Men and Depression

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Disclosure

• Dr. Mays is not on any drug advisory boards, paid for doing drug research, or otherwise employed, funded, or consciously influenced by the pharmaceutical industry or any other corporate entity.
• No off label uses of medications will be discussed unless mentioned in the handout and by the presenter.
• No funny business.

“I am now the most miserable man living. If what I feel were equally distributed to the whole human family, there would not be one cheerful face on earth. Whether I shall ever be better, I cannot tell: I awfully forebode I shall not. To remain as I am is impossible. I must die or be better, it appears to me.”

Robert Wilson, fellow legislator of Lincoln’s, 1836

“He (Lincoln) told me that although he appeared to enjoy life rapturously, still he was the victim of a terrible melancholy. He sought company, and indulged in fun and hilarity without restraint. Still when by himself, he told me that he was so overcome with mental depression, that he never dare carry a knife in his pocket. As long as I was intimately acquainted with him, he never carried a pocket knife.”

Depression

• Depression is a commonly experienced mood and a syndrome. A clinical depression is distinguished from a depressed mood by the intensity and pervasiveness of its symptoms. Depressed people are usually not able to relate to others and may be able to express only a limited range of emotions. They are frequently obsessively focused on themselves and how they are feeling moment to moment. In a primary care setting the following complaints may identify depression: sleep disturbance, fatigue, somatic complaints.

An Alternative Description to DSM

• The present criteria for “Major” Depressive Disorder was the result of a compromise between scientists and analysts in writing the DSM-III. Originally, major and minor types of depression were proposed, but since the analysts worked with “minor” depression, and were afraid they would not be reimbursed for treatment if it was called minor, all the criteria were subsumed into Major Depression. What has been lost is the phenomenology of depression.
The Spectrum of Major Depression  
(Ghaemi 2012)

- Melancholic
- Neurotic
- Mixed
- Pure

Melancholic Depression
- Severe and generally unassociated with anxiety
- Psychomotor retardation
- Marked anhedonia
- No reactivity – patients are not labile and are unresponsive to psychological stressors. (Bad events don’t make them feel worse because they can’t feel any worse.)
- Episodic, not chronic, but lengthy
- More common in bipolar depression than unipolar
- High suicide risk
- Tricyclic antidepressants, Electroconvulsive therapy

Neurotic Depression
- Mix of mild depression and mild anxiety
- High degree of sensitivity to psychosocial stressors
- Chronic, not episodic, although they may be easily pushed into a major depressive episode by stress
- Probably more temperament than disease
- Does not respond to antidepressants any more than to placebos

Mixed Depression
- Major depression with 1-3 manic symptoms
- Core features: irritability, agitation, mood lability
- More common in bipolar disorder, but frequently present in major depressive disorder
- Recent research indicates that more people with mood disorders have mixed symptoms than purely depressive or manic (at least 40% of the total)
- Antipsychotics are more effective than antidepressants

Pure Depression
- Some mood reactivity, some interests, somewhat functional (not melancholic)
- No mania, little or no anxiety (not mixed)
- Episodic (not neurotic)
- The new antidepressants may be the most effective in this group.

Demographics
- Depression is the fourth leading cause of disease burden worldwide, 1st in the United States. Lifetime prevalence may be 7-12% of men, 20-25% of women. High risk groups include Native Americans (19.17%) and Caucasians (14.58%). Asians are at lowest risk (8.77%).
- There is high comorbidity with anxiety disorders (36%) and personality disorder (37%).
- Mortality is high. 46% wish to die. 9% report a suicide attempt. Risk of suicide death is 20x higher – 15% lifetime risk. 30-70% of suicides have a depressive disorder.
Impairment

- 44% of depressed people have some sort of functional work impairment, 11% are unable to work altogether. In 2020, major depression will be second only to heart disease in the amount of disability suffered.
- Cardiac clients have 4x greater risk of depression and depression a month after a heart attack is the best predictor of MI in next year - the risk is the same as being a smoker – 5x more likely to die than healthy peers.

Natural History

- Depression is a lifelong illness, likely to relapse within a few months after the first episode.
- Average age of onset is late 20-40 years old. Symptoms develop over days or weeks.
- Prodromal symptoms include anxiety, panic, phobias, low grade depression.
- Episodes last from 6 to 24 months.
- There is strong evidence that sub-syndromal continuation of symptoms represent a continuation of the illness, and will lead to relapse.

Depression and Clinical Practice

- In clinical practice, the diagnosis of “depression” is used across a wide variety of clinical presentations of depressed mood. It can encompass major depressive disorder, depression in bipolar disorder, dysthymia, reactive depression, an overall sense of dysphoria or pessimism, bereavement, and the depression found in personality disorders, particularly borderline. It may be a sign of many different disorders, similar to “fever” or “inflammation” in medical practice.

Causes of Disability

- Depression
- Heart Dis
- Alcohol
- Stroke
- Diabetes

Risk of Recurrence of Depression (DSM-IV-TR)

- The risk of recurrence of depression increases with each subsequent episode.
- After 1 episode: 10%
- After 2 episodes: 20%
- After 3 episodes: 30%

Symptoms

- Affective
  - Depressed mood
- Vegetative
  - Weight loss or gain
  - Insomnia or hypersomnia (insomnia has a bidirectional relationship to depression – a cause and an effect)
  - Decreased sex drive
- Behavioral
  - Psychomotor retardation or agitation
  - Fatigue
  - Diminished interest or pleasure in most activities
Symptoms

- Cognitive
  - Feelings of worthlessness or guilt
  - Diminished ability to think and concentrate
  - Poor frustration tolerance
  - Negative distortions
  - Affective agnosia and apraxia
- Impulse Control
  - Recurrent thoughts of suicide, homicide, or death
- Somatic
  - Headaches, stomach aches, muscle tension
- Chronic Painful Physical Conditions

Symptoms

- Clients with depression have difficulties with interpersonal relationships, largely related to problems with emotional perception and executive function. They misidentify happy facial expressions as sad, for instance.
- There is evidence of mood state dependent learning - clients don’t remember ever feeling good, increasing the risk of suicide. These memories can be retrieved with proper prompting and cueing.

Comorbidities

- Social anxiety disorder is a major risk factor
- Comorbid personality disorder confers worse prognosis and treatment response
- Obesity and metabolic syndrome – bidirectional
- Coronary artery disease
- 65% increase in risk for diabetes
- Secretion and production of proinflammatory enzymes

Gender Issues

- Depression is “a fixed melancholy.”
  - Emily Dickinson

  Depression is “a rage spread thin.”
  - George Santayana

Gender Issues

- Women are twice as likely to be depressed as men (1/5 vs. 1/10). The gender difference begins at 10 and continues until the mid 50’s. Social and hormonal influences contribute to making adolescence a difficult transition for girls. Estrogen may boost levels of cortisol and inhibit GABA.
- Menopause is strongly associated with new onset depression.
- College education, being in the first marriage, working outside the home lowers risk. Single mothers have 2x the depression risk as mothers with partners.

Hazard Rate for Depression
Women

- More likely to describe themselves as sad or depressed with more symptoms and higher degree of distress
- More “reverse” symptoms (hypersomnia, increased appetite, somatization)
- Friendship networks are larger, which buffers and creates stress.
- Marriage is protective for men, but not for women.

Gender

- Women are more likely to seek healthcare for depression, in part, because women enter the healthcare system more frequently than men due to seeking birth control and/or pregnancy. If men are more likely to attribute their depression to finances, etc., they are less likely to view the healthcare system as the place for help.

Why the Gender Difference?

Why the Gender Difference?

- Genes: Heredity may account for ~40% of the risk of major depression. Certain genetic mutations that are associated with the development of severe depression occur only in women.
- Hormones: The gender difference begins at puberty. Hormonal changes that accompany menstruation bring on mood changes. Some women are vulnerable to depression after childbirth or menopause. But it has not been proven that hormonal changes significantly alter mood in large groups of women.

Gender

Am J Psychiatry, April 2014

- In a large, opposite sex twin study, the following risk factors were defined for each gender:
  - Women: deficiencies in caring relationships and interpersonal loss
    - Neuroticism, divorce, absence of parental warmth and social supports, lack of marital satisfaction
  - Men: failure to achieve expected goals and lowered self-worth
    - Childhood sexual abuse, conduct disorder, drug abuse, financial, occupational, legal stress

Men

- Testosterone may make boys more susceptible to seizures (and possibly autism) due to the increase in GABA, but may protect them from depression later on.
- SSRI’s may work better in the presence of estrogen.
- They are less likely to seek help and 4x more likely to die of suicide than women, although they attempt suicide 3x less often.
Symptoms in Men

- Men are more likely
  - to lose weight when depressed
  - to show OCD symptoms rather than simply anxiety
  - to abuse substances
  - to show anger and irritability
  - to increase risk taking

Suicide Epidemiologic Risk Factors

- Gender, Age, and Race
- Marital Status
- Family History
- Mental Illness History
- Newness in Treatment Program
- Time of Year
- Rural vs. Urban
- Natural/Unnatural Disasters
- The Media

NESARC Data (n=43,093) Suicide Findings

- Among depressed people:
  - Highest suicide attempts – Hispanic, Latino, younger age, low income
  - Comorbidity with any anxiety disorder, personality disorder, substance abuse
  - In men, depression + dependent personality disorder (75% will make a suicide attempt)
  - In women, antisocial personality disorder
  - Most predictive symptom: feeling worthless

Gender

- Gender differences in suicide deaths have complicated attempts to understand the epidemiology of suicide. Women have low suicide mortality, but a higher incidence of the two most significant risk factors – depression and suicide attempts.
- Risk factors of increasing age, single marital status, physical illness, stressful life events, unemployment, and low socioeconomic status apply only to men.

Gender

- The reason for this gender difference is not known. It is suggested that in men, higher rates of substance abuse, violence, and greater social expectation that a real man will “succeed” in a suicide attempt contribute to men using more lethal means than women.
- In contrast, women tend to exhibit more help-seeking behavior, have more social connectivity, have more “permission” to make non-fatal attempts, and may assume more responsibility for the feelings of children and family members.
The Problem

- Suicide rates have not decreased in the last decade, or in the last 110 years. Compare this with progress made in other areas of public health: breast and skin cancer, HIV, automobile accidents, etc. where we have seen a decrease in death rates from 40-80%.

The Problem

- Preventing suicide is not easy. The base rate of suicide is low creating a number of statistical and research problems. Our current approach of using epidemiologic risk factors has no clinical utility. Even the highest odds ratio is not informative at an individual level. (The best predictor is a previous suicide attempt, but 60% of suicides occur on the first attempt.) Furthermore, decades of research have failed to identify any new predictors. We have no biological markers.

The Problem

- People who are at risk of suicide do not seek help. 80% of people who die of suicide have seen a provider prior to their attempt, but did not identify themselves as suicidal, largely because they think they do not need help.
- Treatment is often not optimal. Community treatments (gatekeeper training, school programs) are not coordinated with medical interventions (treatment of mental illness, follow-up.)

The Problem

- Cardiovascular disease and cancer research have studies that include hundreds of thousands of patients. We need that kind of power to determine effective treatments.
- In order to study short-term risk, real time monitoring may provide helpful ideas. Less than 1% of risk factor studies look at the week before the suicide.

The Problem Christensen JAMA May 2016

- Mobile phones
- Certain phrases and use of personal pronouns in blogs/digital footprints on Twitter – machines can learn to detect disturbing tweets.
- Data mining may help uncover risk factors
- Facial and voice characteristics
- Social media can facilitate help seeking and peer support. Suicide prevention apps and websites can deliver assessment and information.

Mariano Sigman, PhD
Shifts in Our Thinking About Depression

- From neurotransmitters to neuroplasticity  
  - Neurogenesis, dendritic pathology...
- From chemical imbalance to neuro-inflammation
- From serotonin and norepinephrine to glutamate
- From oral to parental administration
- From delayed efficacy to immediate efficacy
- From pharmacotherapy to neuromodulation

“Network Model”

- Hypothesis: the problem is not so much with neurotransmitter inadequacy, but rather with networks of cells that are dysfunctional.
- A 2012 meta-analysis of brain scan studies found high baseline activation in the pulvinar, a large nucleus in the thalamus. This structure is part of a fast, unconscious processing stream for priming behavior in the face of a threat, as well as for focusing emotional attention and awareness.

Network Theory

- The amygdala, dorsal anterior cingulate cortex, and insula are all overactive to negative stimuli.
- These data are consistent with the hypothesis that negative cognitive biases play a crucial role in the onset and maintenance of major depression.
- These sensory inputs fail to propagate to the dorsolateral prefrontal cortex, which would ordinarily allow the individual to appraise and correct this negativity.

Bottom Line

- Current imaging research indicates a bias of attention to negative emotional stimuli and a lack of recognition of positive emotional and rewarding stimuli.
- There is increased activity supporting emotion processing and reduced activity in neural systems supporting regulation of emotions (dorsolateral prefrontal cortex.)

Free Depression Outcome Scale

- Patient Health Questionnaire-9 (PHQ-9)
  www.depression-primarycare.org/forms/phq_9/