Divalproex (Depakote ER; Valproic acid)
  - Halves Lamotrigine levels by ↑ clearance:
    - Carbamazepine (Tegretol); Dilantin (Phenytoin); Phenobarbital (Phenobarb); Primidone (Mysoline)

LAMOTRIGINE

- Increases Lamotrigine blood levels:
  - Rifampin (Rifadin; anti TB)
  - BCPs
- No impact on Lamotrigine levels:
  - Lithium (and no impact on Lithium level)
  - Trileptal (Oxcarbazepine)
  - Keppra (Levetiracetam)

LAMOTRIGINE

- Dose strengths: all scored:
  - 25 mg (white)
  - 100 mg (peach)
  - 150 mg (yellow)
  - 200 mg **(blue)**
- Average effective dose: 200 mg, may need up to 600 mg daily (Dr. Bowden)

LAMOTRIGINE

- Risk of rash: same as any med when dosing protocol is followed
- See Doctor ASAP if following occur:
  - Skin rash w/wo hives
  - Fever
  - Swollen glands in neck
  - Painful sores in mouth or around eyes
  - Swelling of lips or tongue

LAMOTRIGINE and BCPs

- If add BCP, may ↓ Lamotrigine blood level
- If stop BCPs, may ↑ Lamotrigine level

- BUT no interference of contraception in women taking Lamotrigine

LAMOTRIGINE

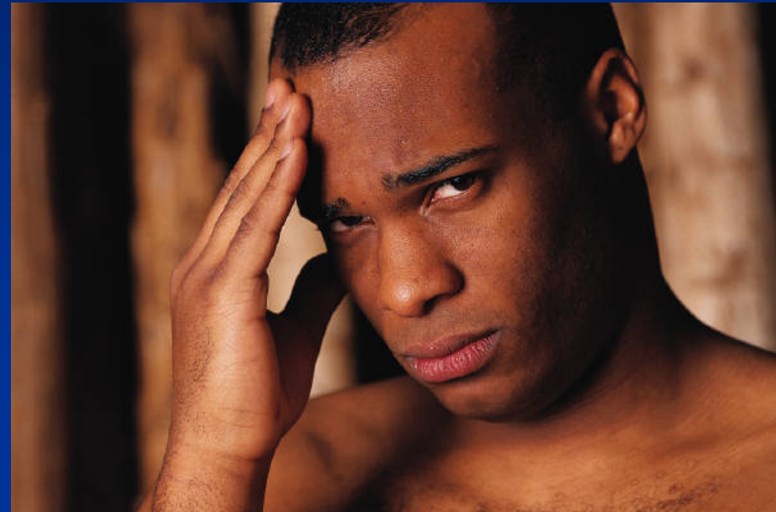
- Class C in pregnancy
  - (Use only if benefits outweigh risk)
- Is passed into human breast milk
- Lamotrigine Pregnancy Registry:
  - 800-336-2176

NEURONTIN

- Not effective in Bipolar Disorder when used as sole mood-stabilizer
- Effective as add-on
- No medication interactions
- Kidney metabolism

NEURONTIN

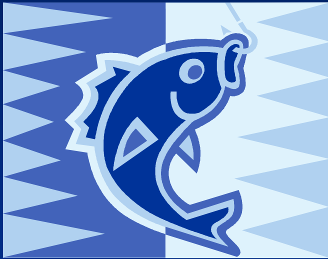
- Indications:
  - Inadequate mood stability with 1st mood stabilizer
  - Significant anxiety component
  - No medication interactions



NEURONTIN

- Caps: 100 mg, 300 mg, 400 mg
- Tabs (generic): 400 mg, 600 mg, 800 mg
- Peaks in 2 hours; ½ life 10 hours
  - Can be used prn acute anxiety or breakthrough mood reactivity
- Starting dose: 300 mg TID or more aggressive depending on acuity/severity

NON-MED TX OPTIONS



- Omega-3-fatty acid
- Psychotherapy “here and now” initially
- Exercise / Sleep
- Phototherapy
- ECT

RECOVERY PSYCHOTHERAPY

- Individual therapy
- Couples counseling
- Family therapy
- Group therapy
- Combination med / therapy group

NON-AA MUTUAL SELF-HELP GROUPS

- Dual Recovery Anonymous (DRA)
- Sobriety Knowledge Is Power (SKIP)
- Women For Sobriety (WFS)
- Self-Management Alcohol Recovery Training (SMART)
- Rational Sobriety (RR)
- Lifering Secular Recovery
- ___________________________

SUMMARY

- Careful initial evaluation
  - Screen all depressed pts for Bipolar Disorder
- History from others
  - Family, friends, etc.
  - Other members of treatment team
    - CDC, therapist, primary care provider, specialists
- Encourage "clean and sober"

SUMMARY

- Treat impairing symptoms first
- Serial, frequent assessments
- Adjust treatment as indicated
- Motivate “clean and sober”
- Collaborate and consult
- Repeat

SUMMARY

- Treat impairing mood reactivity while facilitating and supporting abstinence
    - Rule-out or treat underlying triggers
    - Acute :
        - Depakote ER can achieve therapeutic range in 3 days
        - Lithium in about 7 days
        - Equetro in about 7 days
        - Lamictal in about 4 to 6 weeks
    - Lithium or Divalproex + Zyprexa or Risperidone more effective than either one alone
- Collaborate and consult regularly

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- American Society of Addiction Medicine, 1989