



Clinical Assessment of the Oncology Patient with Emotional Distress

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Disclosures

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.

Disclosures



Learning Objectives

- *Provide a framework that helps characterize mental distress*
- *Familiarize with somatic disorders associated with cancer care*
- *Learn tools that help structure the diagnosis of Psychiatric Disorders during Cancer*
- *Outline pharmacological guidelines*

*A Framework for
Cancer-Related Distress*



Framework for Distress

Definition of Cancer Related Distress

“A multi-factorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis.”

Framework for Distress

Importance of Acknowledging

- Addresses the core issue of stigma
- Normalizes the occurrence, the term is readily understood
- Facilitates communication and helps build trust
- It is inclusive and not limited to psychological problems



Framework for Distress

What causes distress

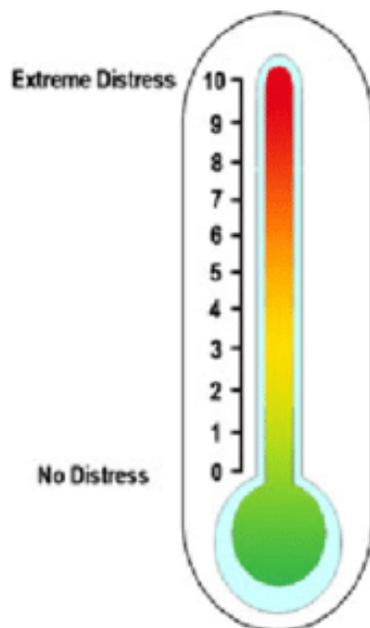
- **Diagnosis:** Cancer has a bad reputation
- **Treatment:** Fear of treatment, side effects
- **Relationships:** Children, communication, fears of being a burden
- **Practical problems:** Financial, housing, transportation
- **Spiritual and Existential concerns**



Framework for Distress

Measuring Distress

First please circle the number (0-10) that best describes how much distress you have been experiencing in the past week including today.



Second, please indicate if any of the following has been a problem for you in the past week including today. Be sure to check YES or NO for each.

YES NO Practical Problems

- Child Care
- Housing
- Insurance/financial
- Transportation
- Work/school

Family Problems

- Dealing with children
- Dealing with partner
- Dealing with close Friend/relative

Emotional Problems

- Depression
- Fears
- Nervousness
- Sadness
- Worry
- Loss of interest in usual activities

- Spiritual/religious concerns

YES NO Physical Problems

- Appearance
- Bathing/dressing
- Breathing
- Changes in urination
- Constipation
- Diarrhoea
- Eating
- Fatigue
- Feeling Swollen
- Fevers
- Getting around
- Indigestion
- Memory/concentration
- Mouth sores
- Nausea
- Nose dry/congested
- Pain
- Sexual
- Skin dry itchy
- Sleep
- Tingling in hands/feet

Other problems



Framework for Distress

Measuring is not Enough

- 50% of patients experience distress
- Great variability in tools used
- Without proper infrastructure, small number of patients receive care
- High prevalence also among family caregivers of patients with advanced cancer

Not seeing the forest for the trees: a systematic review of comprehensive distress management programs and implementation strategies. Current Opinion in Supportive and Palliative Care 14(3):p 220-231

Author	Referrals (% where reported)
Götz <i>et al.</i> 2019 [33]	One in four distressed patients agreed to a referral
Hamilton and Kroska 2019 [34]	24.5% of participants met the distress thermometer cut-off score, referral rates were not reported
Loth <i>et al.</i> 2018 [35]	Before this process, approximately 6% were successfully referred to psycho-oncology; with this process, 13.7% were successfully referred
Pearson and Melton 2020 [37 ^{***}]	Not available
Pichler <i>et al.</i> 2019 [38]	46.2% of all patients experienced elevated psychosocial distress, and 53.9% of those patients declined psychological support
Ploos van Amstel. 2019 [39 ^{***}]	25% of patients received a referral to a psycho-oncology service. Ten patients with anxiety and/or depression were referred to a psychologist. Nine patients with, for example, coping, family, or financial problems were referred to a social worker. One patient was referred to a sexologist. Three patients were referred to an expert center for cancer-related fatigue. Some patients had existing psychological support, which they continued during the study
Tondorf <i>et al.</i> 2018 [42]	Approximately 22% of all patients regardless of distress thermometer score accessed the psycho-oncology service

Framework for Distress

Factors affecting vulnerability

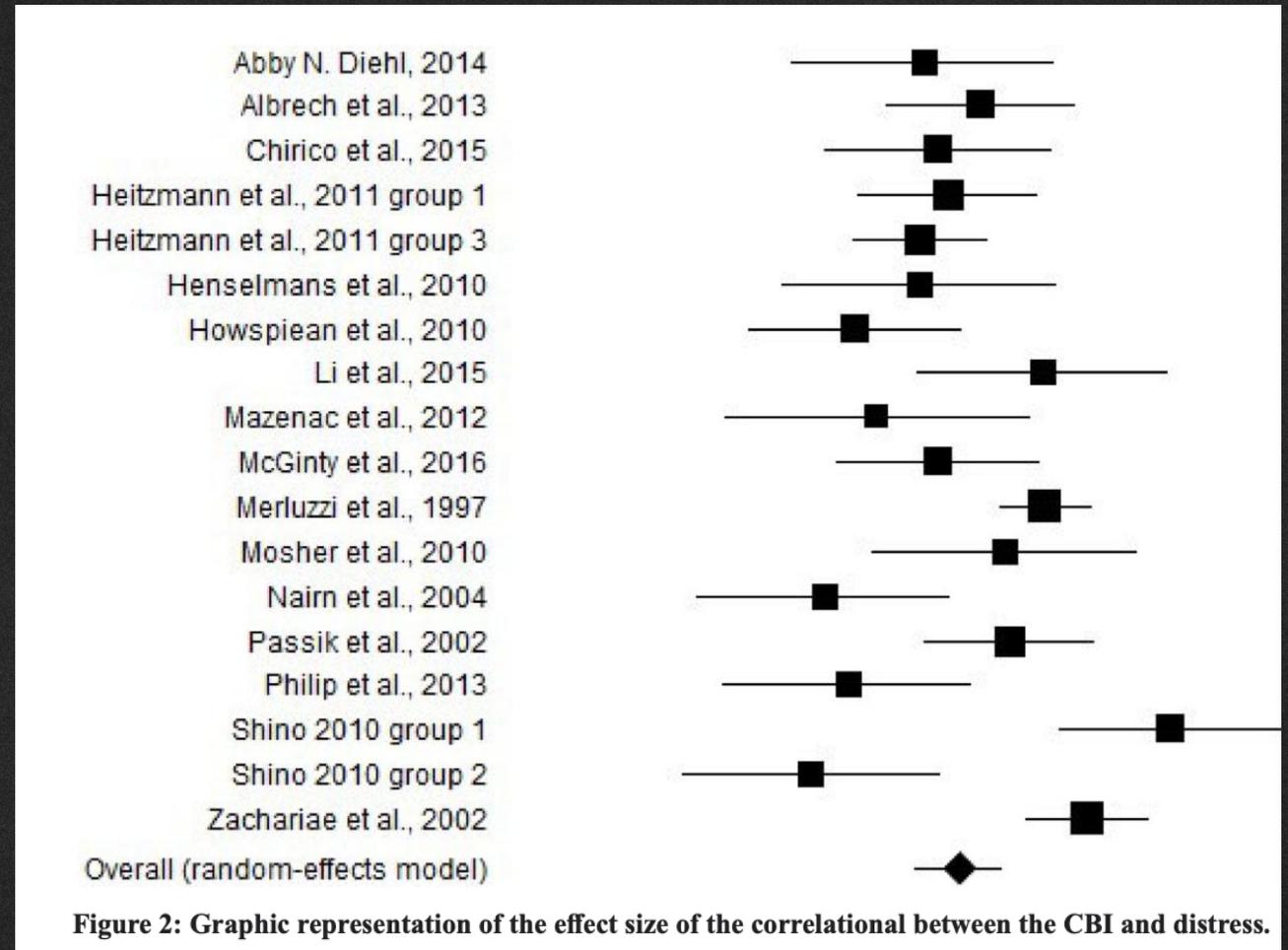
- Stage of emotional development
- Resilience and Self Efficacy
- Coping strategies
- Attachment style
- Psychosocial support



Framework for Distress

Factors affecting vulnerability

- Stage of emotional development
- Resilience and Self Efficacy
- Coping strategies
- Attachment style
- Psychosocial support



A meta-analytic review of the relationship of cancer coping self-efficacy with distress and quality of life.
Oncotarget. 2017; 8: 36800-36811.

Framework for Distress

Factors affecting vulnerability

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Framework for Distress

Factors affecting vulnerability

- Stage of emotional development
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Predictors	<i>b</i>
Depression	
Final model	
No. of physical symptoms	0.20
Secure vs. preoccupied	1.87
Secure vs. dismissing	-0.20
Secure vs. fearful-avoidant	3.57
Death anxiety	
No. physical symptoms	0.42
Secure vs. preoccupied	3.54
Secure vs. dismissing	2.89
Secure vs. fearful-avoidant	6.57

Insecure attachment predicts depression and death anxiety in advanced cancer patients. Palliative and Supportive Care, 16(3), 308-316

Framework for Distress

Factors affecting vulnerability

- Stage of emotional development
- Resilience and Self Efficacy
- Coping strategies
- Attachment style
- Psychosocial support



Framework for Distress

Helping the Distress Patient: Goals

- Improve communication, respect and trust
- Generate alternative coping strategies
- Help reclaim personal control
- Improve morale and self-esteem
- Help patient gain independence



Framework for Distress

Helping the Distress Patient: Basics

- Acknowledge distress and the experience
- Clarify diagnosis, Tx options and side effects
 - Ensure understanding
 - Educate and support through transitions
- Witnessing, Validation and Normalization
- Assist with problem solving
- Cognitive coping, reframing and modification
- Stress reduction and relaxation exercises

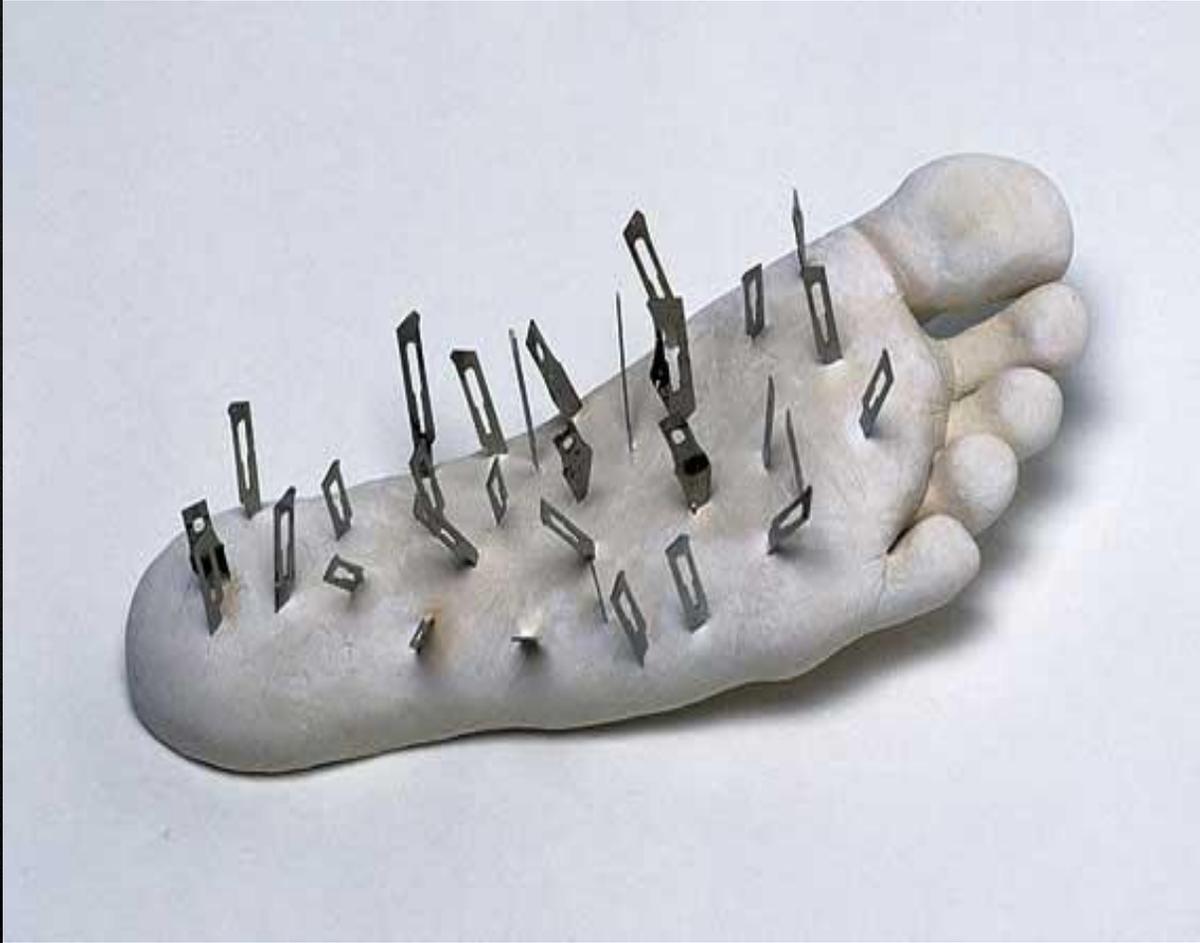


Physical Distress During Cancer



Physical Distress

Pain



- Most feared symptom
- Etiology and type of pain
 - Bone pain
 - Neuropathic pain
 - Pain from inflammation
 - Nerve compression
- Risk factors for under treatment: children, elderly, women, minorities, hx of PSA or psych
- Treatment: Opioid + Non-Opioid + Pain modulator + CBT

Physical Distress

Fatigue



- Most frequently reported, most distressing than pain, and most debilitating impact on functioning (Williams, 2016)
- Up to 77% of Individual with Cancer (Van Lancker A. 2014)
- NCCN recommends a one-item, 0-10 scale: “Since your last visit, how would you rate your fatigue on a scale of 0-10?”
- Treatment: CBT for Energy Mgt, Yoga, Graded Exercise, Stimulants

Physical Distress

Sleep

Table 1 Sleep and activity during putative daily wake span

Sleep and activity variable	Mean and standard error	
	Cancer patients (n = 33)	Reference population (n = 35)
Mean daily activity (min)	92.8 ± 5.63	127 ± 17.11
Mean activity during wakefulness (min)	117.5 ± 7.11	182.6 ± 25.08
Mean duration of sleep during wakefulness (min)	195.0 ± 25.03	46.5 ± 41.05
% of wakefulness spent sleeping	21.8 ± 2.93	4.7 ± 3.92
Number of sleep episodes during wakefulness	17.8 ± 1.82	5.4 ± 5.06

Table 2 Sleep and activity during putative daily sleep span

Sleep and activity variable	Mean and standard error	
	Cancer patients (n = 33)	Reference population (n = 35)
Frequency of long naps	9.5 ± 1.08	2.1 ± 1.96
Duration of wakefulness during night sleep (min)	134.1 ± 14.94	31.1 ± 21.53
Number of sleep interruptions nightly	14.6 ± 1.35	6.9 ± 4.52
% of sleep span actually spent sleeping	71.2 ± 3.09	93.0 ± 4.88
Nightly average duration of long sleeps (min)	112.5 ± 13.22	225.6 ± 100.8

Levin 2005

Physical Distress

Sexual Dysfunction



- Very high incidence, and little discussions about it
- Most commonly studied in breast and prostate cancer
- Factors affecting sexual function
 - Treatment related factors
 - Physical Changes
 - Psychological factors
- Sterility should be timely discussed

Illustration by

*Diagnosing Mental Disorders
In Cancer Patients*



Diagnosis

Challenges

ANXIETY

DEPRESSION

Terminology

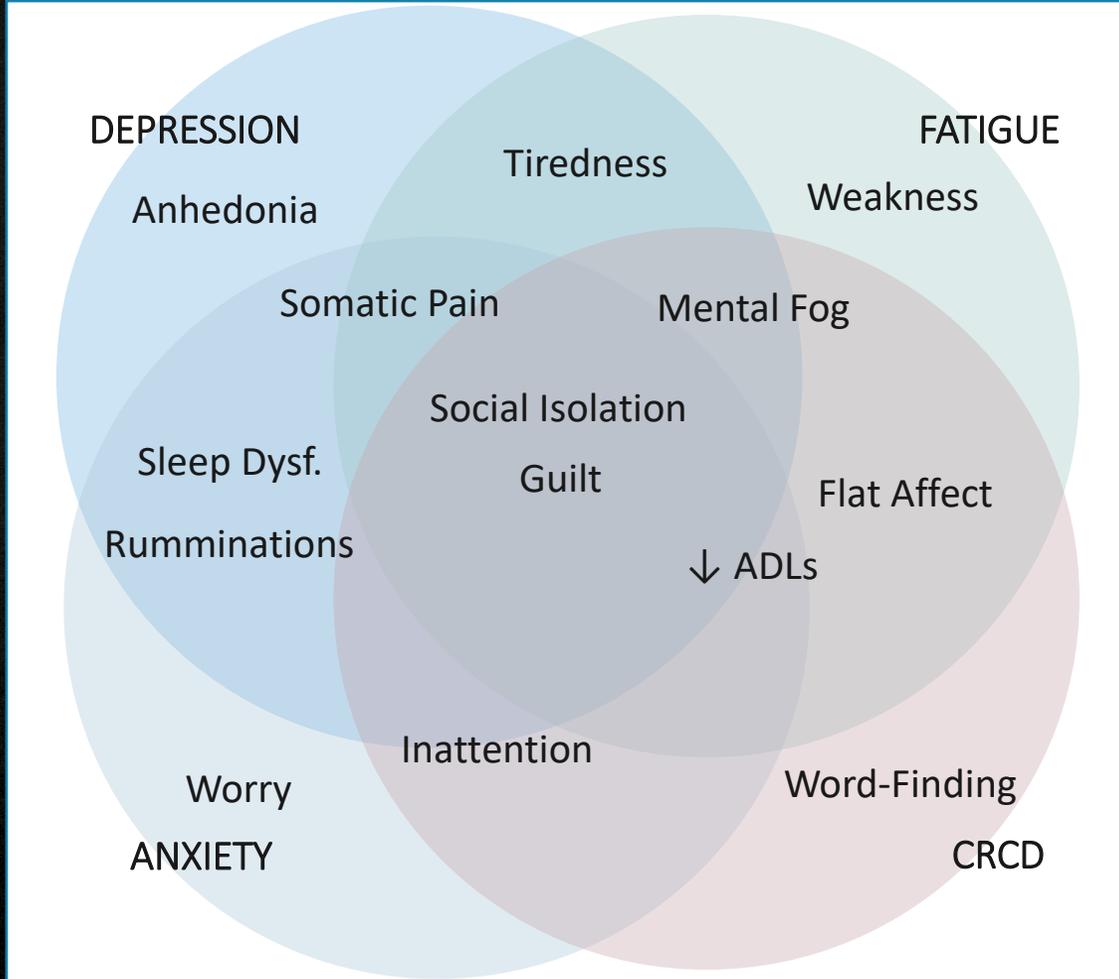
Overlapping Symptoms

Inconsistent Report

Stigma

Diagnosis

Challenges



Terminology

Overlapping Symptoms

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Diagnosis

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Terminology

Overlapping Symptoms

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Stigma



Diagnostic Tips for the Big Three

Diagnosis

Depression: Endicott Criteria

Physical Symptoms		Psychological/Cognitive Symptoms
Change in Appetite		Tearfulness Depressed Appearance
Sleep Disturbance		Social Withdrawal Decreased Talkativeness
Fatigue		Brooding Self-pity Pessimism
Psychomotor agitation/retardation		Lack of reactivity

Diagnosis

Depression: Suicide

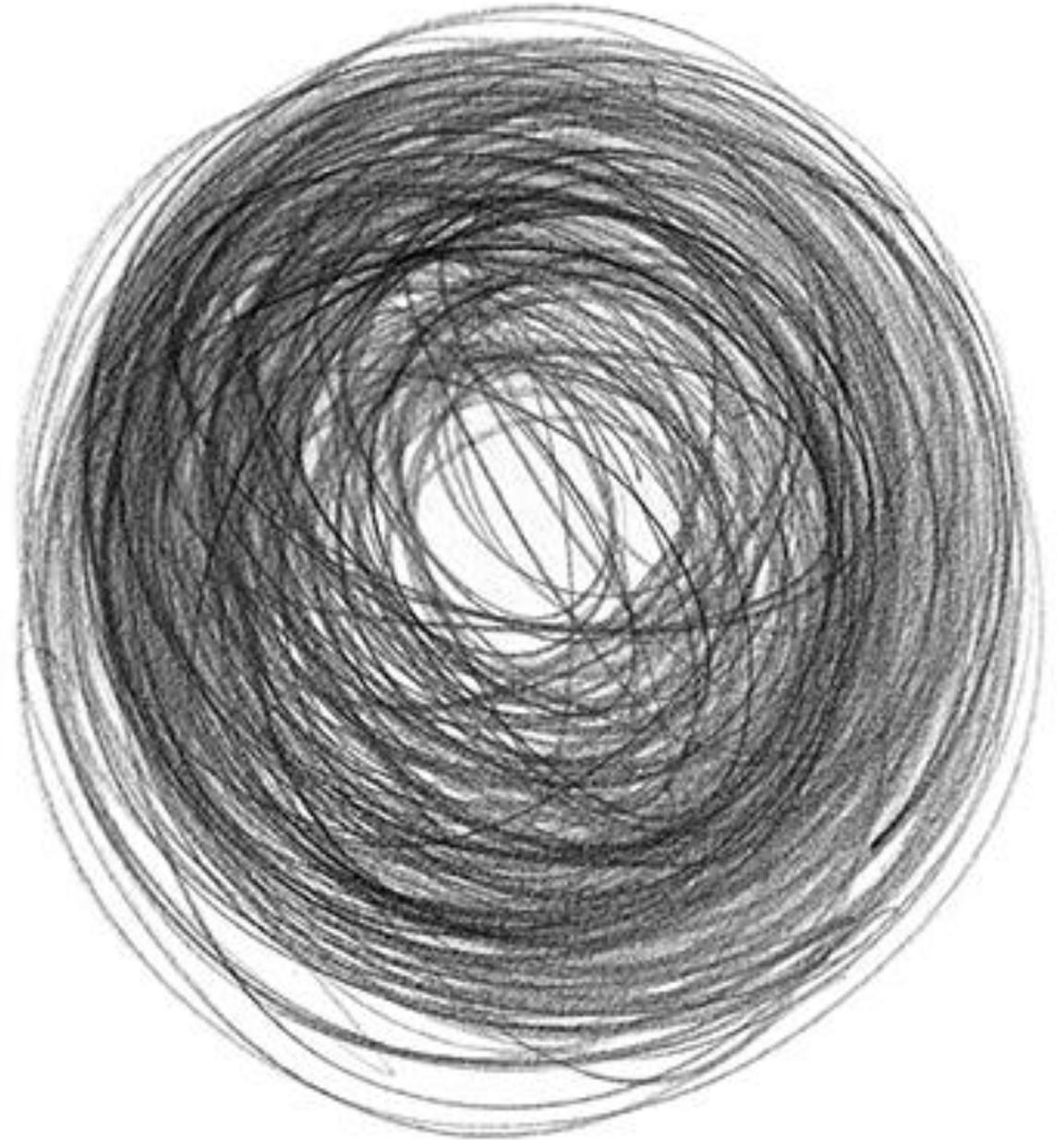


- The suicide rate among cancer patients is 4.4 times higher (Zaorsky, 2019)
- Men have more than double the prevalence ($\approx 2.2x$ higher) compared to women (Rafiei, 2024)
- Findings on Disease Site vary greatly
- Risk of completed suicide was higher within the six months of diagnosis (Lin Du, 2020)

Diagnosis

Multiple Shapes of Anxiety

- Situational anxiety
- Organic anxiety
- Psychiatric anxiety
- Existential anxiety



Diagnosis

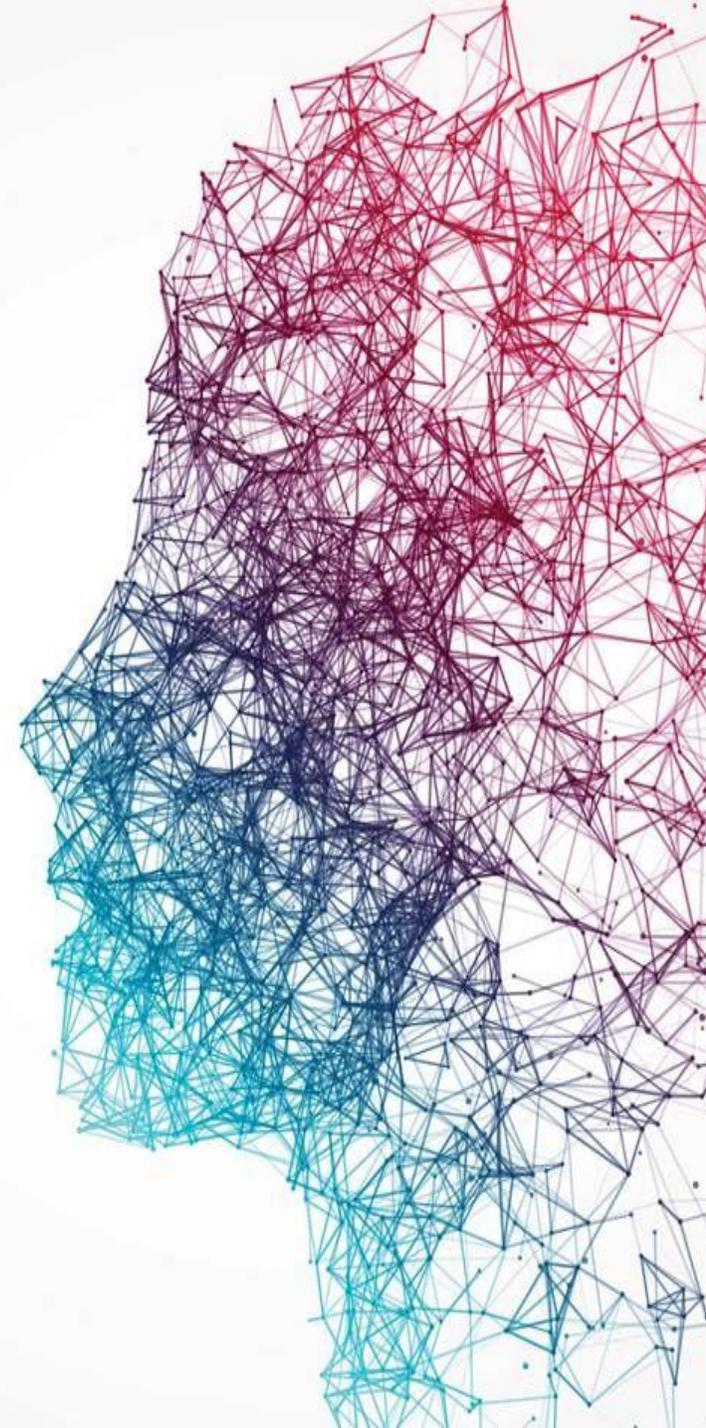
Teasing out Cognitive Impairment

- Chemotherapy Related Cognitive Dysfunction
- Delirium
- Major Neurocognitive Disorder

Short Term Memory

Word Finding

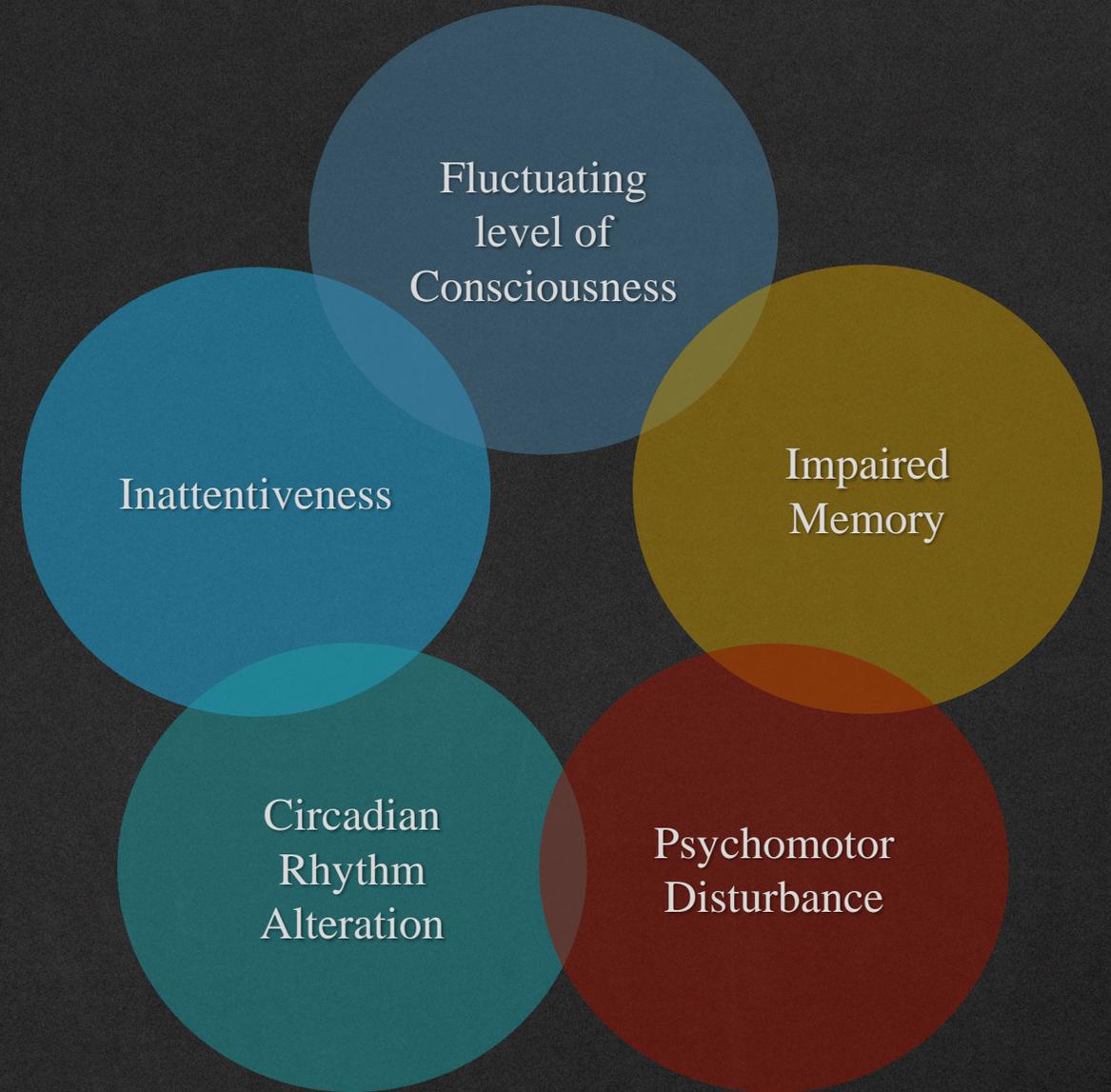
Planning and Multi-tasking



Diagnosis

Teasing out Cognitive Impairment

- Chemotherapy Related Cognitive Dysfunction
- Delirium
- Major Neurocognitive Disorder



Diagnosis

Teasing out Cognitive Impairment

- Chemotherapy Related Cognitive Dysfunction
- Delirium
- Major Neurocognitive Disorder

- Cancer and treatment increases risk
- It is not just about memory:
 - Learning and memory
 - Language
 - Executive function
 - Complex attention
 - Perceptual-motor
 - Social cognition
- Screening tool: MOCA test
www.mocatest.org
- Neuropsychological testing

Differential Diagnosis: Think Broad



Differential

Broad Approach



When encountering a Cancer patient with a neuropsychiatric symptoms:

- *Broad view to other disease contributors beyond psychological distress*
- *Develop a methodological approach to formulating a differential diagnosis*
- *Use all elements necessary for a multidisciplinary treatment approach*

Differential

CNS: Primary Impact

1

Toxic Leukoencephalopathies

*Relapsing Remitting focal symptoms –
Vision loss, weakness, rigidity
Relevant Sxs: Cognitive impairment,
Mood Swings, anxiety, fatigue*

2

Leptomeningeal Disease

*Headache, difficulty with walking, limb
weakness, seizures, dizziness and
sensorineural deafness
Relevant Sxs: **Confusion, Lethargy***

3

Immune-mediated Encephalitis

*Relevant Sxs: **Decreased alertness,**
focal Neuro sxs, **personality change,**
seizures, **encephalopathy, catatonia***

4

Cerebral Vasculitis

*Large-medium: Hemiparesis, **aphasia** or
focal neurological sx
Small: HA, **cognitive impairment** and
seizures
Systemic Sxs: Fever, **fatigue,** flu-like sxs*

Differential

CNS - Secondary Impact

- Infections

Aspergillosis - AMS 86%, seizures 41%, focal deficits 32%

HHV-6 - Limbic encephalitis (irritability, memory impairment, confusion)

- Posterior Reversible Encephalopathy Syndrome (PRES)

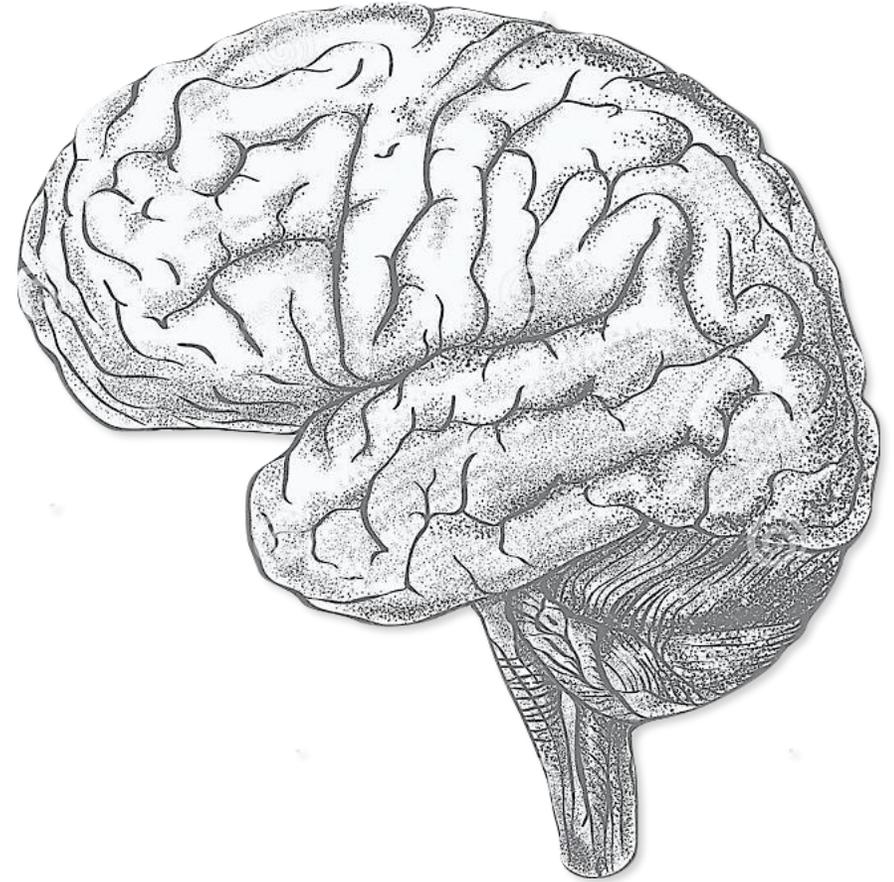
Seizures, AMS, visual disturbances, HTN, headaches

- Post Treatment Lymphoproliferative Disorders

Fever, malaise, fatigue

- Tx Induced Malignancies (>10 years)

GBM, Astrocytoma, Lymphoma, Meningioma



Differential

Chemical Abnormalities

- Hyponatremia

Paraneoplastic SIADH 2ry to syndrome, SCLC, NSCLC, mesothelioma, pancreatic, duodenal and endometrial cancer, lymphoma/leukemia

Associated with lung infections, cerebral tumors, brain injuries, and medications

Lethargy and confusion are attributable to cerebral edema

- Hypercalcemia

Metastatic lesions to the bone or with tumor-related ectopic production of parathyroid hormone-related protein

Nausea, vomiting, constipation, confusion, can progress to coma and renal failure

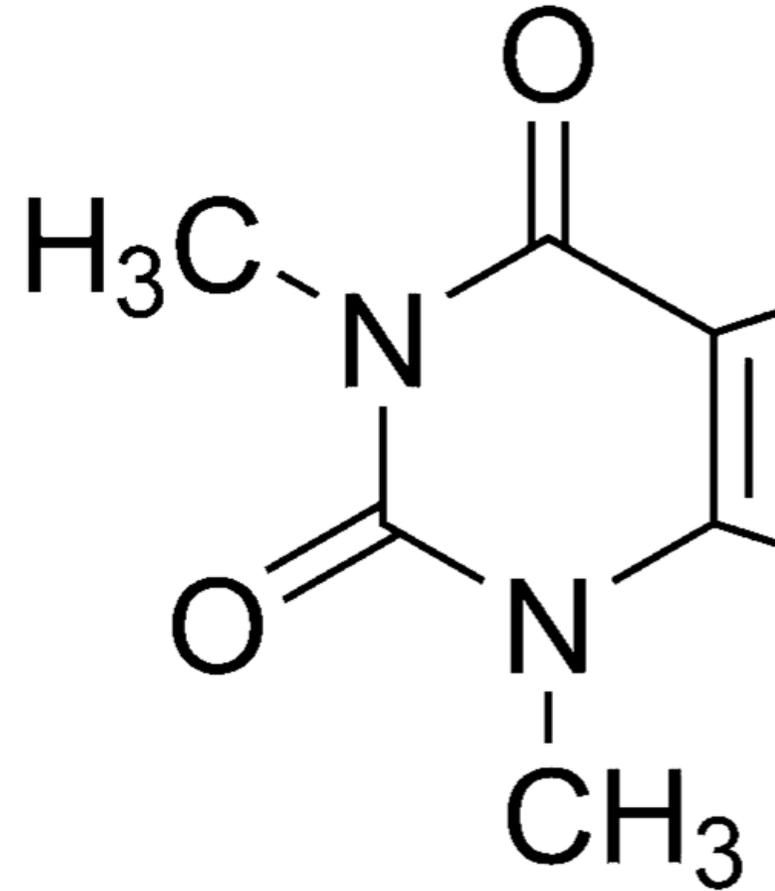
Treatment: diphosphonates, hydration, and diuresis.

- Idiopathic Hyperammonemia (IHA)

Plasma ammonia level >2x the upper limit and normal LFTs

Lethargy, confusion, ataxia, seizures, coma, and death

Hematologic malignancies who are neutropenic following STC and MM patients



Differential

Endocrine

- Thyroid Dysfunction

Sxs: Fatigue, cold intolerance, low mood, hypersomnia, constipation

Risk factors: TBI, Bulsulfan regimens, Hodgkin's Dz, younger patient

- Hypoadrenalism

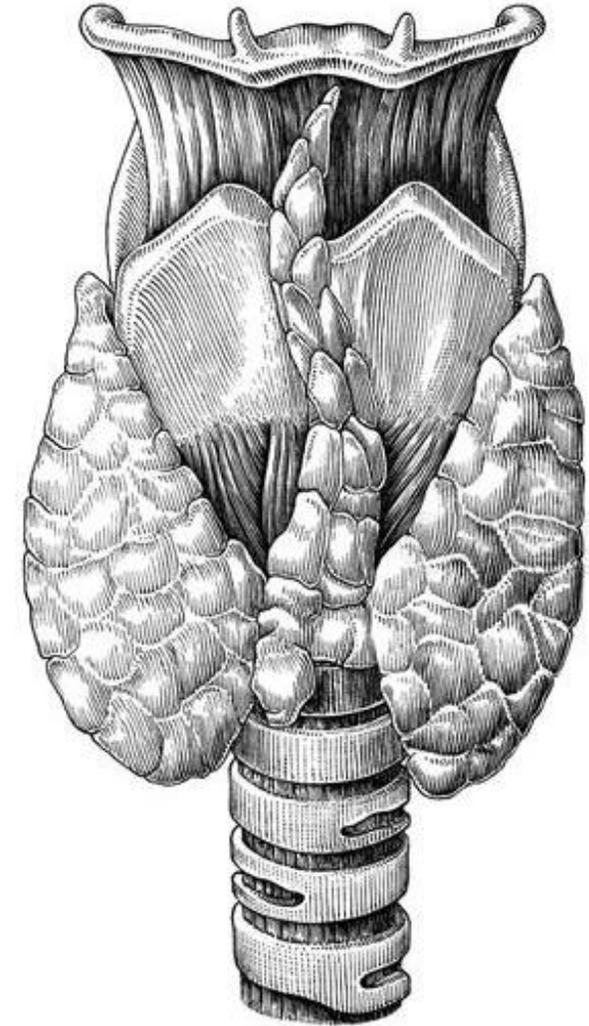
Sxs: Fatigue, weight loss, ↓ sex drive, nausea, craving salty foods

Risk Factors: > 3 months of steroid therapy

- Ovarian Failure

Sx: Hot flashes depression, mood lability, cognitive impairment

Risk Factors: Alkylating agents, TBI, baseline ovarian reserve



Differential

Nutritional

- Vitamin B1: *Wernicke's encephalopathy (ophthalmoplegia, ataxia, confusion); Korsakoff dementia*
- Vitamin B6: *Depression, confusion, fatigue, nausea, Anemia, susceptibility to infections, skin rashes or dermatitis*
- Vitamin B12: *Neuropathy, fatigue, cognitive impairment*
- Vitamin C: *Fatigue, fever, loss of appetite, bleeding gums, rashes, coiled hair, apathy, irritability, muscle weakness, and weight loss*



Differential

Other Organs

- Vascular

Subdural Hematomas – Prolonged thrombocytopenia

Ischemic Strokes / Thrombotic diseases / Pulmonary Embolism

Intraparenchymal Hemorrhages

Hyper viscosity Syndrome - Triad of focal neurological changes, vision abnormalities, and bleeding

- Hepatic

Sinusoidal Obstruction Syndrome: Edema, jaundice, hepatomegaly, in severe cases delirium

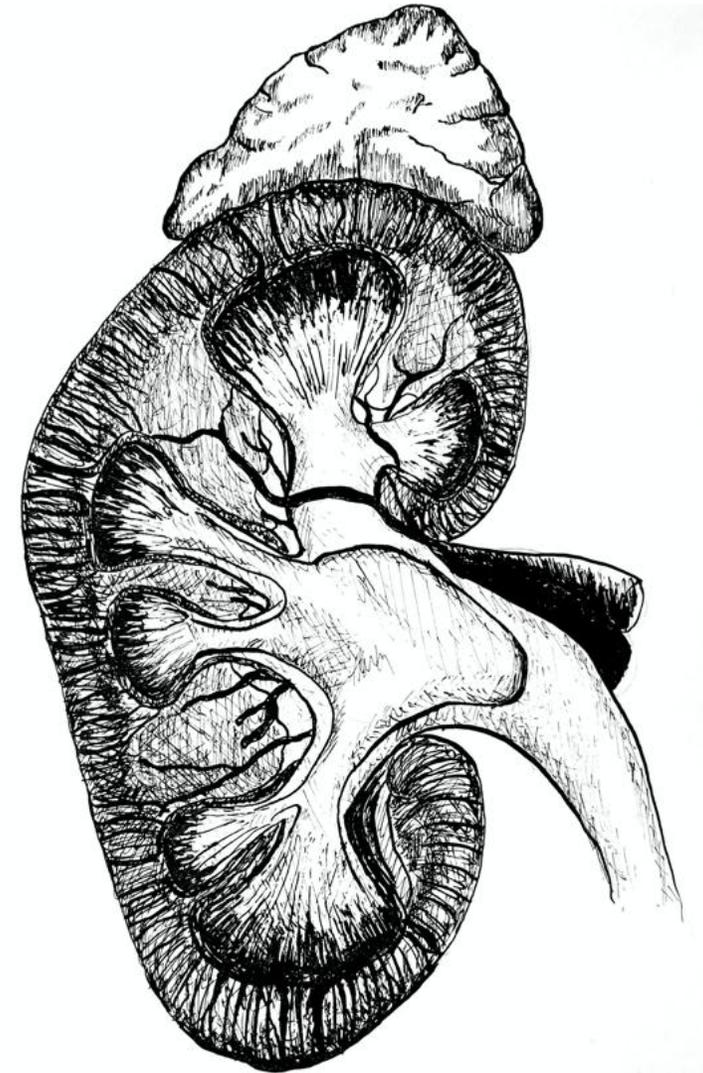
Autoimmune Hepatitis: Fatigue, anorexia, hepatic tenderness, dark urine

Idiopathic Hyperammonemia: Lethargy, motor dyscoordination, alkalosis

- Renal

Pre-renal, renal and obstructive (hemorrhagic cystitis)

Uremia symptoms: Fatigue, nausea, loss of appetite, a metallic taste in the mouth, confusion



Differential

Pharmacology

Medication	Toxicity
Cyclosporin A	PRES, Confusion, tremor, ataxia, seizures
Methotrexate	Leukoencephalopathy, headache, lethargy, dysarthria
Busulfan	Seizures
Fludarabine	Acute toxic leukoencephalopathy
Thiotepa	Headache, encephalopathy, seizures, paresthesia
Rituximab	PML
Blinatumomab	Encephalopathy, headache, aphasia, ataxia, tremor, seizures
Sorafenib	PRES
imipenem	Seizures, tremor, vertigo, paresthesia, delirium
Cefepime	Headache, paresthesia, encephalopathy
Voriconazole	Headaches, seizures, vision changes, hallucinations, delirium
Amphotericin B	Headache, encephalopathy, vision changes
Foscarnet	Headache, vertigo, paresthesia, seizures, delirium
Ganciclovir	Headache, numbness, tremor, seizures

Therapeutics: One size does not fit all



Therapeutics

Treatment Modalities



Support/Psychoeducation

Empathic Listening / Support
Coping Skills / Problem Solving
Education and Insight



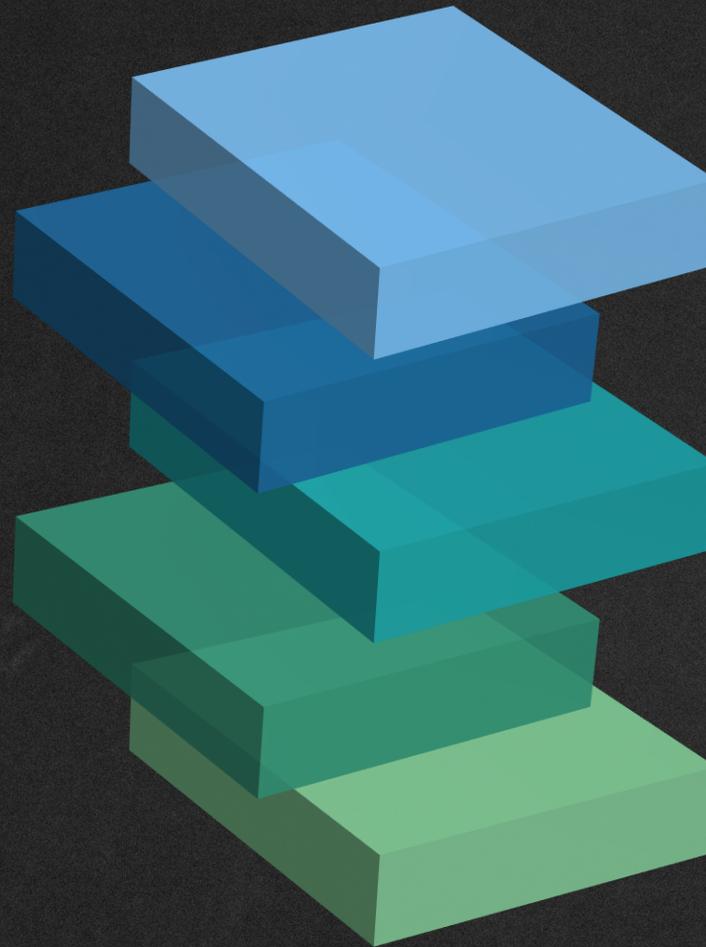
Psychotherapy

Cognitive Behavioral Therapy
Interpersonal Therapy
Psychodynamic Psychotherapy



Complementary Medicine

Body/Mind treatments
Supplements / Nutrition
Acupuncture



Psychopharmacology

Symptom Management
Disease Modifying



Somatic Therapies

Electroconvulsive Therapy
Transcranial Magnetic Stimulation
NMDA receptor antagonist



Pharmacology

Prescribing Considerations

- Protein binding
- Cytochrome P450 isoenzymes
- Pharmacodynamic Interactions



MASSACHUSETTS
GENERAL HOSPITAL

CANCER CENTER

Pharmacology

Prescribing Considerations

- Protein binding
- Cytochrome P450 isoenzymes
- Pharmacodynamic Interactions

Psychotropics > 90% bound	Psychotropics < 90% bound	Chemotherapies > 90% bound
Fluoxetine	Citalopram	Etoposide-VP16
Sertraline	Escitalopram	Teniposide-VM26
Paroxetine	Mirtazapine	Paclitaxel-taxol
Duloxetine	Venlafaxine	Docetaxel-taxatere
Nefazadone	Bupropion	Tamoxifen
Valproic Acid	Methylphenidate	
	Carbamazepine	
	Lithium	



Pharmacology

Prescribing Considerations

- Protein binding
- Cytochrome P450 isoenzymes
- Pharmacodynamic actions

<u>3A4 Substrates</u>	<u>Psychotropics active at 3A4</u>
Anastrozole	<u>3A4 Inhibitors:</u>
Doxorubicin	Fluoxetine
Cyclophosphamide *	Sertraline
Ifosfamide *	Nefazadone
Etoposide	Mirtazapine
Erlotinib (Tarceva)	
Teniposide	<u>3A4 Inducers:</u>
Vincristine	Carbamazepine
Vinblastine	Oxcarbazepine
Paclitaxel *	Modafinil
Docetaxel *	Topiramate
Tamoxifen *	
Tacrolimus	

*Must be metabolized to active compound



Pharmacology

Prescribing Considerations

- Protein binding
- Cytochrome P450 isoenzymes
- Pharmacodynamic actions

<u>System</u>	<u>Adverse Reactions</u>
Cardiovascular	QTc Prolongation (AD, AP) Hypertension (SNRIs) Tachycardia (Stimulants)
Metabolic	SIADH (SSRIs) Diabetes/Hyperlipedemia (AP)
Neurological	Seizures (Bupropion) Movement Disorders (AP)
Hepatological	DILI (TCA, AED, CPZ, SNRIs) LFT ↑ (AP, Mirtazapine)
Renal	CKD (Lithium) Electrolyte imbalances



Pharmacology

Prescribing Considerations

- Protein binding
- Cytochrome P450 isoenzymes
- Pharmacodynamic actions

<u>System</u>	<u>Better Agent</u>
Cardiovascular	QTc Prolongation (Sertraline) Hypertension (SSRIs) Tachycardia (Modafinil)
Metabolic	SIADH (Mirtazapine) Diabetes/HL (Aripiprazole)
Neurological	Seizures (SSRIs) Movement Dx (Quetiapine)
Hepatological	DILI (Escitalopram, SGA)
Renal	CKD (SGA) Electrolyte imbalances (Monitor)



Takeaways

- *Distress is almost universal, but not all distress is equal*
- *Acknowledging and educating is the first step in helping distress*
- *Simple interventions can go a long way*
- *Physical distress is within the realm of the CL Psychiatrist*
- *Differential MUST be broad*
- *Pharmacology is a balancing act*

A photograph of a modern glass skyscraper at dusk. The building features a prominent skybridge connecting to another structure on the right. The sky is a deep blue, and the building's glass reflects the ambient light. The text 'Thank you!! Questions' is overlaid in the center in a white serif font.

Thank you!!
Questions