Global Mental Health: A growing problem and a downward spiral
Depression is a Major Public Health Problem

- 40K suicides/yr (vs. 13K homicides) 22 veterans/day
- Bed days/mo 2<sup>nd</sup> only to heart disease. WHO: #1 cause of disability by 2020
- Depression increases mortality of the aged; e.g. death from MI 4x higher in patients with documented depression
- 1 of 6 worldwide has or will have depression
Where is the Light

My mood is black. I've lost all hope.
I've sunk into despair.
The tentacles of gloom grip tight
I must escape. But where

Am I to go? I've lost desire
To live or love or laugh.
I feel no pleasure, just dull pain.
I see my epitaph,

Yet it is blank. This endless gloom
From which I must escape
Yields no promise of afterlife.
I recognize no shape

Nor color, taste, passion, joy;
Just foul and acrid mood.
I cannot work, I cannot play
I lie in bed and brood.

Shall I end this worthless life?
Have I the motivation?
I guess I'll just maintain this state
Of endless dissipation.

—Mark M. Rasenick 12/7/99
Stressors

• Endogenous
• Financial
• Traumatic (violence, war, natural disasters)
1 OF EVERY 6 PEOPLE SUFFER DEPRESSION

300+M worldwide
15M in US

<50% diagnosed

<25% treated adequately

one-third of treated fail to respond

Stigma

2013 US Annual Cost estimate--$500B

7/2/13 NYT

Slide adapted from John Greden, U. Michigan
Antidepressant Therapy

- Cognitive
- Direct Stimulation (ECT, TMS, AVS, DBS)
- MAO inhibitors (phenylzine, iproniazid)
- Tricyclics (amitriptyline, imipramine, chloipramine)
- SSRI (fluoxetine, sertraline, paroxetine, citalopram)
- Others (venlafaxine--DA uptake/5HT & NE antagonist)
- Combinations (as seen on TV)
Are new antidepressants needed?

• Doesn’t everybody get better with escitalproam?
• 30% respond well to any given treatment
• 40% have a partial response
• 30% do not respond
• Some of these are refractory to all treatment and are at risk of death from suicide
With each level of treatment, remission rates decrease and relapse rates increase. An estimated 30% continue to experience significant impairment after 4 levels of treatment. These people are at risk for suicide.

Is this the result of repeated failure?

What’s the problem?

• Stigma discourages many from seeking treatment
• Most current depression therapy requires 6-12 week lag before improvement of symptoms
• Settling for response rather than recovery.
• Designing new drugs based on existing drugs.

What’s the solution?

• Approaching depression and other psychiatric problems as a neurobiology issue (end stigma)
• Understanding the molecular/cellular basis of depression.
• Identifying clear, easily-obtainable biochemical/genetic hallmarks for diagnosis and treatment (biomarkers).
Disability Adjusted Life Years (DALYs) in 2020: Depression #2 worldwide and #1 in developing world

86 % suicides and 75% global burden of neuropsychiatric disorders are in low and middle income countries

Murray and Lopez Lancet, 1997
Economic Burden of Noncommunicable Diseases 2011-2030

US Annual Costs > $300B for SMI (Insel, AJP, 2008)
Global $2.5T, 2010; $6T, 2030

Treatment has increased over the past decade

A. Antidepressant prescriptions

B. Antipsychotic prescriptions

(millions of prescriptions in US market – IMS Health)
Inconvenient Truth #1

Increased treatment, worldwide, as measured by epidemiology, prescriptions, expense

No decrease and, in some areas, increase in morbidity and mortality

Explanations:

Effective treatments, but prevalence is increasing
Effective treatments, but delivery is inadequate
Current treatments are not effective enough to influence public health outcomes

From W.Z. Potter
Inconvenient Truth #2

At a time of increased need, most Pharma companies have left CNS R&D.

U.S. federal funding has dropped 25% over past decade. No new targets

Explanations:

Market saturation w generics
Preclinical studies not predictive
Expensive Phase 3 failures

From W.Z. Potter
Remission Harder To Achieve With Each Treatment Failure

Significance of Moderate Levels of Prior Treatment Failure

With each level of treatment, remission rates decrease and relapse rates increase. An estimated 30% continue to experience significant impairment after 4 levels of treatment.

These people are at risk for suicide.

Is this the result of repeated failure?

<table>
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<th>Country</th>
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Completed Suicides by Method, USA

Fatality Rate by Suicide Method

- Firearms: 90%
- Suffocation/Hanging: 60%
- Falls: 30%
- Poisoning/Overdose: 5%
- Cutting: 1%

(Bar chart showing fatality rates for different suicide methods in the USA.)
<table>
<thead>
<tr>
<th>Country</th>
<th>Crude Suicide Rates (per 100 000 Population)</th>
<th>Proportion of Firearm Suicides, %</th>
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Availability of Treatment

• Psychiatrists/population:
  • Western Europe, 1:10,000
  • Central Africa, 1:400,000
• But faith healers abound

• Is there a fix?
• More Psychiatrists?
• More prisons?
Global Strategy

- Will “throwing money at it” help?
- Psychiatrists not the answer
- Cultural competence
- Private funders
- Global mental health laboratory
- Family involvement ala Cuba