DEPRESSION

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Psychiatric Diagnosis

- **No pathognomonic** signs or symptoms
- Psychiatric disorders are clinical **syndromes**
  - **Pathophysiology** not well understood
  - **No Lab, No Imaging, No Post-Mortem Confirmation**
  - **Heterogeneous** –
    - **Symptoms**
    - **Course**
    - **Treatment Response – NNT ≥ 1.5**
- **Clinical Dx** → CC HPI SUD PψHx FHx ROS PE MSE

Psychiatric Diagnosis

'Who's your daddy?' **Stephen M. Stahl MD Mood Disorders**

Is there a Family History of:

- Mood Disorder – Depression, Manic Depression, Bipolar, SCZA, SCZ
- Psychiatric Hospitalizations
- Suicide
- ECT
- Medications: Lithium, Mood Stabilizers, Antidepressants, Antipsychotics

Psychiatric Diagnosis

'Where's your Mommy?' **Stephen M. Stahl MD Mood Disorders**

Is there a Family History – especially of Mania:

- When depressed, patients may not recall episodes of mania or hypomania – they may lack insight and often under-report
- Mother, spouse or someone else close to the patient may help enhance the data base

Diagnosis of Depression

- **Depressive Symptoms** – extremely common
  - **human reaction to adversity and loss –**
  - **Occur in a wide variety of clinical syndromes, only some of which reflect Mood D/O and require AD medications**
  - **in any one semester 17% of college students have thought of suicide**
- **Depressive Disorders =**
  - **↓Mood + Symptoms + Impairment**
  - **↓Mood – persistent and pervasive**
  - **Symptoms – multiple and disrupt function**

Depressive Disorders

- **Common and Costly**
  - **NIMH:** Depression afflicts 6.7% of US adults ≥ 18
    - **Archives of General Psychiatry, 2005 Jun; 62(6): 617-27**
  - **Lifetime Prevalence –** 20-26% women 8-12% men
    - Journal of the American Medical Association, 1996
  - **Lifetime Prevalence** – Anxiety (28.9%) Impulse (24.8%) Mood (20.8%) SUD (14.6%) Any Psychiatric D/O (50%)
    - Archives of General Psychiatry. 2005 Jun;62(6):593-602.
  - **WHO:** Depression = 2nd leading cause of disability
- **80% get no Treatment at all - 24% PCP 20% Non-MD 12% Psych**
- **Age of Onset**:
  - 50% of all mental d/o occur by age 14, 75% by age 24.
  - Anxiety (11) Borderline D/O (18?) SUD (20) Bipolar Disorder (25) Depression (30)
    - Arch Gen Psychiatry. 2005 Jun;62(6):593-602.

Symptoms of Depression

- **Depression = ↓ Mood + SIG E CAPSS**
- **SIG E CAPSS – easy to remember mnemonic**
- **PHQ 9 – patient self-report instrument**
  - **Very useful in the office for**
    - **Diagnosis and**
    - **monitoring response to treatment**

Symptoms of Depression

SIG E CAPSS

- **S**leep
- **I**nterest/Pleasure
- **G**uilt/Worthlessness
- **E**nergy
- **C**oncentration
- **A**ppetite ↓↑
- **P**sychomotor
- **S**ex (Libido)
- **S**uicide

PHQ - 9

- **Patient Health Questionnaire**
  - J Gen Intern Med. 2001 Sep; 16(9): 606–613.
- self-administered version of PRIME-MD
- The PHQ-9 is the depression module, which scores each of the 9 DSM-IV criteria as “0” (not at all) to “3” (nearly every day).
- Over the last 2 weeks, how often have you been bothered by any of the following problems?

PHQ - 9

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless
3. Trouble falling or staying asleep, or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down
7. Trouble concentrating on things, such as reading the newspaper or watching television
8. Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual
9. Thoughts that you would be better off dead or of hurting yourself in some way

PHQ - 9

- Contains the Diagnostic Criteria
- Make the Diagnosis – PHQ 9 $\geq$ 10
  - A cut-off score of 10 may result in many false negatives in hospital settings, while more false-positive results may be seen in primary care.
  - http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3281183/
- Assess the Severity
- Monitor Response to Treatment

CASE 1

ID: 48 MWM, recently divorced, three children, tennis player, college varsity and one of the best players in his club
HPI: since his separation and subsequent divorce, he has become increasingly depressed, with significant symptoms
Past ψ Hx: None
SUD: Occasional alcohol, MJ in college
FHx: none known, no FHx suicide, Bipolar, SCZA, SCZ
PE: BMI 23 BP 115/78 P 62 No AIM
LAB: normal TSH
ROS: middle insomnia, anhedonia, stopped tennis 'too tired', can't focus at work, ↓ appetite ↓ weight , ↓ libido
MSE: depressed, moves slowly, 'failed my children', burden to his coworkers, pessimistic, SI w/o intent or plan, no delusions

CASE 1 – Major Depression

- Divorce and Unemployment are common precipitants, but
- The Existence of a Reason for the Depression is not a Reason to Ignore the Existence of Depression

Case 1 – Major Depression

Persistently ↓ Mood + 9/9 SIG E CAPSS

- **Sleep**
- **Interest**
- **Guilt/Worthless**
- **Energy**
- **Concentration**
- **Appetite**
- **Psychomotor**
- **Sex (Libido)**
- **Suicide**

CASE 1 – Major Depression

Start SSRI – Citalopram 20 QHS + Trazodone 50 QHS

+/- Folate 2 mg QAM

Educate re SSRI unwanted effects:

- Jittery insomnia – 'wired and tired'
- Headache
- Bruxism
- Sexual Side Effects – TRZ → Priapism - not all are bad
- ↑ Suicidal Ideation

Refer for Psychotherapy – CBT or IPT

F/U Email re SE/SI in 1 week* and RTC 2 weeks **

Emergency Plan ***

CASE 1 – Major Depression

Two Week Follow Up

- 'A little better' with ↓ PHQ 9 score
- Met with therapist – 'very nice…I feel comfortable talking to her.'
- Sleeping better on Trazodone
- No SI = hope has been restored
- But still depressed, guilty, pessimistic, with difficulty concentrating at work → worries he will lose his job

Plan

- Increase Celexa 20 → 40 QHS (Optimize)
- Continue Psychotherapy
- RTC 2 weeks, Email if worse
- Emergency Plan ***

CASE 1 – Major Depression

Four Week Follow Up

- 'Much better' with ↓ PHQ 9 score = 2
- Therapist – 'very helpful…better perspective on life'
- Sleeping well
- No SI = more optimistic about life after divorce
- Not depressed, guilty, pessimistic,
- concentrating better at work and no longer worries that he will lose his job

Plan

- Continue Celexa 40 QHS – review side effects
- Continue Psychotherapy
- RTC 4 weeks
- Emergency Plan ***

CASE 1 – Major Depression

Goal Of AD Treatment = Full Remission (no Sxs)

Response rates to current AD are disappointing

Each AD gives Response in ~ 65-70% = NNT ~1.5

- Response ≥ 50% improvement

Risk of Relapse is High

Continue Treatment - 9-12 months after remission

CASE 1 – Major Depression

First AD Trial (STAR*D study)

Remission 30%

- HAM-D < 7 or QIDS < 5
- may still have Sx

Response 40%

- 50% ↓ in HAM-D or QIDS
- Continue to have significant Sx
- Risk of Relapse is High

No Response 30%

CASE 1 – Major Depression

Response rates to subsequent AD are disappointing

AD Trial # 2 20%
AD Trial # 3 6-7%
AD Trial # 4 6-7%

After the 4th AD Trial ~67% have remitted

Common Residual Symptoms:
Most: insomnia, fatigue, pain, concentration, lack of interest
Least Common: depressed mood, SI, psychomotor ↓

CASE 1 – Major Depression

Treatment Resistant Depression (TRD)

Definition

- Non-response after adequate trial = 6 weeks at 'adequate dose'
- Adequate = max tolerated* vs mid-therapeutic
- Should 'partial responders' be included?

NB: Common Causes of 'Pseudo-Resistance

- 50% do not receive an adequate AD trial;
- Unrecognized Etoh (includes 'moderate')
- Anxiety Disorder → predisposes to chronicity
- Subclinical Hypothyroid (~50%)
- Noncompliance – support, encourage, close follow-up

CASE 1 – Major Depression

Management of TRD

Switch to another AD in new class (e.g. Effexor, Remeron)

- Optimize (max tolerated) before Switching
- Switch for intolerable side effects
- Switch for Non-Response

Combine by Adding AD Drug in new class

- Optimize (max tolerated) before Adding
- Augment for Partial Response
- Wellbutrin, Remeron, TCA, Effexor

Augment by Adding non-AD Drug

- Optimize (max tolerated) before Adding
- Augment for Partial Response
- Lithium, Cytomel (T3), Second Generation Antipsychotic, Stimulants, Pindolol, etc.

CASE 1 – Major Depression

Management of TRD (Continued)

ECT – Electroconvulsive Therapy

- Works in 50-85% of AD non-responders
- Effective for Severe and Psychotic Depression
- Generally Well-Tolerated
- No Weight Gain

TMS – Transcranial Magnetic Stimulation

- Lindner Center (Keck) – 50% remission, 75% response
- Very well tolerated, treatment takes 50 minutes, patients can drive to and from appoinment
- No Insurance company will currently pay

CASE 2

ID:56 MWF, mother of 2 adult children; she lives with her husband, SVP Finance of Fortune 500 corporation.
HPI: Feeling down for several months. In response to a call from his wife's friends, expressing concern about her emotional state, her husband returned home unexpectedly early from a business trip to find her in the garage, the car running and a hose attached to the exhaust. Her husband calls you, his PCP, asking for guidance.
Past ψ Hx: Yes, ambulatory treatment with AD meds
SUD: No **FHX**: mother was depressed, ECT
PE: no AIM, BMI = 31 LAB: normal TSH
MSE: bradykinetic, poor eye contact, denies she is depressed, unable to explain why she was in the garage,

CASE 2 – Severe Depression

Referred to ED for admission
Discharged 10 days later, on AD, 'improved' but not well
Follow-up at a well-known private clinic
Over the next 4 months – trials of 3 more AD
Followed by a trial of an investigational agent
ECT never offered
On the advice of a physician family friend, underwent ECT – better by the 8th treatment, well by the 12th

CASE 2 – Severe Depression

~30% of severely depressed patients will deny depression

ECT is indicated and effective – often rapidly effective - for severe symptoms and high risk

CASE 3

ID: 37 NMWF, employed as a cashier, despite graduating from a good college,
HPI: depressed since mid-20's, socially isolated, no close friends, no boyfriends, knows she is 'under-performing'
Past Ψ Hx: brief psychotherapy in college – dropped out because 'he never talked, he just looked at me.'
SUD: None
FHX: MGM and two maternal aunts were depressed
ROS: hypersomnia, over-eating, low energy
PE: BMI=33
LAB: normal TSH
MSE: depressed, apathetic, pessimistic, no SI, no delusions

CASE 3–Persistent Depressive D/O

Depressed mood that occurs for most of the day, for more days than not, **for at least 2 years** (at least 1 year for children and adolescents).
During periods of depressed mood, at least two of the following six symptoms from are present.

- Poor appetite or overeating
- Insomnia or hypersomnia
- Low energy or fatigue
- Low self-esteem
- Poor concentration or difficulty making decisions
- Feelings of hopelessness

CASE 3–Persistent Depressive D/O

- Consolidation of DSM-IV-defined Chronic Major Depressive Disorder and Dysthymic disorder.
- Major depression may precede persistent depressive disorder, and major depressive episodes may occur during persistent depressive disorder.
- Individuals whose symptoms meet major depressive disorder criteria for 2 years should be given a diagnosis of persistent depressive disorder as well as major depressive disorder (Double Depression)

CASE 3–Persistent Depressive D/O

Treatment – Combined Medication and Psychotherapy
Keller et al NEJM (2000)

- CBT 48%
- AD Meds 48%
- Combined 75%

"The combination of the two was whoppingly more effective than either one alone … People suffering from chronic depression often have longstanding interpersonal difficulties, and the virtue of combined treatment in this case may be that it simultaneously targets both depressive symptoms and social functioning."

CASE 4

ID: 54 MWM, wife is an MD, 3 children, 'steady…good father'. Employed as a senior state government manager
HPI: depressed for ~ 3 weeks, wife increasingly concerned, 'not like him', cannot get an appointment with a psychiatrist, calls you.
Past Ψ Hx: one episode of depression in early 20's
SUD: None
FHx: Father severely depressed, treated with ECT, paternal uncle committed suicide
ROS: insomnia, no appetite
MSE: when asked about depression – 'not really', when asked when he last thought of suicide – 'on the way to your office, voices told me to jump out of the car.'

CASE 4 – Psychotic Depression

- Severely ill, very high risk
- Admitted to psychiatric hospital for ECT
- Better by the third treatment, discharged without symptoms by the sixth treatment.

CASE 5

ID: 54 MWF, 2 adult children, Employed as a DSS administrator

HPI: depressed for ~ 2 weeks, husband increasingly concerned,

Past Ψ Hx: one episode of mania in early 30's, preceded by postpartum depression after birth of second child

SUD: None

FHx: Mother severely depressed, PGF 'Manic Depressive', paternal uncle committed suicide

ROS: insomnia, no appetite, increased energy 'wired'

MSE: depressed, anxious, irritable, pressured, restless, SI without plan

CASE 5 – Bipolar Depression

- you see her and refer to a local psychiatrist
- He starts her on Prozac,
- over the next week she worsens, develops the delusion that her husband is the devil and will try to kill her,
- Convinced of this, she stabs him in the shoulder - severe Brachial plexus injury
- Admitted to psychiatric hospital, in 3 weeks she is better on Zyprexa and Lithium

CASE 5 – Bipolar Depression

- Diagnostic Clues – FHx, Hx Hypomania and/or
  - Early Age of Onset
  - Frequent Depressive Episodes
  - Rapid Onset and Resolution
  - Frequent Job or Relationship Changes
- Severely ill, very high risk – hospitalize
- Antidepressants may produce manic switch and severe illness
- Medications for Bipolar D/O – SGA – Risperdal, Zyprexa, Seroquel, Abilify, Lithium, Depakote
- Consider Wellbutrin if AD needed

CASE 6

ID: 56 DWF, lives alone, no children (3 miscarriages), accountant and owns her own small firm

HPI: Depressed for six weeks in the aftermath of the unexpected death of her mother in a MVA; Very close to her mother – 'my best friend'

Past Ψ Hx: None

SUD: Glass of wine with dinner

FHx: unremarkable

PE: unremarkable **LAB:** normal TSH

ROS: middle insomnia, loss of appetite, difficulty concentrating at work,

MSE: depressed mood, intense pangs of sadness, crying spells, No suicidal ideation, no guilt, no worthlessness, no psychotic symptoms

CASE 6 – Acute Grief

Acute Grief – ICD 10 43.20
Yearning for and Persistently Missing the deceased-
Emotional Pain
some improvement at 6-12 months
Less severe than depression, but suffering is significant
≠ Depression –
Controversy – pathologizing or over-medicalizing vs missing patients with treatable disorder –
'I wish God would take me' vs. 'I want God to take me'
"Is grief a disease?" - George Engel MD

CASE 6 – Acute Grief

- Human CNS – hardwired for attachment – relationships are central to our feeling of well-being and belonging.
- Attachment is Central to Health
- Losses Accumulate – 'Freud's Law of the Heart'
- ''Grief is a form of Love" a continuation of lost relationship
  - M. Katherine Shear MD – Columbia University
- Acute Grief has all the symptoms of major depression except worthlessness and suicidal ideation

  (Aaron Lazare MD 1978)
- Natural History – Acute Grief → Integrated Grief
- Prognosis without Treatment – good,
  - Acute Grief → Integrated Grief for ~85-90%.
  - but 10-15% develop complicated grief

CASE 6 – Acute Grief

6 Month Follow Up

"A little better…but I miss her so much.'

Sleeping normally, appetite returned, no SI

Psychologist – declines referral, 'I can deal with this'

Bereavement Support Group

- 'If you don't deal with grief, grief will deal with you…if you try to avoid it , it will find you,
- 'I kept my grief buried deep inside, where it would do the most harm.
- I realize that I am forever changed, you don't get over it, you just learn to live with it, incorporate it into who you are

CASE 6 – Complicated Grief

Complicated Grief - ICD 10 43.21

- Persistent, Problematic, Severe grief reaction
- does not abate over time
- ≤ 15% of bereaved individuals = ~ 1 Million New Cases/Year in USA
- ≠ Depression – but some patients with grief are depressed
  - different core symptoms - Yearning for and Missing Deceased
  - no response to AD
- But impairment may be severe – suicide, Substance Use Disorder
- Complicated – Elements of Depression, PTSD, Addiction
- Untreated Course – Chronic and Unremitting
- Responds to Evidence Based Psychotherapy (e.g. Complicated Grief Treatment CGT > IPT or CBT)
- Ongoing Research comparing CGT to combined CGT and AD Meds
- Reference: http://complicatedgrief.org/

CASE 6 – Complicated Grief

Complicated Grief (CG)

- Nosology in Flux
  - DSM V (Provisional) 'Persistent Complex Bereavement Disorder (PCBD)
  - ICD 11 – 'Prolonged Grief Disorder' (PGD)
- Intense Grief that is Persistent, Pervasive and Produces Impairment
- Unrelenting Pain
- 'Not Knowing What is happening
- A World Defined by Absence

http://complicatedgrief.org/

CASE 6 – Complicated Grief

Complicated Grief (CG)

- NEJM - http://www.nejm.org/toc/nejm/372/2 pp 153-160
- Complicated Grief
- M. Katherine Shear, M.D.
- N Engl J Med 2015; 372:153-160January 8, 2015DOI: 10.1056/NEJMcp1315618

- Share:
- Complicated grief is intense grief after the death of a loved one that lasts longer than expected according to social norms and causes functional impairment. Psychotherapy directed at the loss and at restoring activities and effective functioning is recommended.

http://complicatedgrief.org/

CASE 6 – Complicated Grief

Unrelenting Pain

- We use the term “complicated” to mean that something is getting in the way of coping with the death of a loved one. When grief is complicated the pain can be unrelenting and life seems empty of any possibility for happiness. We want to help lessen the pain. We want to make it possible to honor grief as a form of love.
- See more at: http://complicatedgrief.org/#sthash.R3twTK2d.dpuf

http://complicatedgrief.org/

CASE 6 – Complicated Grief

Not Knowing What is Happening

- Even though bereavement is a universal human experience, acute grief is often a disconcerting experience that is unique to each person and each loss.
- We want to help you understand how grief emerges naturally after a loss and seeks its rightful place in ongoing life and how to recognize and deal with complications that can stall or halt this process. –
- See more at: http://complicatedgrief.org/#sthash.R3twTK2d.dpuf

http://complicatedgrief.org/

CASE 6 – Complicated Grief

A World Defined by Absence

- One of the difficult things about complicated grief is the feeling that everything in life is infused with a sense of absence and return of the deceased person is all that could relieve the pain. We want to help people find ways to restore meaningful connections to others, a sense of purpose and the possibility for happiness.
- See more at: http://complicatedgrief.org/#sthash.R3twTK2d.dpuf

http://complicatedgrief.org/

CASE 7

ID: 58 MWM, lives with second wife, 4 adult children, employed as assistant to CIO for a regional bank. No Legal Hx

HPI: increasingly depressed over the past 4 weeks, cautioned at work for lateness; 'I'm depressed, so I drink more.'

Past Ψ Hx: None

SUD: heavy binge drinker since college, now daily 1 ½ pints of Vodka, describes himself as a 'social drinker' – no legal problems related to Alcohol

FHx: Both parents have alcoholism, father died of cirrhosis, 3 of 4 siblings have alcoholism

ROS: middle insomnia, mid-epigastric pain

PE: ruddy complexion, BP 155/95

LAB: BAL=349 6 weeks ago in ED after a fall

MSE: depressed, irritable, SI without plan, no delusions

CASE 7 – Alcohol Use Disorder (AUD)

- DSM–IV described two distinct disorders, alcohol abuse and alcohol dependence, with specific criteria for each.
- DSM–5 integrates the two DSM–IV disorders, alcohol abuse and alcohol dependence, into a single disorder called alcohol use disorder (AUD) with mild, moderate, and severe sub-classifications.
- Legal Criterion eliminated in DSM-5
- Craving Criterion added in DSM-5
- 2/11 Criteria = AUD
- Mild = 2-3 Moderate = 4-5 Severe= 6+

CASE 7 – Alcohol Use Disorder (AUD)

- The causal vector points Alcohol → Symptoms and not the other way around
- Treat the Alcoholism, when drinking ceases, depressive symptoms get better ~7-14 days
- SSRI may make Alcoholism worse in some patients
- Naltrexone, Campral, Antabuse, Baclofen, Topiramate, Varenicline – all effective for some patients
- Gabapentin very helpful for anxious alcoholics
- At 3 AA meetings/week 98% of people are sober
  (John Kelly PhD MGH)

SUMMARY

- Depressive Symptoms are common and occur in many medical syndromes– not all of them reflect depression
- Antidepressant Medications can be very helpful, indeed life-saving, but can also harm
- Ron Fegelman MD
- Sir William Osler – 'To see patients without reading books is to set sail on uncharted seas, but to read books without seeing patients is never to leave the harbor.'
- You have all already left the harbor…

CASE 8 – Borderline D/O

ID:
HPI:
Past ψ Hx:
SUD:
PE:
LAB:
MSE: