



INTEGRATIVE MEDICINE APPROACH TO DEPRESSION & ANXIETY

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DISCLOSURES

- No financial or other disclosures to make

OUTLINE

- Case Presentations
- Background
- Review of Standard Treatments
- Herbs & Supplements
- Other Modalities
- Back to the Cases

CASE 1: SL

- HPI: 41yo healthy female presenting for consultation regarding anxiety, panic attacks, PTSD, and fatigue
- History of physical abuse from brother (8-11yo) and sexual / emotional abuse from ex-boyfriend (25-35yo)
- Developed symptoms of weekly panic attacks, PTSD, and anxiety in 2013
- Treatments:
 - CBT & Mindfulness-based yoga program in 2014
 - Started on Zoloft 50 mg and it helped, but has since discontinued
 - Xanax as needed, uses rarely
 - Currently sees a therapist weekly
- Now in a new relationship and symptoms worsening, would like to know other options
- Also with worsening tension / aches and pains in shoulders and neck, would like recommendations
- PHQ-9 10, GAD-7 12

CASE 2: JN

- 46yo female w/ history of migraines, insomnia, and depression previously on Celexa (discontinued 1 year ago) presents for worsening depression & anxiety
- Reports baseline “anxiety & irritability.” Celexa helped, but felt sluggish & worse in some ways – flat affect, less productive at work
- Symptoms gradually worsening since d/c Celexa
- Snapping at kids and husband for small things, like wrapping presents too slowly
- Tried CBT, did not like it / not helpful
- No current exercise. Diet is OK



- ROS:
 - Frequent nighttime awakenings; cannot fall back to sleep
 - Hot flashes intermittently and worsening
- PHQ9: 4
- GAD7: 18

CASE 3: MR



- 23yo male with worsening depression, lack of energy, over-sleeping
- Low self-esteem, has difficulty leaving home. Still functioning OK at work; reports good social support. Lives at home with parents.
- Otherwise healthy. Not on any medications. Does not want to start SSRI due to concern for sexual side effects
- Not in therapy; has not tried other therapies
- ROS: Otherwise negative
- PHQ9: 20
- GAD7: 6

CASE 4: DS

- DS is a 43yo male presenting for anger / irritability issues
- Upset because he is snapping at his wife for “silly things” like dishes or clutter around the home. Also with stress at work, struggling with insomnia
- Has never been seen for depression or anxiety before, but would like treatment
- Lifestyle: Healthy diet, exercises most days during week but less lately. Lives with wife and children
- ROS otherwise negative.
- PMHx: HTN and gout. On Lisinopril and allopurinol
- PHQ9: 12
- GAD7: 15

CASE 5: JT

- JT is a 76yo female presenting for several vague concerns and is requesting labs to find cause:
 - Change in bowel habits – some increased urgency and has to go after meals
 - Decreased appetite in the morning
 - Cold intolerance
 - Energy crash and fatigue in afternoons
- Significant history of loss and grief.
 - Her husband passed away five years ago and the anniversary is next week (always a hard time of year).
 - Her brother passed away in December 2017, and also two other recent deaths of people she knew well (a close friend, and a previous client)
- PMHx: Essential HTN and BPPV.
- Social History: Retired, lives alone. Previously worked as psychotherapist and as a nurse. Has good friends who she spends time with weekly

BACKGROUND: DEPRESSION

DSM 5 Criteria: At least 5 of 9 symptoms present most days over 2 weeks period

- 1) Depressed mood most of the day
- 2) Diminished interest or pleasure in activities
- 3) Decrease or increase in appetite
- 4) Insomnia or over-sleeping
- 5) Psychomotor agitation or slow movements
- 6) Fatigue or loss of energy
- 7) Feelings of worthlessness or inappropriate guilt
- 8) Difficulty concentrating, or indecisiveness
- 9) Recurrent thoughts of death / SI

DSM 5 – Major Depressive Disorder

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: _____ DATE: _____

Over the last 2 weeks, how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
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	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3

add columns + +

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. If you checked off <i>any</i> problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all	_____
	Somewhat difficult	_____
	Very difficult	_____
	Extremely difficult	_____

BACKGROUND: ANXIETY

DSM5 for Generalized Anxiety Disorder (GAD), 3 or more of 6 symptoms for most days over 6 month period

- 1) Restlessness, feeling “on edge”
- 2) Easily fatigued
- 3) Difficulty concentrating
- 4) Irritability
- 5) Muscle tension
- 6) Sleep disturbance

GAD-7

Over the <u>last 2 weeks</u> , how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

Total Score — = Add Columns — + — + —

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all

Somewhat difficult

Very difficult

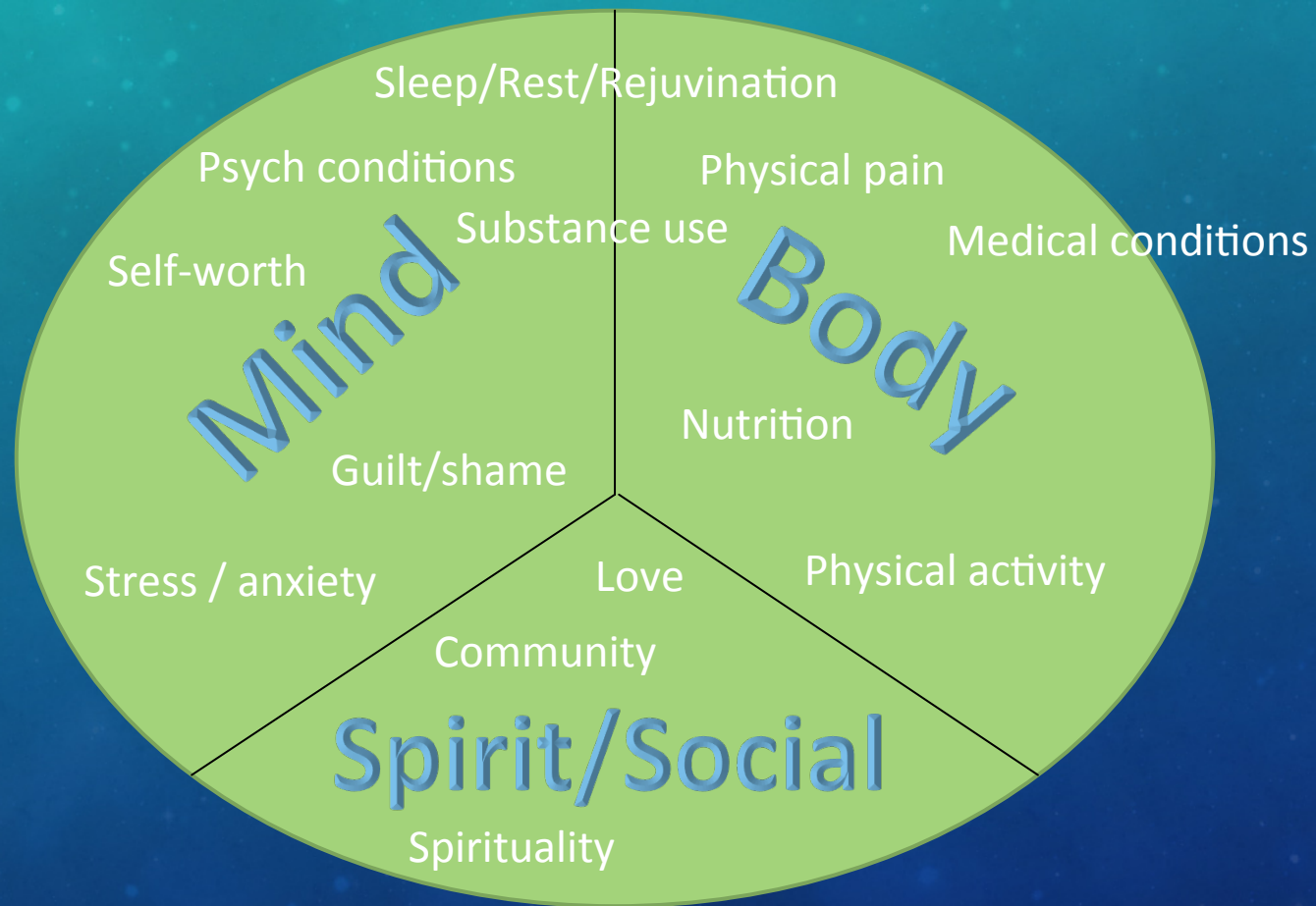
Extremely difficult

BACKGROUND: DEPRESSION & ANXIETY

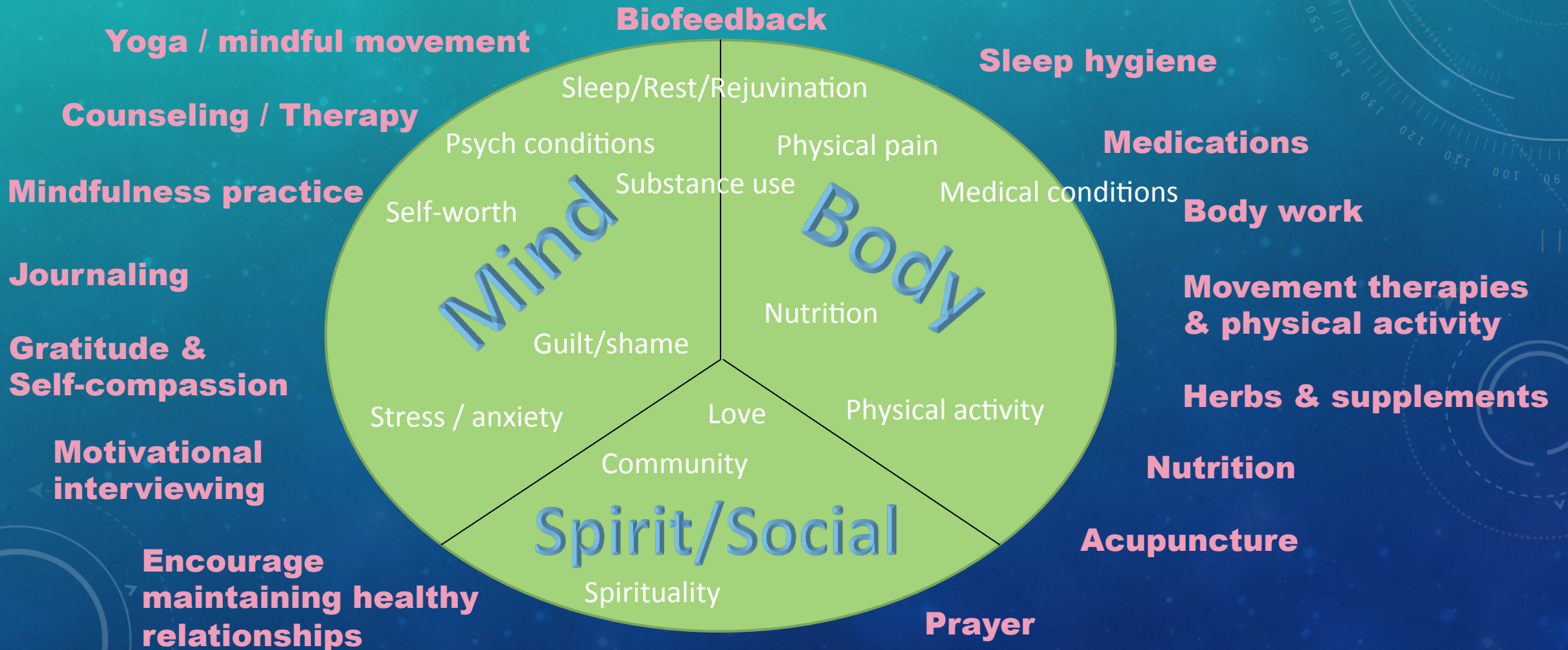
- Depression & Anxiety are often comorbid and exist together along a spectrum
- Very common
 - Adult U.S. Prevalence: 10% for depression, 18.1% for anxiety disorders
 - Over 100 million prescriptions annually for antidepressants
 - Common condition for which integrative and alternative therapies desired
- Subtypes are common
 - Depression: Dysthymia (persistent mild depression), Seasonal Affective Disorder
 - Anxiety: GAD, OCD, Panic Disorder, Phobias, PTSD
- Individuals with depression & anxiety seek primary care services at higher rates than others
- Psychosomatic symptoms are common (GI, headaches, palpitations)

CDC: Prevalence of Depression Among Adults Aged 20 and Over: United States, 2013–2016.

INTEGRATIVE MODEL



INTEGRATIVE MODEL



LIFESTYLE: EXERCISE

- Several studies demonstrate that exercise is as effective as antidepressants or psychotherapy, and superior in preventing recurrence of depression (1, 2)
- Exercise + medications are more effective than either alone
- Total energy expenditure more important than times per week. Benefit for aerobic and anaerobic exercise
- High intensity work-outs superior to low-intensity (3)
- **BOTTOM LINE:** Write an exercise prescription for all patients; tailor the type of exercise to something the patient enjoys. Best to diversify exercises with aerobic, anaerobic, and stretching.



LIFESTYLE: NUTRITION

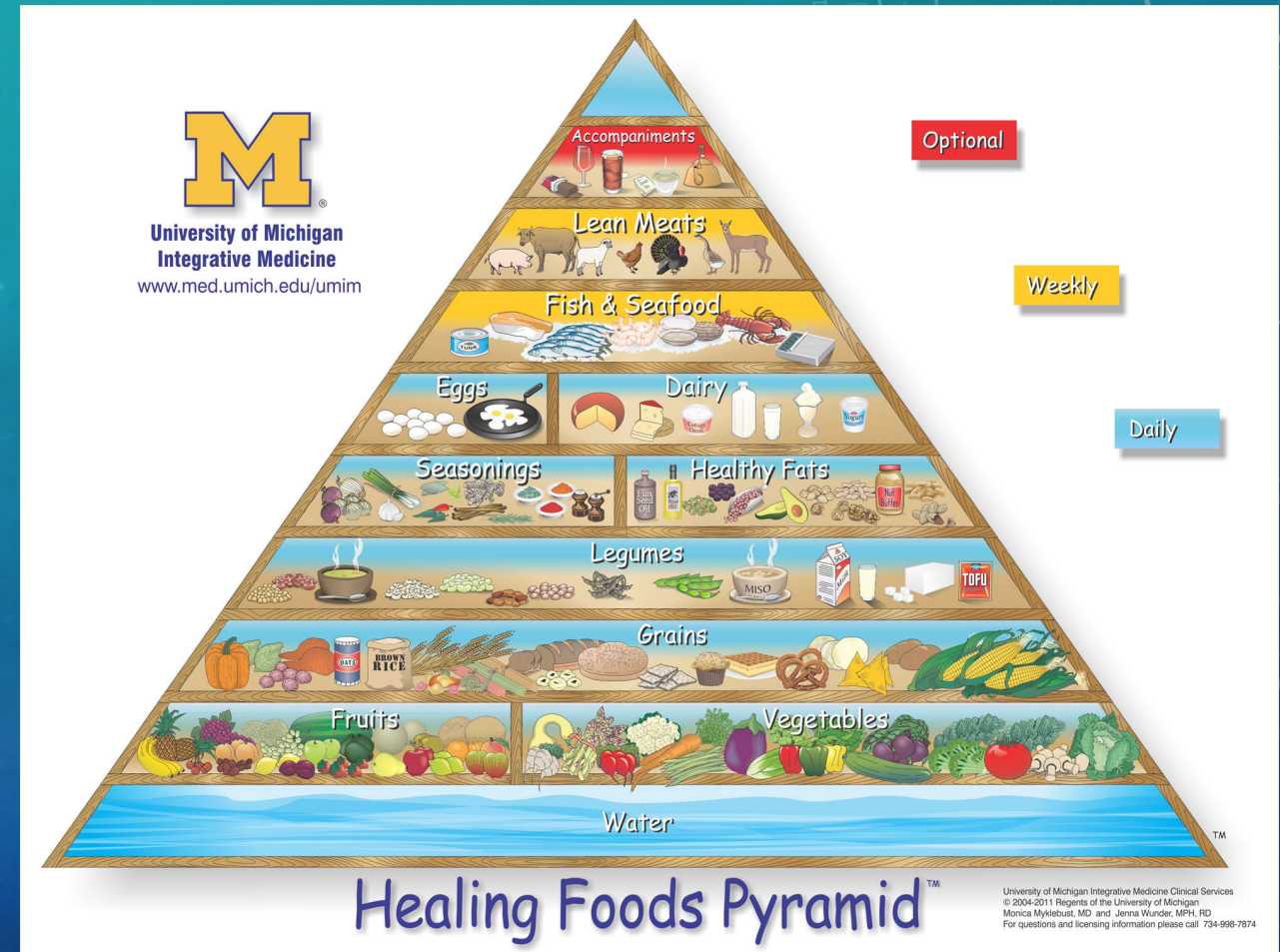
1) Limit simple sugars & alcohol

- Increased consumption of simple sugars and processed foods in depressed & anxious individuals (1)
- Alcohol problems more common in depression & anxiety, and reduction improves symptoms

2) Mediterranean-style diet > Western diet

3) Improve omega 3 : omega 6 ratio through diet and/or supplementation.

- Supplement: >60%EPA, aim for at least 1000 mg combines EPA + DHA daily. Consumption of 2-3 servings of cold-water fish (herring, mackerel, salmon, sardines) weekly is comparable



1. Westover AN, Marangell LB. A cross-national relationship between sugar consumption and major depression. 2. Peet, D.F. Horrobin: A dose-ranging study of the effects of ethyl-eicosapentaenoate in patients with ongoing depression despite apparently adequate treatment with standard drugs.

MEDICATIONS

- SSRI Medications

- 1) Fluoxetine (Prozac) 20-80 mg / day
- 2) Sertraline (Zoloft) 50-100 mg / day
- 3) Citalopram (Celexa) 20-60 mg / day
- 4) Escitalopram (Lexapro) 5-20 mg / day
- 5) Paroxetine (Paxil) 20-60 mg / day

- First-line for treatment of depression and anxiety
- Common side effects:
 - GI side effects when first starting medication, usually improves with time
 - Sexual side effects
 - Drowsiness, insomnia, worsening agitation

MEDICATIONS

- Serotonin Norepinephrine Reuptake Inhibitors (SNRI)

- 1) Venlafaxine (Effexor) 75-375 mg / day
 - Similar side effects as SSRI, less sexual side effects
 - Best for: failed SSRI, comorbid menopausal symptoms (hot flashes), or comorbid anxiety
- 2) Duloxetine (Cymbalta) 20-60 mg / day
 - Best for: failed SSRI or comorbid chronic pain

- Dopamine Norepinephrine Reuptake Inhibitors

- 1) Bupropion (Wellbutrin) 150-450 mg / day
 - Most activating; good for low-energy, apathetic patient
 - Can combine with SSRI

- Serotonin & alpha-2 receptor blocker

- 1) Mirtazapine (Remeron)
 - Promotes sleep and increases appetite / weight gain

PSYCHOTHERAPY

- Useful as monotherapy, and more beneficial than medication alone for depression and anxiety
- Meta-analysis evaluated for differences between seven different types of psychotherapy for mild-moderate depression and found all were helpful with no statistically significant differences:
 - Cognitive-behavior therapy
 - Nondirective supportive treatment
 - Behavioral activation treatment
 - Psychodynamic treatment
 - Problem-solving therapy
 - Interpersonal psychotherapy
 - Social skills training

SUPPLEMENTS & BOTANICALS: ST. JOHN'S WORT

- Flowering plant that grows in temperate regions worldwide. Used for centuries to treat depression
- Mechanism of action:
 - Affects serotonin, dopamine, norepinephrine, and GABA reuptake inhibitors
 - Inhibits IL-6 and increases cortisol production
 - In vitro: affects monoamine oxidase and L-glutamate
 - Clinical effect is likely summative of multiple weak mechanisms



SUPPLEMENTS & BOTANICALS: ST. JOHN'S WORT

- **Safety:** Generally safe. Main precaution is with CYP3A4 induction. Precaution with several drugs: macrolide antibiotics, HIV drugs, benzodiazepines, CCBs, statins, contraceptives, warfarin
- **Side effects:** Much less than SSRIs. GI and headaches most common
- **Cochrane Review 2008:** Superior to placebo and as effective as standard antidepressants (SSRI) for major depression, with fewer side effects
- **Dosing:**
 - General dosing range 900-1200 mg daily
 - Start 300 mg or 450 mg daily & increase every 3-5 days to goal dose of 300 mg TID or 450 mg BID
 - Avoid after 6pm, can be activating
 - Standardized to 0.2%-0.3% hypericin, or 3-5% hyperforin



SUPPLEMENTS: RHODIOLA ROSEA

- Traditional medicine cultures have used Rhodiola rosea as an herb to promote work endurance, resistance against fatigue, depression, and other conditions
- May enhance mood via effects on central biogenic amines and endorphins
- May stimulate norepinephrine, serotonin, dopamine, and acetylcholine receptors in brain
- Good safety profile



SUPPLEMENTS: RHODIOLA ROSEA

- High-quality RCT compared Rhodiola versus sertraline 50 mg for mild-moderate depression and found both better than placebo, and equally effective
- Rhodiola with fewer side effects and smaller drop-out rate
- Dosing: 200-400 mg 1-2 times daily
- Side effects: anxiety / jitteriness



SUPPLEMENTS: S-ADENOSYLMETHIONINE (SAM-E)

- SAME: Methyl-donor involved in production of norepinephrine, dopamine, and serotonin
- Evidence: Small studies demonstrate effectiveness. Some show no benefit over placebo (1-2)
- Safety: Extremely safe; though caution use with SSRIs due to similar mechanism
- Side effects: minor; can cause nausea/diarrhea
- Dosing: Goal dose of 800 mg twice daily. Start 200 mg twice daily and increase over 2 weeks



1. R. Delle Chiaie et al: Efficacy and tolerability of oral and intramuscular S-adenosyl-L-methionine 1,4-butanedisulfonate (SAME) in the treatment of major depression: comparison with imipramine in 2 multicenter studies. 2. Mischoulon, L.H. Price, L.L. Carpenter, et al.: A double-blind, randomized, placebo-controlled clinical trial of S-adenosyl-L-methionine (SAME) versus escitalopram in major depressive disorder.

SUPPLEMENTS: HYDROXYTRYPTOPHAN (5-HTP)

- 5-HTP is a precursor to serotonin, and likely works similarly to SSRIs with fewer side effects
- Evidence: Cochrane review found only 2 of 108 trials of sufficient quality, but both showed 5-HTP superior to placebo (1)
- Generally safe; caution with SSRIs
 - Case reports of eosinophilia-myalgia syndrome in patients taking 5-HTP, which is what caused L-tryptophan to come off-market in 1989. Believed to be due to contaminants (2)
- Side effects: GI side effects most common
- Dosing: 50-300 mg TID. Start at 50-100 mg and go up from there



SUPPLEMENTS: L-THEANINE

- L-Theanine
 - Amino acid found in green tea
 - Antagonist to glutamate, an excitatory neurotransmitter
 - Increase alpha-waves, creating state of “relaxed alertness”
 - Increase dopamine levels and reduce norepinephrine levels in brain
 - No high-quality studies about L-Theanine for anxiety disorders



SUPPLEMENTS: VALERIAN ROOT

- Botanical that has been utilized in Europe for anxiety for hundreds of years
- Anecdotally useful for acute anxiety and insomnia
- May take several weeks to see full benefit
- No high-quality studies showing benefit
- Dosing: 300-450 mg at night or divided BID



SUPPLEMENTS: KAVA (PIPER METHYSTICUM)

- Botanical option to treat GAD
- Derived from pulverized roots of subspecies of pepper plant
- Recognized by health authorities in Europe as relatively safe remedy for anxiety
- Meta-analysis: 6 RCTs found kava to be superior to placebo in symptomatic treatment of GAD
- Mechanism of action: Unclear. Likely combination of GABA receptors and limbic system (amygdala, hippocampus)
- Dosing: 50-70 mg purified extract TID PRN



SUMMARY OF SUPPLEMENT RECOMMENDATIONS

Supplement	Specific Indication	Dosing
St. John's Wort	Depression and/or Anxiety	Start: 300 mg or 450 mg daily and increase over 3-5 days to 300 mg TID or 450 mg BID
SAM-E	Depression and/or Anxiety	Goal dose 800 mg twice daily Start 200 mg twice daily and increase over 2 weeks
5-HTP	Depression and/or Anxiety	50-300 mg three times daily
Rhodiola rosea	Depression, low energy, fatigue	200-400 mg 1-2 times daily Start with once daily dosing, and avoid after 6pm
L-Theanine	Anxiety	250-500 mg up to TID
Valerian Root	Anxiety, insomnia	300-450 mg at night or divided BID
Kava	Anxiety	50-70 mg purified extract TID PRN

SUPPLEMENTS: OTHER

- Magnesium (200-800 mg daily):
 - Helpful for anxiety with comorbid headaches, fatigue, fibromyalgia, constipation
 - No high-quality studies for depression/anxiety
- B-Vitamins & Folate (400-1000 mcg daily)
 - Methyl donors for brain neurotransmitters and synthesis of SAMe and serotonin
 - Large-scale studies are lacking
- Vitamin D (1000-2000 IU daily)
 - Deficiency associated with 8-14% increase in depression
 - Meta-analysis concluded that vitamin D supplementation improved depression symptoms



OTHER THERAPIES - YOGA

- 2013 systematic review and meta-analysis (12 RCTs, 619 subjects) on yoga for depression (1)
 - Short term improvements in depression compared to usual care, relaxation, or aerobic exercise
 - Meditative yoga subgroup had most significant effect vs exercise or complex yoga groups
- 2015 review on yoga for prenatal depression
 - Yoga superior to standard prenatal care, antenatal exercise groups, and social support for depression scores in depressed and non-depressed pregnant women
 - Integrated yoga (with meditation) superior to exercise-based yoga



OTHER THERAPIES

- Mindfulness Meditation & Mind-Body Medicine
 - Active participation of individual to learn from their symptoms compared to passive process of taking medication or supplement
- MBSR & MBCT
 - 8-week courses (2 hours weekly) that focus on allowing distressing emotions, thoughts, and sensations to come and go without grasping onto the need to suppress, fight, or escape them
 - MBCT is specifically designed for depression
 - Useful for treatment and to prevent recurrences



OTHER THERAPIES

- Biofeedback
 - A type of therapy that teaches a person to change and control physiological processes through practice with immediate feedback
 - Heart-rate variability, EMG, neurofeedback
 - Useful for situational stress, panic attacks, specific phobias, depression and GAD (1)
- Acupuncture
 - UN WHO: Safe monotherapy for depression
 - Cochrane Review: Insufficient evidence to make recommendation (2)
- Phototherapy
 - 30-60 minutes of bright, white light (10,000 Lux)
 - Superior to placebo, and effective as adjunctive therapy (3)
 - Safe and low-cost option



1. Glick RM, Greco CM. Biofeedback and Primary Care. 2. C.A. Smith, P.P. Hay, H. Macpherson: Acupuncture for depression. *Cochrane Database Syst Rev.* (1): 2010. 3. Rakel D: Integrative Medicine, 4th edition. 2017

CASE 1 SL: TREATMENT PLAN

- HPI: 41yo healthy female presenting for consultation regarding anxiety, panic attacks, PTSD, and fatigue
- Lifestyle:
 - Continue regular exercise most days per week for 30 minutes or more
 - Maintain and foster healthy relationships
 - Continue mindfulness practices (yoga, meditation)
 - Heartmath.org, biofeedback resource
- Nutrition:
 - Mediterranean-style diet; Continue to avoid triggers
- Supplements:
 - Theanine Serene by Source Naturals (Theanine 200 mg, GABA 500 mg, Magnesium 300 mg, Taurine, Holy Basil Leaf). 1-2 capsules 2 times daily as needed for anxiety (instead of Xanax)
 - Turmeric 400-500 mg as needed for joint pain
- Pharmaceuticals:
 - Restart Sertraline 50 mg daily. Start 25 mg for 1 week then increase to 50 mg daily

CASE 1 SL: UPDATE 6 MONTHS LATER

- Doing well. Theanine was helpful and no longer using benzodiazepines
- Still seeing therapist weekly
- Still maintaining mindfulness techniques
- Engaged and considering pregnancy. Had messaged through the portal and I suggested stopping supplements due to lack of data in pregnancy
- Patient began slow wean off Zoloft as well, now taking $\frac{1}{4}$ tablet daily. Symptoms returning a bit



CASE 1 SL: UPDATE 6 MONTHS LATER

- Supplements & Anti-Depressants in Pregnancy:
 - Most supplements for depression recommended against due to lack of data
 - SSRIs are Category C, but risk considered low
 - Risks of untreated depression / anxiety in pregnancy include low birth weight, preterm delivery, poor nutrition, reduced adherence to prenatal care, and suicide
 - Ideally should be discussed before conception



CASE 2: JN TREATMENT PLAN

- 46yo female w/ history of migraines, insomnia, and depression previously on Celexa (discontinued 1 year ago) presents for worsening depression & anxiety
- Also with hot flashes in the evening
- Checked TSH - normal
- Effexor: Start at 37.5 mg and go up by 37.5 mg weekly to goal of 150 mg daily
- Theanine Serene twice daily
- Continue regular exercise, healthy diet
- Information given on mindfulness apps and book resources
- Discussed sleep hygiene

CASE 2: JN TREATMENT PLAN

- 6-month update
 - Initially doing great with this plan
 - 2nd follow-up: Felt “too chill.” Now GAD-7 of 0, but PHQ-9 of 8, with low motivation
 - Updated plan: Stop theanine and reduce Effexor to 75 mg daily
 - 3rd follow-up: Doing great, PHQ9 & GAD7 of 0
- Checked TSH - normal
- Effexor: Start at 37.5 mg and go up by 37.5 mg weekly to goal of 150 mg daily
- Theanine Serene twice daily
- Continue regular exercise, healthy diet
- Information given on mindfulness apps and book resources
- Discussed sleep hygiene

CASE 3: MR TREATMENT PLAN

- 23yo male with worsening depression, lack of energy, over-sleeping
- Wants to avoid SSRI due to side effects
- Lifestyle: Need to pursue something in terms of hobbies and exercise. Encouraged leaving the house for walks outdoors – most days per week. Discussed light box for SAD. Healthy diet.
- Medications/Supplements:
 - St. John's Wort
 - 300 mg for 5 days, then 300 mg BID, then 600 mg in morning and 300 mg in evening. Increase to 600 mg twice daily and follow-up
- Meet with SW for psychotherapy

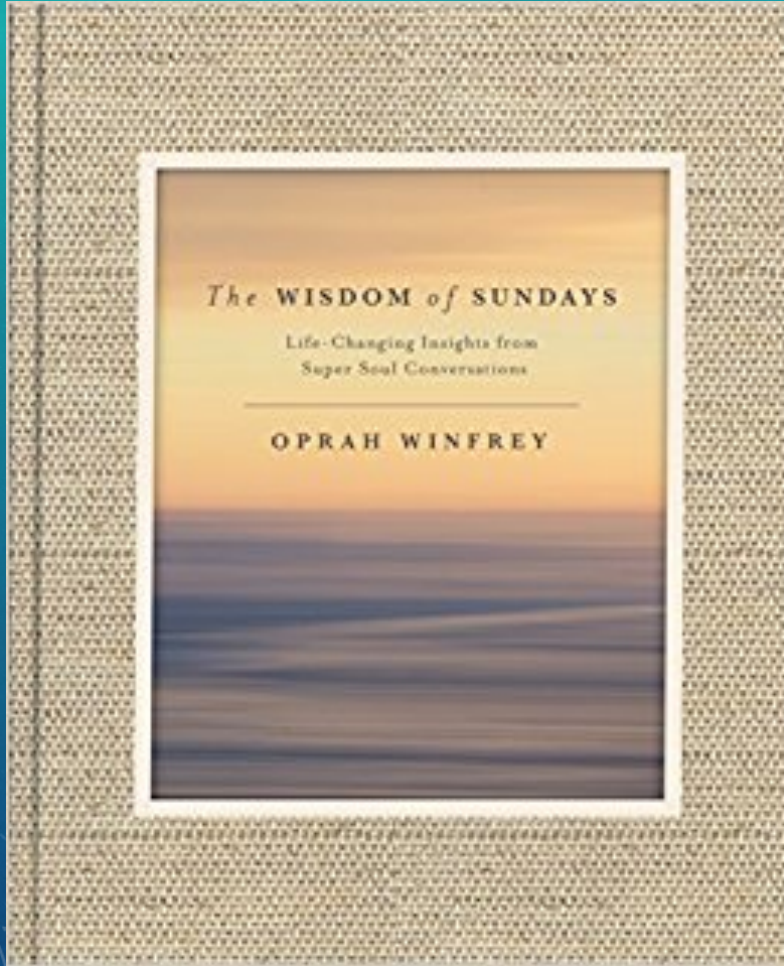
CASE 4: DS TREATMENT PLAN

- DS is a 43yo male presenting for anger / irritability issues with symptoms of mild depression, significant anxiety/irritability, and insomnia
- Medications: Lexapro, start 5 mg daily and increase to 10 mg after 6 days
- Melatonin for sleep: 3-10 mg at night
- Lifestyle: Increase exercise to more days during the week at gym. Discussed sleep hygiene
- Therapy: Meet with SW for psychotherapy

CASE 5: JT TREATMENT PLAN

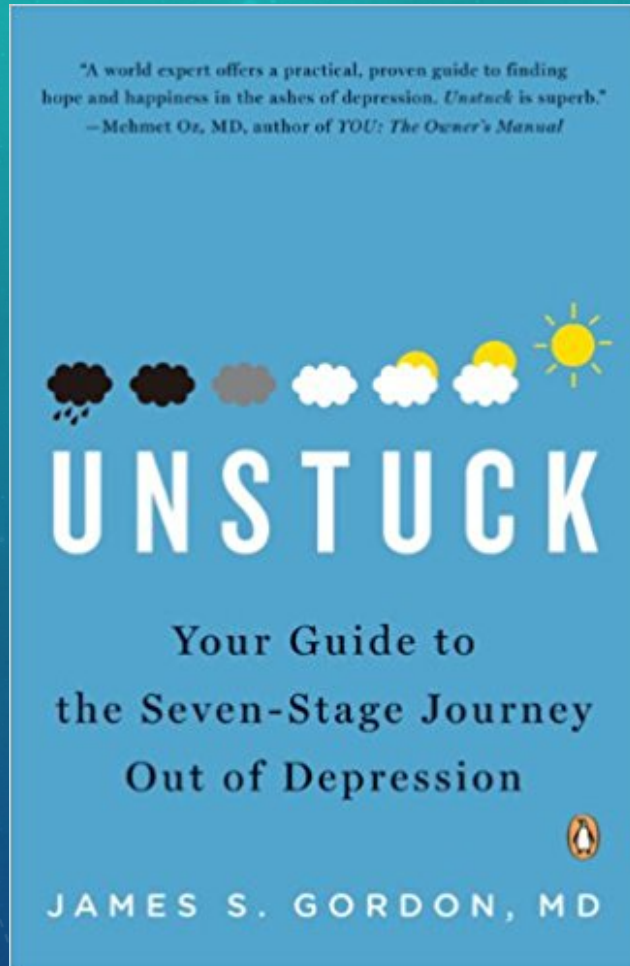
- JT is a 76yo female presenting for several vague concerns and is requesting labs to find cause:
 - Change in bowel habits – some increased urgency and has to go after meals
 - Decreased appetite in the morning
 - Cold intolerance
 - Energy crash and fatigue in afternoons
- Review of mental health and stressors:
 - Significant history of loss and grief. Her husband passed away five years ago and the anniversary is next week (always a hard time of year). Her brother passed away in December 2017, and also two other recent deaths of people she knew well (a close friend, and a previous client).
- Work-up: TSH, CBC, CMP, iron studies: all normal
- Discussed with patient that vague symptoms of fatigue, decreased appetite, change in bowel patterns may be related to mild depression and grief. Patient receptive to this idea
- Discussed options and patient elected for psychotherapy
- Recommended staying social and active, avoiding isolation
- Recommended book on spirituality: “The Wisdom of Sundays” compiled by Oprah Winfrey

RESOURCES



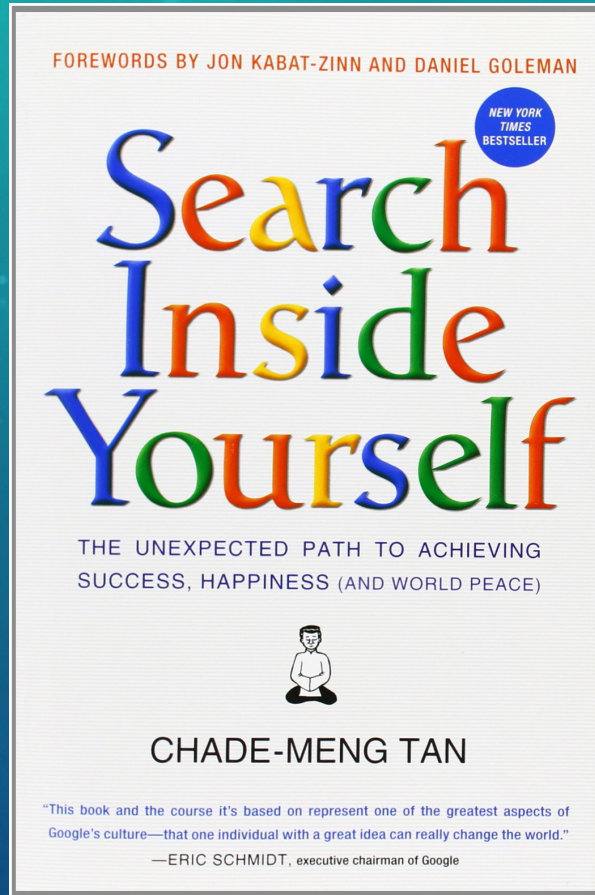
- Excerpts from inspirational conversations with thought leaders from various fields
- CHAPTERS
 - Awakening
 - Intention
 - Mindfulness
 - Spiritual GPS
 - Ego
 - Forgiveness
 - Broken Open
 - Grace & Gratitude
 - Fulfillment
 - Love & Connection

RESOURCES



- Guidance by psychiatrist James Gordon on a seven-stage program for depression symptoms - through food and nutritional supplements; Chinese medicine; movement, exercise, and dance; psychotherapy, meditation, and guided imagery; and spiritual practice.

RESOURCES



- Written by Google Engineer who pioneered mindfulness program at Google
- Provides methods to enhance emotional intelligence and mindfulness at work and at home
- Several guided meditation prompts

RESOURCES

- SMARTPHONE APPS:
 - Headspace
 - Insight Timer (free guided meditations)
 - Downward Dog (free guided yoga sessions)
 - Jon Kabat-Zinn series (JKZ 1, JKZ 2, JKZ 3)
 - 10% Happier (also a book by Dan Harris)

TAKE-HOME POINTS



- Management of depression and anxiety disorders takes a comprehensive, mind-body-lifestyle approach
- Treatment is unique to each individual, with tons of options. Doctor-patient relationship and patient buy-in and participation are important
- Start low and up-titrate on medications or supplements. Less likelihood of side effects and discontinuation with slow approach
- If not having success with one type of treatment, try changing it up
- Frequent follow-up is important when changing doses or starting new medication

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QUESTIONS?

