Rethinking Depression and Its Treatment

Eric Goldberg D.O.

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Disclosures:

Consultant for Sunovian, Forrest and Astra Zeneca.

I do not own stock an any pharmaceutical/medical companies.

Rethinking Depression and Its Treatment

- Objectives
  - Recognize and diagnose different types of Depression
  - Review the more common treatments
  - Provide new options and ways to treat the tough cases

Rethinking Depression and Its Treatment

- #1 Contributor to Disability Worldwide[1]
- 16 Million adults affected in the US[2]

1 World Health Organization Global burden of disease 2008

2 NIMH. Major Depressive Disorder among adults.Available from www.nimh.nih.gov/statistics/1mdd_adult.shtml

Rethinking Depression and Its Treatment

- 48% are not receiving any treatment[1]
- 70% are either partial or nonresponders[2]
- 40% experienced significant side effects[3]
- 90% experienced moderate to very severe functional impariment[4]

1 Available fromwww.nimh.nih.gov/statistics/1mdd_adult.shtml

2 Knoth RL, et al. *Am J Manage Care*. 2010:16(8):e188-e196

3 Trivedi MH, et al. *Am J Psychiatry* 2006:163:28-40.

4 Kessler RC, et al *JAMA*, 2003;289(23):3095-3105

How many Depressive Disorders are in the DSM 5?

- A 1-2
- B 3-4
- C 5-6
- D 7-8

Depressive Disorders

- 1-Disruptive Mood Dysregulation Disorder
- 2-Major Depressive Disorder
- 3-Persistent Depressive Disorder
- 4-Premenstrual Dysphoric Disorder
- 5-Substance/Medication Induced Depressive Disorder
- 6-Depressive Disorder Due to Another Medical Condition
- 7-Other Specified and Unspecified Depressive Disorders

Disruptive Mood Dysregulation Disorder

- Essential feature Per DSM5: Severe temper outbursts with underlying persistent angry or irritable mood
  - Temper outburst frequency: Three or more time a week
  - Duration: Temper outbursts and the persistently irritable mood between outbursts lasts at least 12 months
  - Severity: Present in two settings and severe in at least one
  - Onset: Before age 10 but do not diagnose before age 6.
  - Can not diagnose for the first time after age 18.
  - Common rule-outs:
    - Bipolar disorder, intermittent explosive disorder, depressive disorder, ADHD, autism spectrum disorder, separation anxiety disorder,
    - Substance, medication or medical condition
    - If ODD present, do not also diagnose it

For a Major Depressive Disorder how many symptoms have to be present for how many weeks or more?

- A 4 symptoms for 1 week
- B 5 symptoms for 1 week
- C 4 symptoms for 2 weeks
- D 5 symptoms for 2 weeks

Major Depressive Disorder

- Essential features for Major Depressive Disorder per DSM5
  - A. At least five of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: at least one of the symptoms is either 1) depressed mood or 2) loss of interest or pleasure.
    - 1. Depressed mood most of the day, nearly every day, as indicated either by subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)
    - 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
    - 3. Significant weight loss when not dieting or weight gain or decrease or increase in appetite nearly every day
    - 4. Insomnia or hypersomnia nearly every day
    - 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
    - 6. Fatigue or loss of energy nearly every day
    - 7. Feelings of worthlessness or excessive or inappropriate guilt
    - 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day
    - 9. Recurrent thoughts of death , recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan for committing suicide

Persistent Depressive Disorder (Dysthymia)

- Essential feature per DSM5: Depression that persists for two years or longer (one year or longer in children and adolescents)
  - May include major depressive episodes

Premenstrual Dysphoric Disorder

- Essential feature per DSM5: Five or more affective symptoms that emerge in the week prior to menses which quickly dissipate with the onset of menses –
  - Duration: Present in all menstrual cycles in the past years and documented prospectively for two menstrual cycles

Treatment Essentials – Safety First

- Determine Suicidality
  - Active vs Passive Suicidal Ideation
  - You are not going to put the idea in their mind
  - They will likely feel relieved if you ask as people are generally afraid/embarrassed to talk about it
  - Document why they want to stay alive
  - Discuss weapons in the home
  - Establish support system especially if you are going to allow them to leave the office

Treatments

- Eliminate/Manage possible causes of depression
  - Situational
    - Relationship
    - Occupational
    - Financial
    - Legal
  - Medical
    - Thyroid
    - Medications
    - infection
    - “Low T”

- Antidepressants cause people to kill themselves
  - TRUE
  - False

"Ask your doctor if taking a pill to solve all your problems is right for you."

Treatment with Medications

- Black Box Warning about increased risk of suicide with antidepressants
- Document that this was discussed with patients
- Why do antidepressants cause and increased risk of suicidal thoughts and behaviors?

Treatment with Medications

- Rule out Bipolar Disorder especially if you are going to treat with medications
  - Have you ever gone several days on end with little to no sleep, felt on top of the world, like you had super powers, you were invincible, bullet proof, racing thoughts, sex drive through the roof, spent lots of money and felt phenomenal ---- ALL at the same time?
  - Someone who has tried multiple antidepressants and "they all only worked for a little while"

"Rethinking Depression"

- Depression and Anxiety go hand in hand
- You really need to be comfortable treating both at the same time.
- Try to determine if you are treating a primary:
  - Depressive Disorder
  - Anxiety Disorder
  - Both
- It generally takes higher doses of medications to treat anxiety than it does depression.
  - If the anxiety is not well controlled it is going to be hard to treat the depression
- If people are not sleeping because of anxiety or depression it is going to be hard to treat both of them.

Rethinking Depression

- Generalized Anxiety Disorder
  - "Would have, Should have, Could have"
  - Hard time turning their mid off
  - Frustration, irritability, concentration difficulties, muscle tension
- Panic Disorder
  - The fear of having future Panic Attacks
    - Heart Racing
    - SOB
    - Fear of losing control, Dying, or going "Crazy"
    - Numbness, tingling, lightheaded, Dizziness

Treatments with Medications

- Tricyclics
- SSRIs
- SNRIs
- Others

Treatment with Medications

- Tricyclics
  - We generally do not use them much anymore
  - Tend to be more lethal in overdose
  - Tend to have more side effects
    - Weight gain
    - Dry mouth
    - Sedation
  - Can be useful for difficult to treat depression

All Antidepressants are created equally

- True
- False

I am _____ about picking the right antidepressant for my patient

- Not confident at all
- Somewhat confident
- Confident
- Very confident

32 yr old C female presents with depression

- Low Energy
- Does not enjoy much of anything but she is usually very outgoing when not depressed
- does NOT want to gain weight because this will make her more depressed
- Has a hard time turning her mind off and controlling the "what ifs"
- Low Libido
- Has been on sertraline150mg for years and one other one that she cannot remember but it stopped working which is why she changed to sertraline.

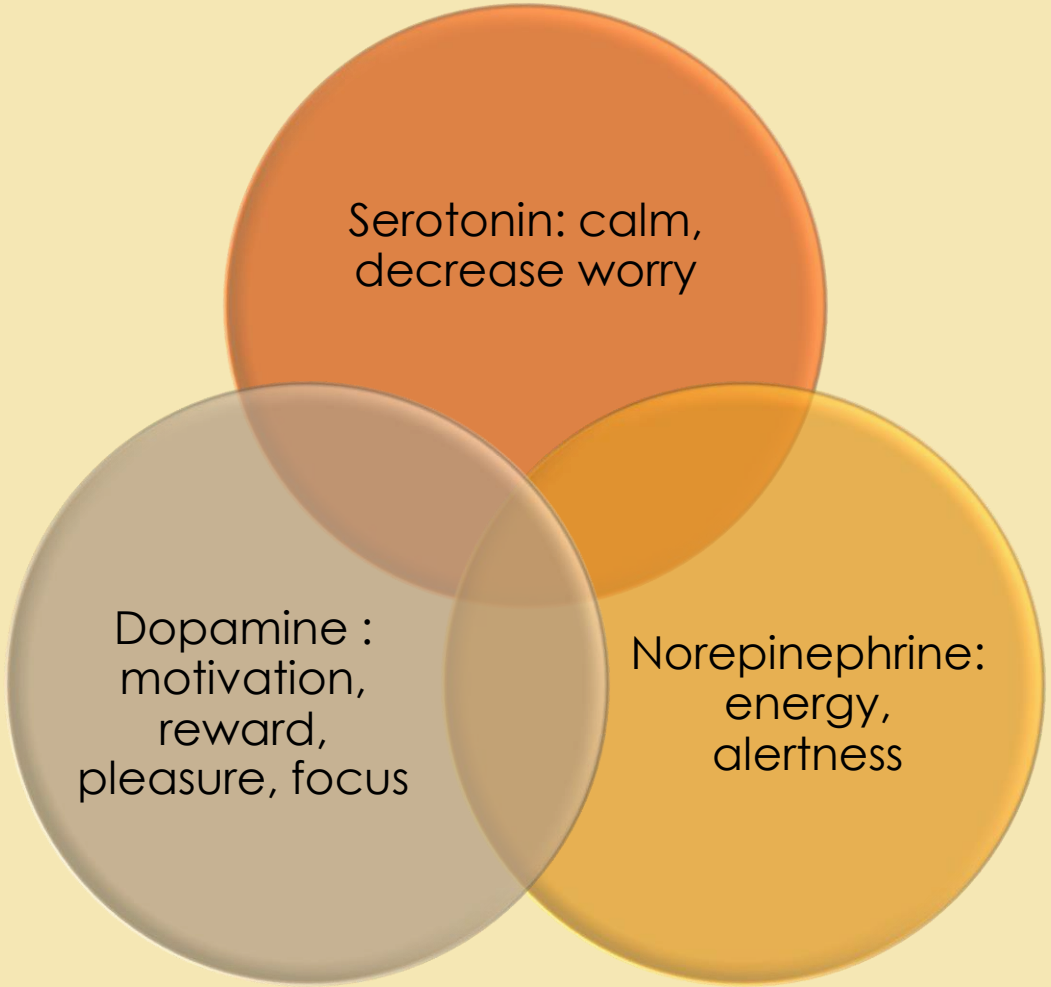
What would you do?

- A- Increase the sertraline ?
- B- Change to another SSRI
- C- Change to or Add buproprion
- D- Change to SNRI
- E- Add and atypical antipsychotic

"Siri – Navigate to……"

Soo many choices

Neurotransmitters all good for depression but how do you choose?



SSRIs

- Fluoxetine
  - ½ life
  - activating
- Paroxetine
  - Sedating
  - Weight gain
  - Harder to come off of
- Sertraline
  - GI upset
- Citalopram
  - QT prolongation above 40mg
  - Consider if there are liver concerns

SSRIs

- Escitalopram
  - Limited titration
  - Consider if there are liver concerns
- Fluvoxamine
  - Most serotonergic
  - Gold Standard for OCD
- Vilazodone
  - Low risk of weight gain
  - Low risk of sexual side effects
  - Must take with food

SNRIs

- Venlefaxine
  - Difficult to discontinue
- Desvenlefaxine
  - Lower risk of sexual side effects
- Duloxetine
  - Good for chronic pain
  - Indication for fibromyalgia, neuropathic pain and chronic musculoskeletal pain
- Levomilnacipran
  - The most noradrenergic to date

“Other” Antidepressants

- Buproprion
  - Great for energy and motivation but watch out for anxiety
- Mirtazepine
  - Sedating at lower doses and more energizing as the dose increases
  - Appetite stimulating
- Vortioxetine
  - 66 hour half life


PROZAC
20 mg

Try to Match the Patient to the Med

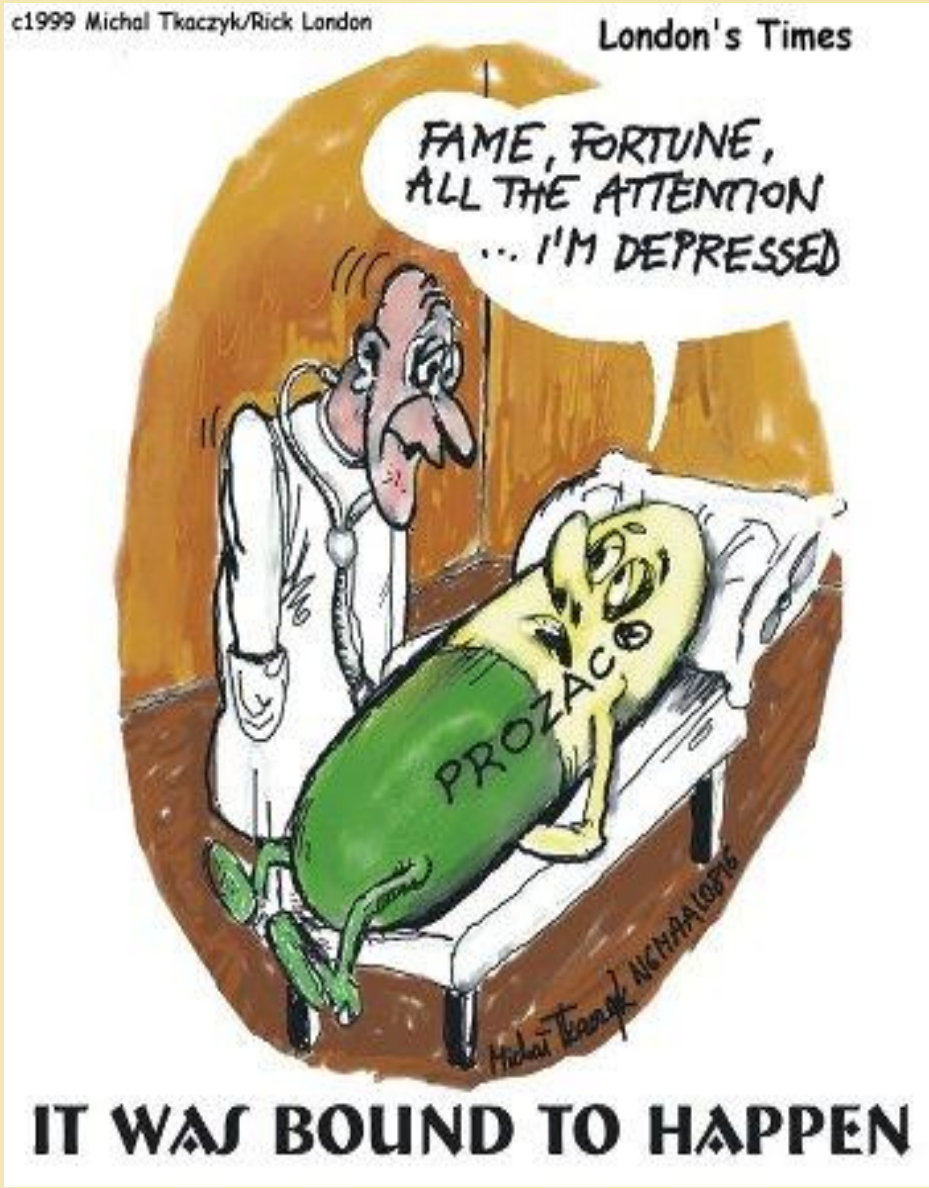
- Buproprion
  - Usually outgoing higher energy people without a great deal of anxiety
- SSRIs (automatic transmission Ford Taurus)
  - Patients who are new to antidepressants and very concerned about/sensitive to side effects with a significant amount of anxiety and need a simple med regimen
- SNRIs (manual transmission – Ferrari)
  - Patients who have been on several antidepressants and want more energy and don't mind tinkering with the meds

“Rethinking Depression”

- How long should you try a medication?
  - Generally at least two weeks before making a change
  - If you have pushed the dose and have no results at a month it is time to try a new med
  - If time is of the essence consider augmenting earlly

Nothing that you told us so far is working and she is still depressed

- Combine meds/antidepressants
- Use atypical antipsychotics
- Add low dose Lithium
- Add low dose thyroxine
- Consider testosterone for males
- Consider hormonal assessment/treatment for females
- Continue to look for other medical causes
- Consider referring them to a therapist


c1999 Michal Tkaczyk/Rick London
London's Times
FAME, FORTUNE, ALL THE ATTENTION ... I'M DEPRESSED
PROZAC
IT WAS BOUND TO HAPPEN

Medication combinations

- Adding buproprion can be very helpful as long as anxiety is under control
  - Start with buproprion XL 150mg and increase by 150mg every 3-4 weeks with current antidepressant up to 450mg
  - Monitor for increase in anxiety
- Generally not a great idea to combine two SSRIs, two SNRIs or an SSRI and SNRI
- California Rocket Fuel
  - Venlefaxine and Mirtazapine

If all else fails I am _____ comfortable using atypical antipsychotics

- A Very
- B Somewhat
- C Not


I think someone
needs one large
mocha Prozac vodka
latte, complete with
whipped cream and
Valium sprinkles.

Atypical Antipsychotics- Don't be afraid of them

- Movement towards referring to them as "Psychotropics" because " I ain't crazy doc"
- Can see results as quickly as 4-7 days
- Warn patients about
  - Tardive Dyskinesia
  - Elevated Cholesterol
  - Elevated Glucose
- Use very small doses to start
  - Aripiprazole 1-5mg HS – can be activating
  - Quetiepine 25-100mg HS – very sedating
  - Risperidone 0.25mg to 1mg HS – slightly sedating
  - Olanzepine 1.25 – 5mg HS – stimulates the appetite

Lithium

- Lithium is known to have good antidepressant properties and to be beneficial when added to antidepressants
- Check baseline CBC, TSH, and Kidney panel
- Start with 150mg qd and increase by 150mg roughly every week as tolerated.
- Make sure they stay hydrated
- Check a lithium level every several weeks while titrating and then every six months

Thyroxine

- Consider adding 0.25mcg and increasing by 0.25 mcg every 3-6 weeks as tolerated
- This can be done even if the thyroid levels are normal but especially if they are approaching hypothyroidism.
- Evidence based medicine does not support this but significant improvement is seen is some cases

"Rethinking Depression"

- TREAT TO REMISSION
- "Better" is not good enough
- The sooner you can get them to remission the less likelihood of relapse
- Allowing residual symptoms to persist greatly increases the rate of relapse

“Rethinking Depression”

- How long should I treat them?
  - First episode: 6-9 months
  - Second episode: 1-2 yrs
  - Third episode: lifetime management

“Rethinking Depression”.

- Risks of Relapse
  - After first episode 50% chance
  - After second episode 75-90% chance
  - By the third episode it is most likely going to be recurrent

Conclusions

- Safety first
  - Assess for suicidal and homicidal/violent ideation
- Make the right diagnosis
  - Rule out bipolar disorder
  - Rule out anxiety
- Try to match the medication to the patient
  - SSRI
  - SNRI
  - Other
  - Augmentation
- Treat to remission and don’t give up

Questions

- Thank You for Attending
- Time for Questions