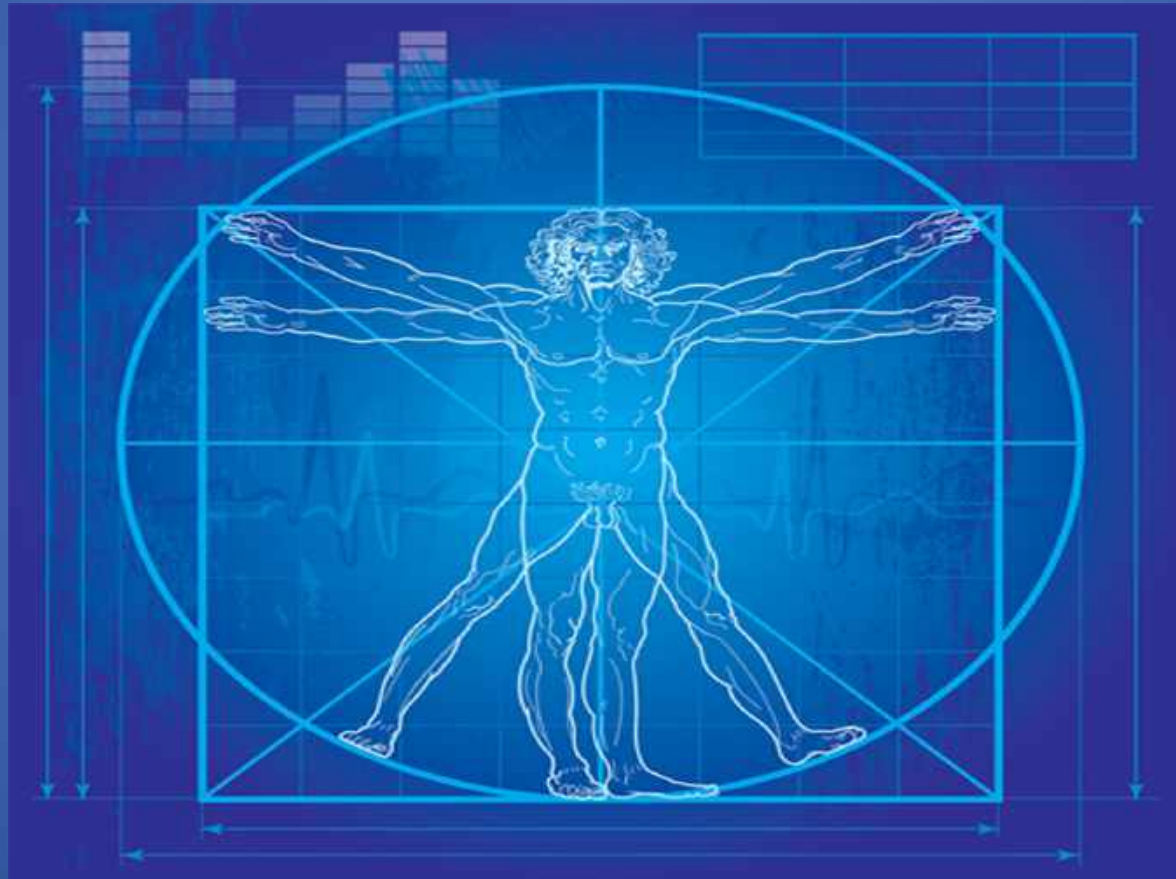


Part II Dr. Stuller, MD PPT

MMI Sept 2020 – Virtual Covid -19

The Essentials of Neuro-immuno-endo- psychopharmacology and Neuroimaging:

A Modern Neuroscience Approach to Understanding and treating
the Child and Adult Brain in Clinical Practice



Part II

Elizabeth A. Stuller, M.D.

ABPN Board Certified in Adult and Addiction Psychiatry

FAPA, FASAM

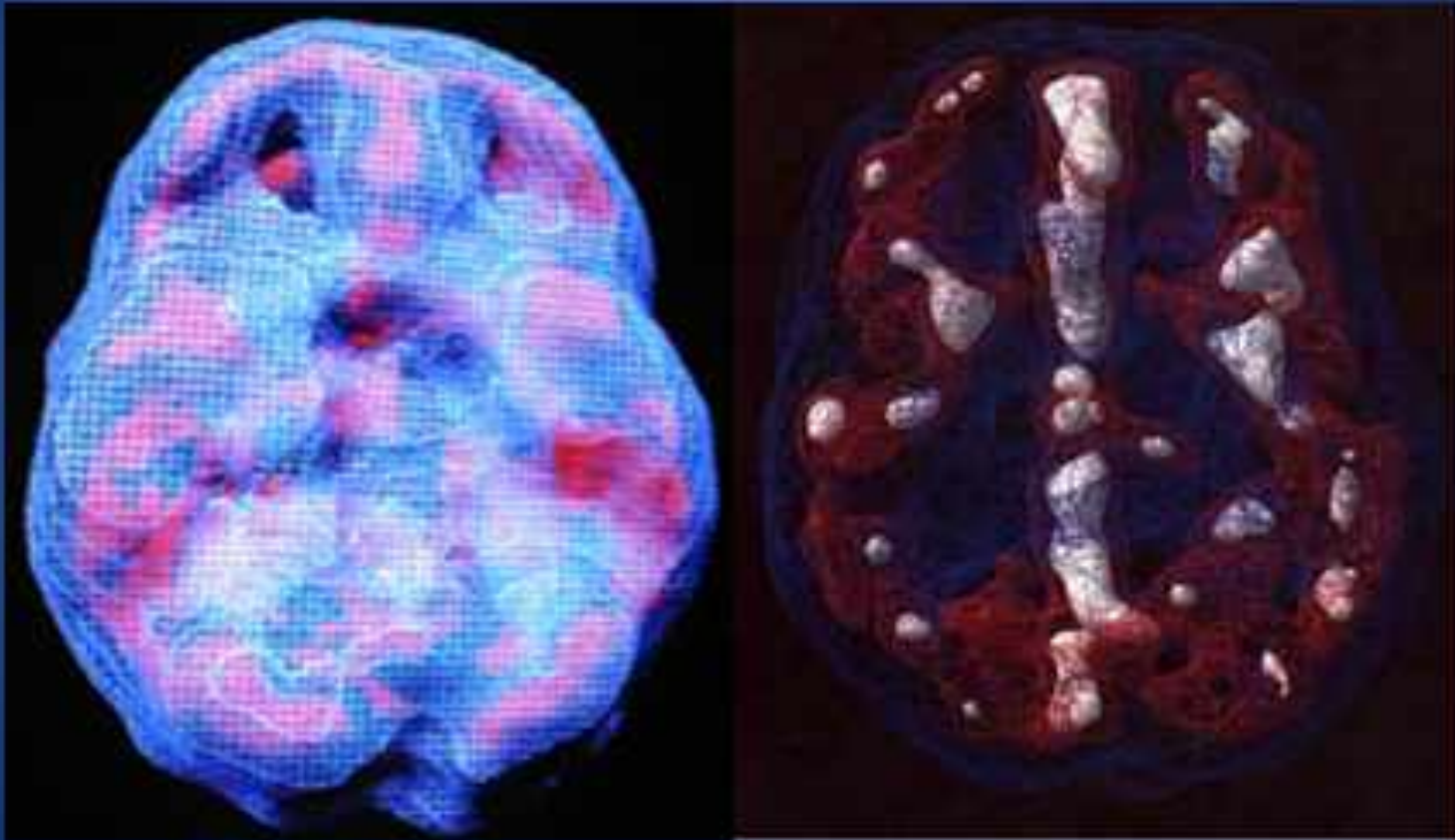
The Revolving Door

Chronic Metabolic Syndrome

Addiction and Mental Health Disease



The Inflamed Brain



Depression



Anxiety



Irritability, Anger, Mania, Psychosis



Insomnia



Panic



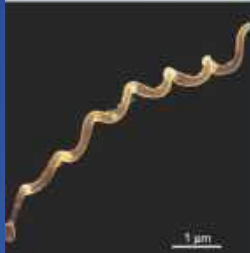
AFFECTIVE NEUROSCIENCE

ANTERIOR AROUSAL HYPOTHALAMUS EXPERIENCE FRONTAL TEMPORAL PREFRONTAL
STRUCTURES FACIAL BROADLEAF ACCUMBENS NUCLEUS AMYGDALA
ATTENTION PARIETAL PREDOMINATING EMOTION INSULIN CEREBELLAR STUDY
FEARFUL CRITICAL AMBIGUOUS POSITIVE AFFECTIVE ROLE ACTIVATED AUTONOMIC
INVOLVE COMPREHENSION

Find the Root Cause of Inflammation



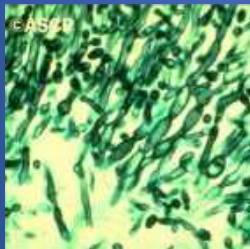
Chronic illness cannot be resolved without identifying the root cause



Bacteria



Viruses



Fungi



Mycobacteria

The Great Psychiatric Imitator

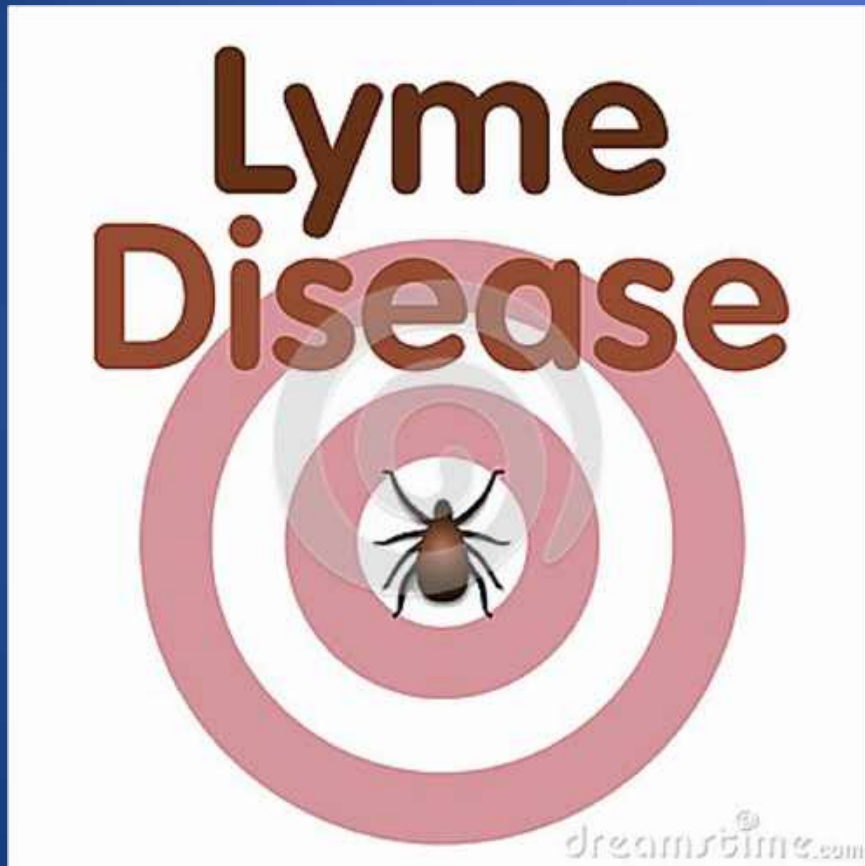




Photo courtesy: California Department of Public Health



Lyme Disease Rash (Erythema Migrans)- otherwise known as a Bull's Eye Rash.



Bartonella Rash courtesy LDA and Martin Fried, MD, Jersey Shore University Medical Center

Bartonella Rash



Rocky Spotted Mountain Fever Rash



Does your patient have Lyme Disease?

Fever

Headache

Arthritis

Musculoskeletal pain

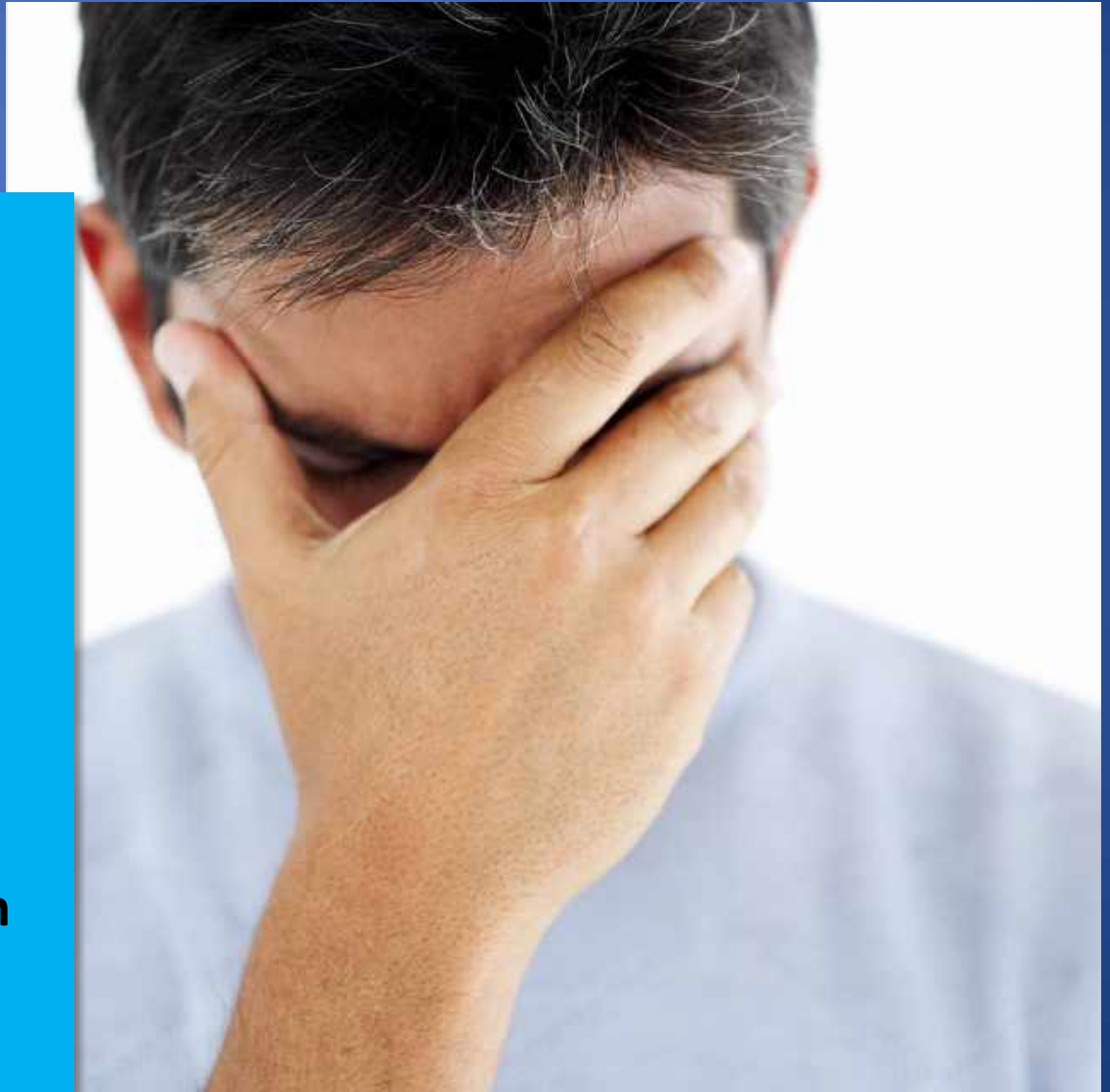
Neuropathy

Depression

Memory loss

Cognitive dysfunction

Sleep disturbances



Reported Cases of Lyme Disease -- United States, 2001



1 dot placed randomly within county of residence

Reported Cases of Lyme Disease -- United States, 2010



1 dot placed randomly within county of residence for each confirmed

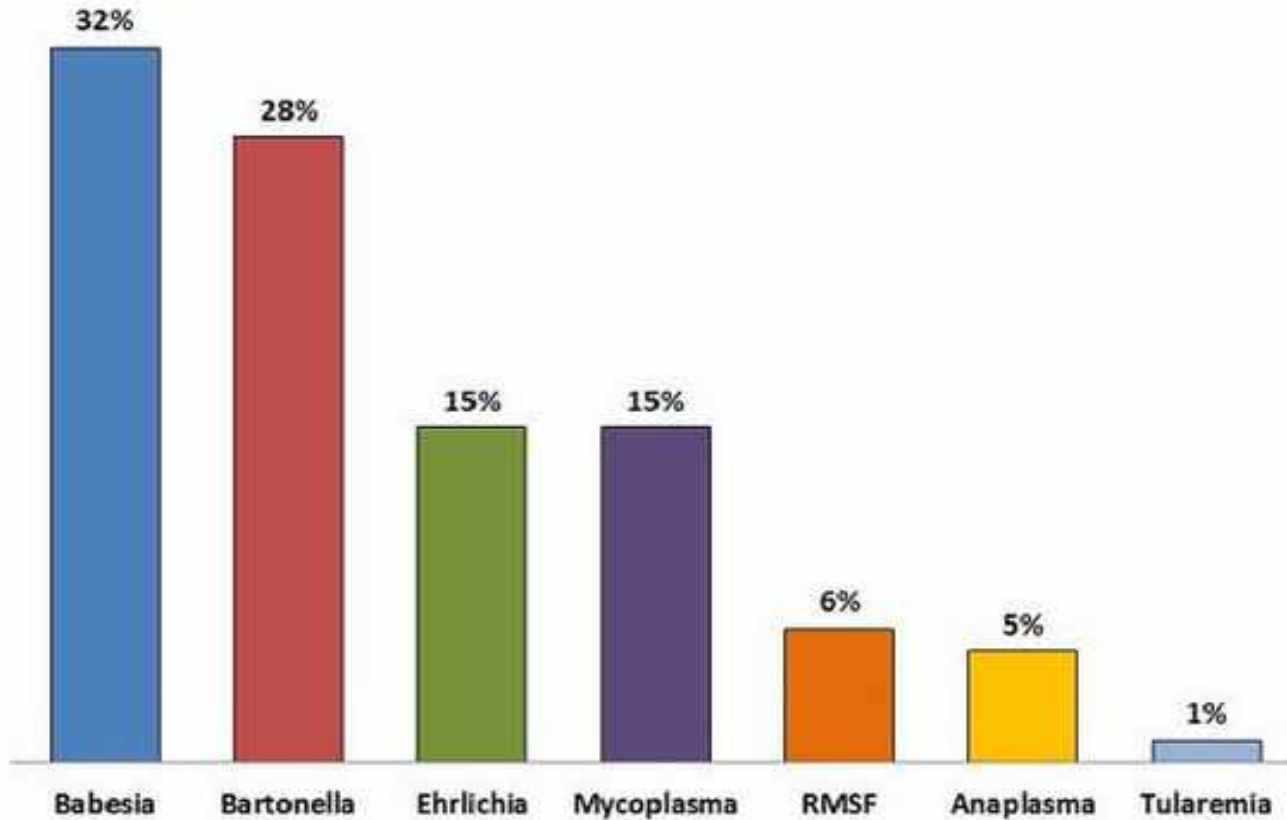
Reported Cases of Lyme Disease -- United States, 2016



1 dot placed randomly within county of residence for each confirmed case

What's In Your Tick

The Most Commonly Reported Co-Infections
U.S. Patients with Lyme Disease



lymedisease.org

Advocacy, Education and Research



LYME DISEASE: A BACTERIAL INFECTION



ILADS

International Lyme and
Associated Diseases Society

Lyme CRAZY

Neuropsychiatric symptoms

Cognitive Difficulties

- Simple and complex attention
- Slow processing—visual and auditory
- Visual-spatial difficulties—e.g. trouble finding things, getting lost
- Auditory processing disorders
- Visual processing disorders
- Sensory integration disorders
- Short-term and working memory difficulties
- Word-finding, word generation and communication difficulties
- Decline in executive functions—planning and organization
- Confusion, decline in overall intellectual performance

As with many patients who have multiple sclerosis, chronic fatigue syndrome and other chronic illnesses, many Lyme patients' neuropsychiatric symptoms are mistaken for mental illnesses, and they are prescribed psychiatric medications that they may need. This Band-Aid approach may cover up symptoms and allow an active Lyme infection to cause ongoing damage.

Emotional/Behavioral Difficulties

- Anxiety, often with panic attacks
- Depression
- Irritability/rage attacks/impulse dyscontrol/violent behavior/oppositional defiance disorder
- Sleep disorders
- Rapid mood swings that may mimic bipolarity (mania/depression)
- Obsessive Compulsive disorder (OCD)
- Hyperactivity
- Autism Spectrum-like disorders
- Antisocial disorders
- Eating disorders

Like syphilis, Lyme disease bacteria can infect the brain and cause severe symptoms that may mimic clinical depression, anxiety, obsessive-compulsive disorder, bipolar disorder, and even schizophrenia.



LYME DISEASE SYMPTOMS

EARLY LYME*

Fatigue	76%
Headache	70%
Rash	<70%
Fever	60%
Sweats	60%
Chills	60%
Muscle Pain	54%
Joint Pain	48%
Neck Pain	46%
Sleep Issues	41%

CHRONIC LYME**

Fatigue	79%
Joint Pain	70%
Muscle Pain	69%
Other pain	66%
Sleep Issues	66%
Cognitive	66%
Neuropathy	61%
Depression	62%
Heart Related	31%
Headaches	50%

* (Aucott 2013) ** (Johnson 2014, Moderate to very severe symptoms)

Estimates of rash rates range from 25-80%

Lyme disease effects multiple systems

Stage 1 – Days to Weeks

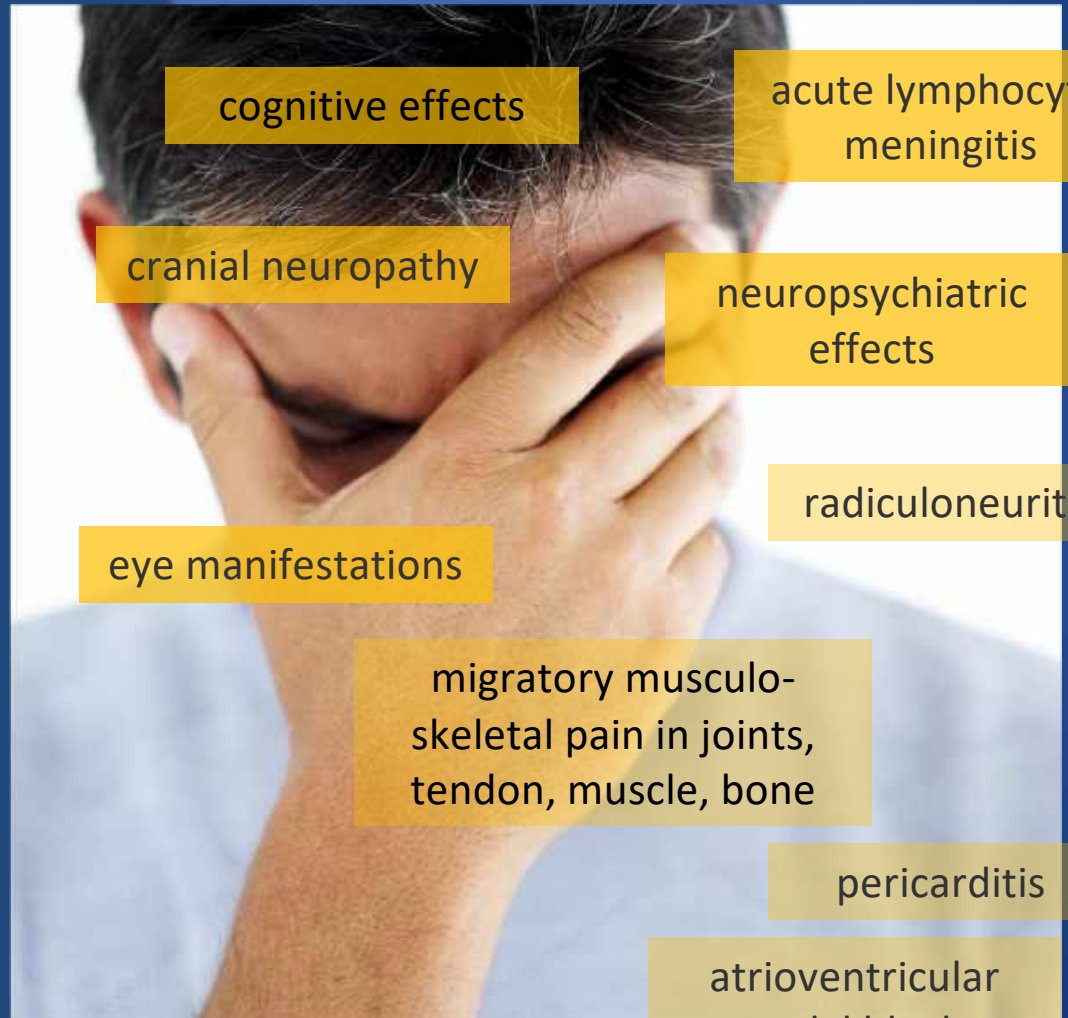
Early infection localized to skin
(Pt may report flu-like symptoms)

Stage 2 – (Months to Years) Disseminated infection

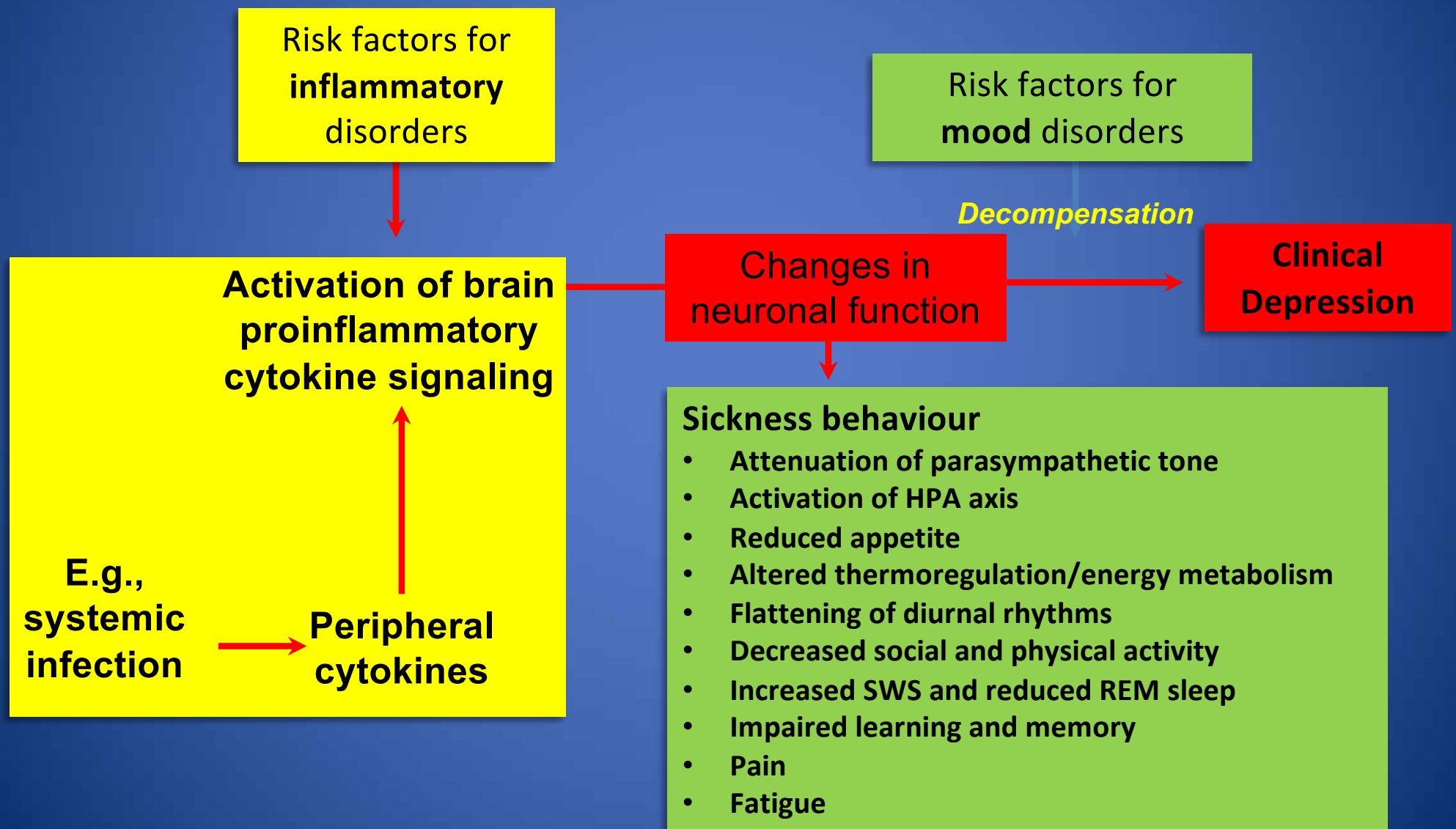
Stage 3 – (Remissions and Exacerbations)

Persistent infection

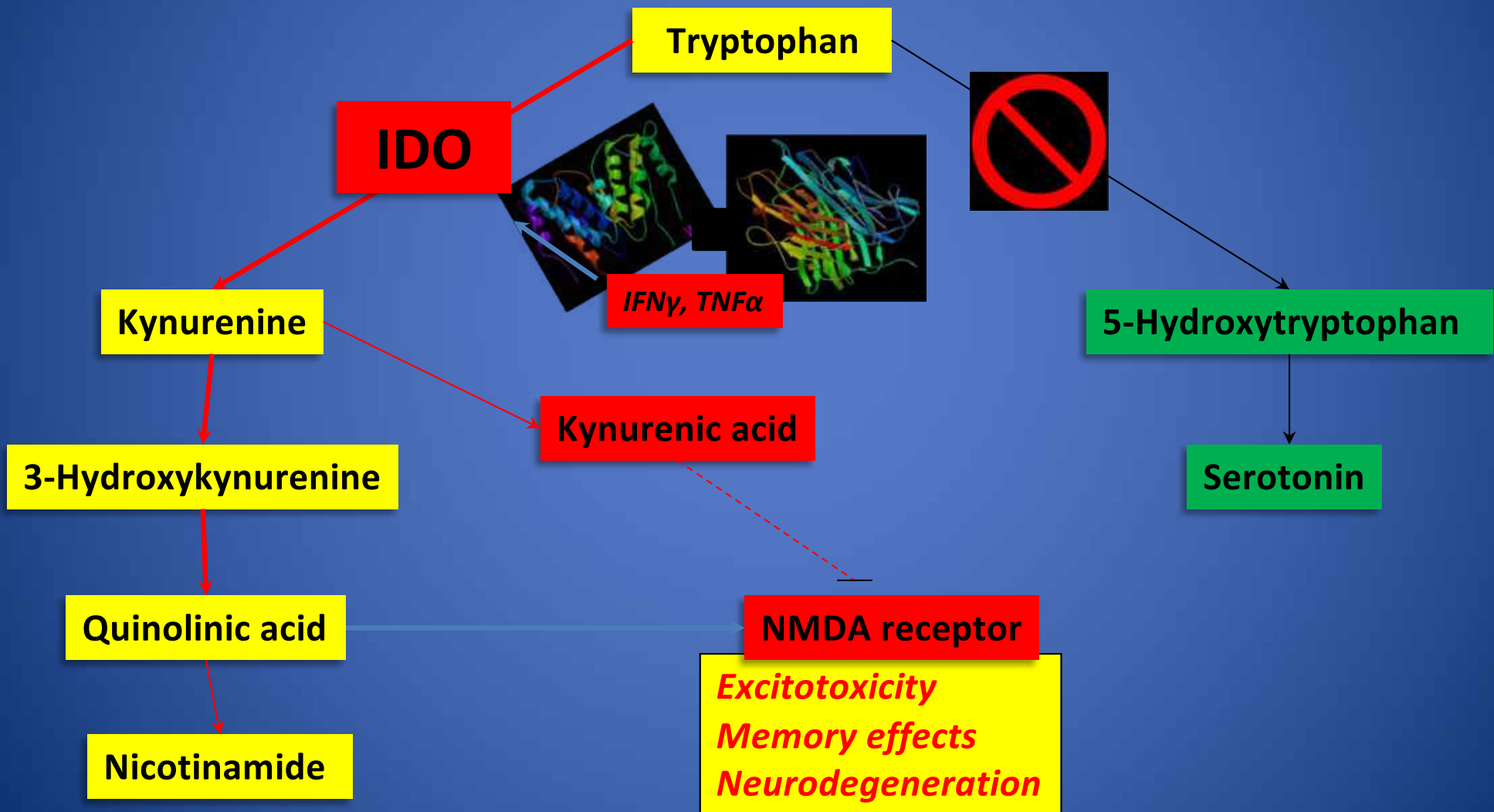
Variable manifestation of stages
in different patients



How can inflammation lead to neuro/mood symptoms?



Depression: The inflammation-serotonin link



IDO: indoleamine 2,3-dihydroxyoxygenase

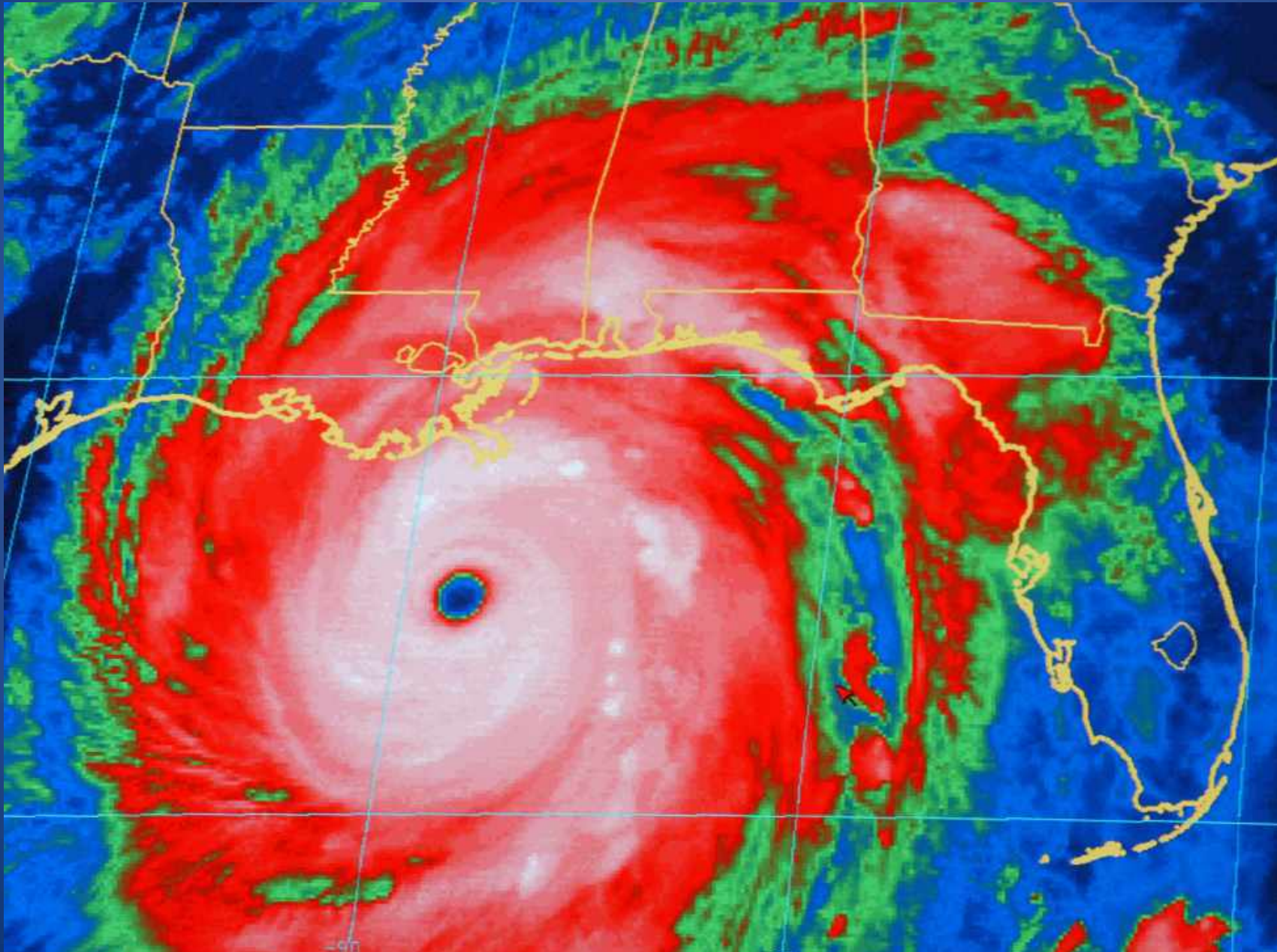
Adapted from Dantzer R et al. (2008). *Nat Rev Neurosci.* 9(1):46-569:46-57.

Mycotoxins



Hurricane Katrina

August 28, 2005



2005

Rita
23 September

Dennis
10 July

Katrina
28 August

Wilma
21 October

Emily
17 July





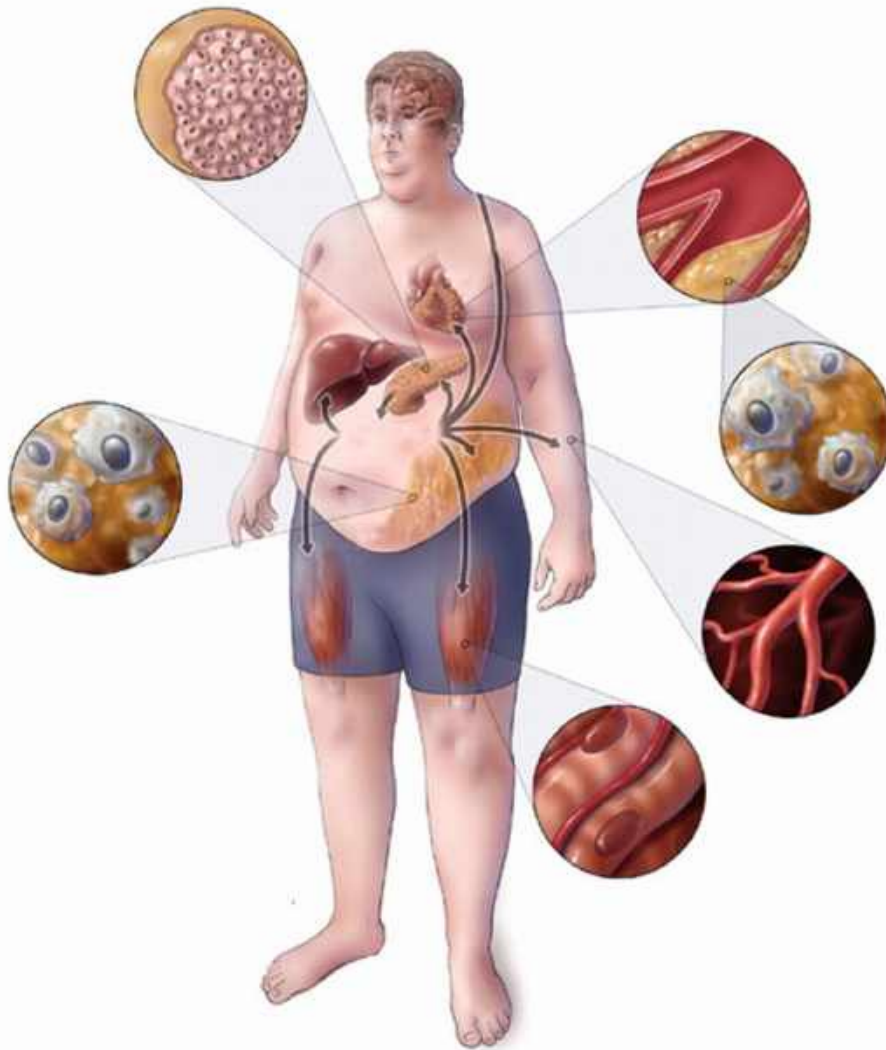








SYMPTOMS OF METABOLIC SYNDROME



IF YOU HAVE ANY THREE OF THE FOLLOWING SYMPTOMS:

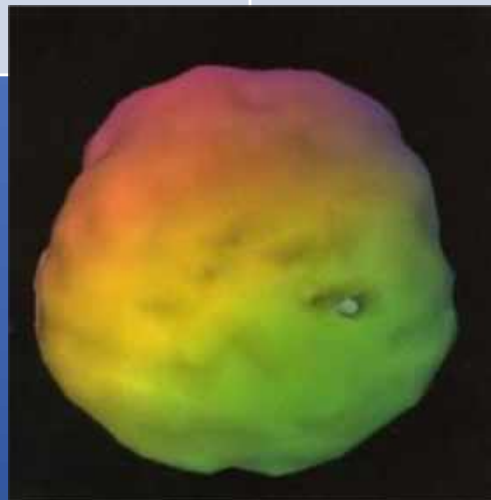
- ✓ BLOOD PRESSURE HIGHER THAN 130 OVER 85
- ✓ FASTING BLOOD SUGAR OVER 100
- ✓ A WAIST LARGER THAN 40 INCHES FOR MEN OR 35 INCHES FOR WOMEN
- ✓ HDL CHOLESTEROL UNDER 40 FOR MEN AND UNDER 50 FOR WOMEN
- ✓ TRIGLYCERIDES OVER 150

Dorm Rooms and Apartments

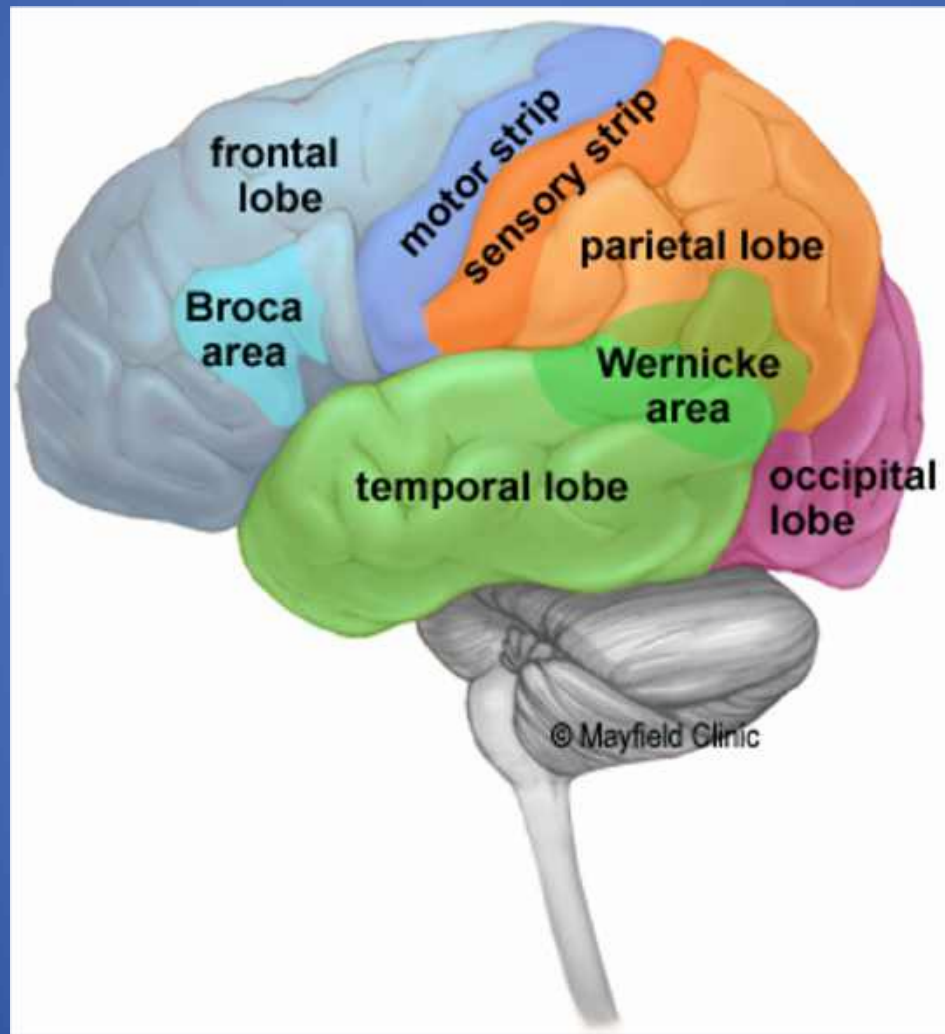


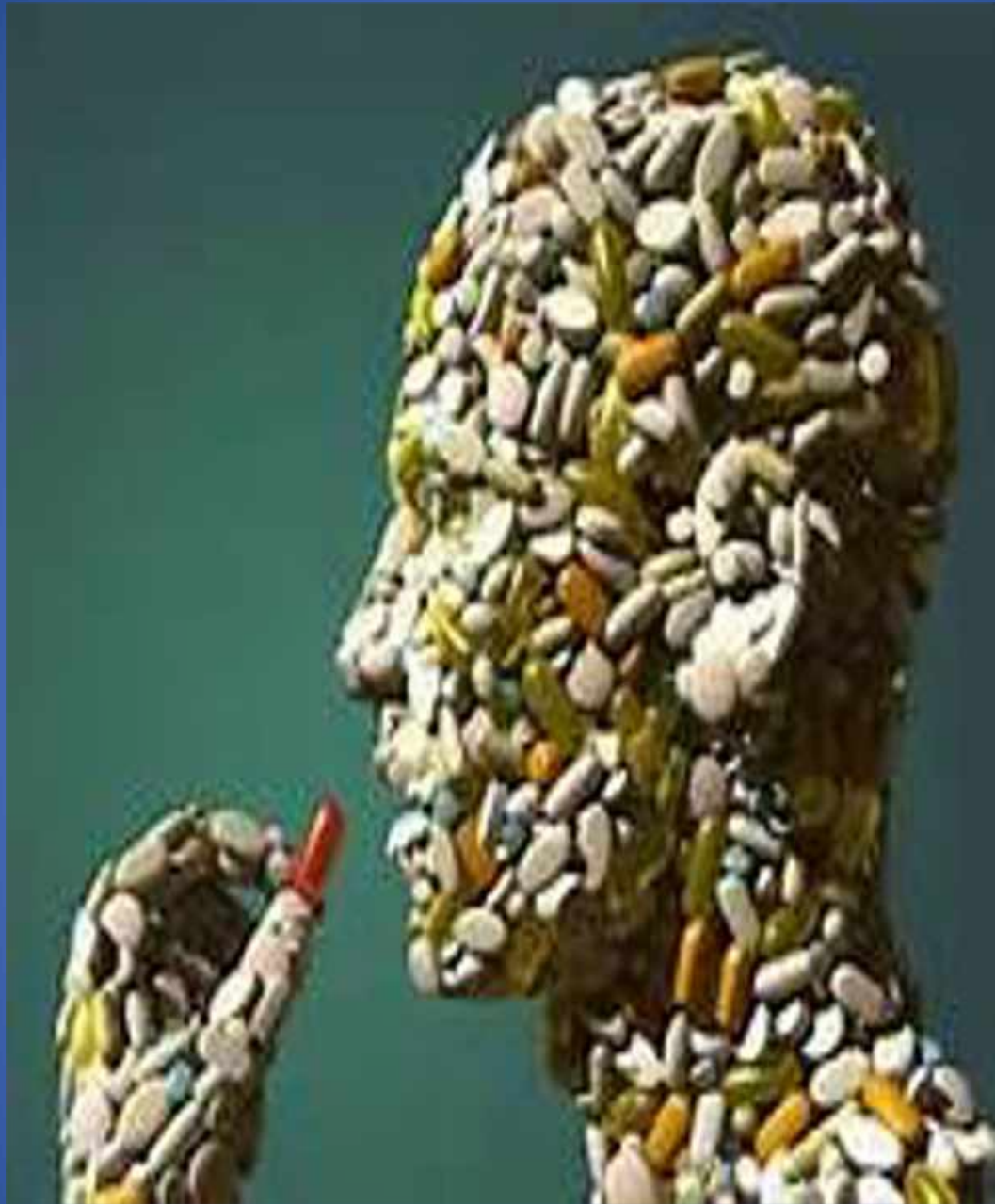
Mycotoxin Testing

Test	Value	Result	Negative	Equivocal	Positive
Ochratoxin	3.4 ppb	Positive	<2.0 ppb	2.0 ppb	>2.0 ppb
Aflatoxin	0 ppb	Negative	<1.0 ppb	1.0 ppb	>1.0 ppb
Tricothecene	0.16 ppb	Negative	<0.2 ppb	0.2 ppb	>0.2 ppb
Gliotoxins					

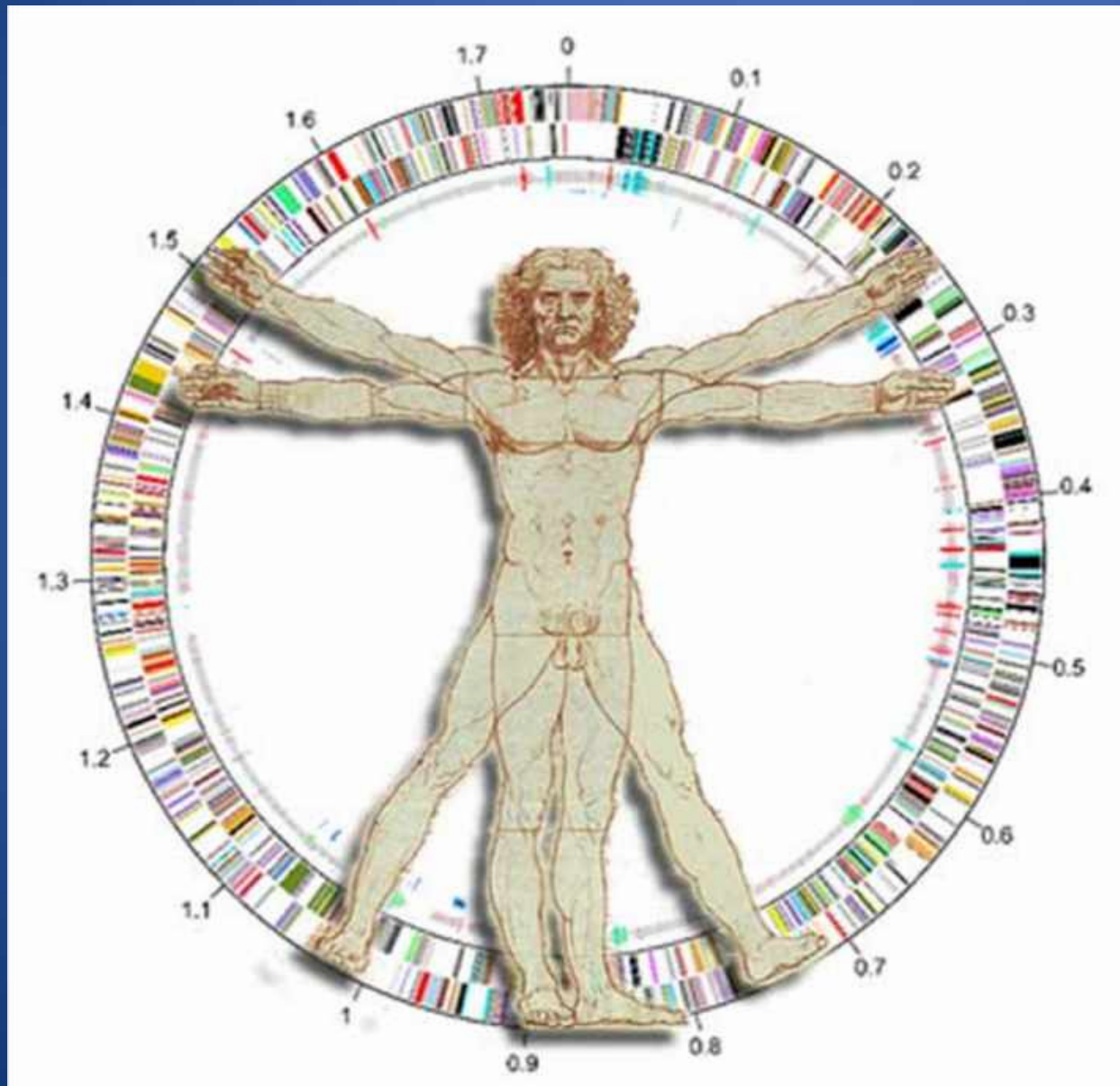


Neuro-immuno-endo-**psychopharmacology**



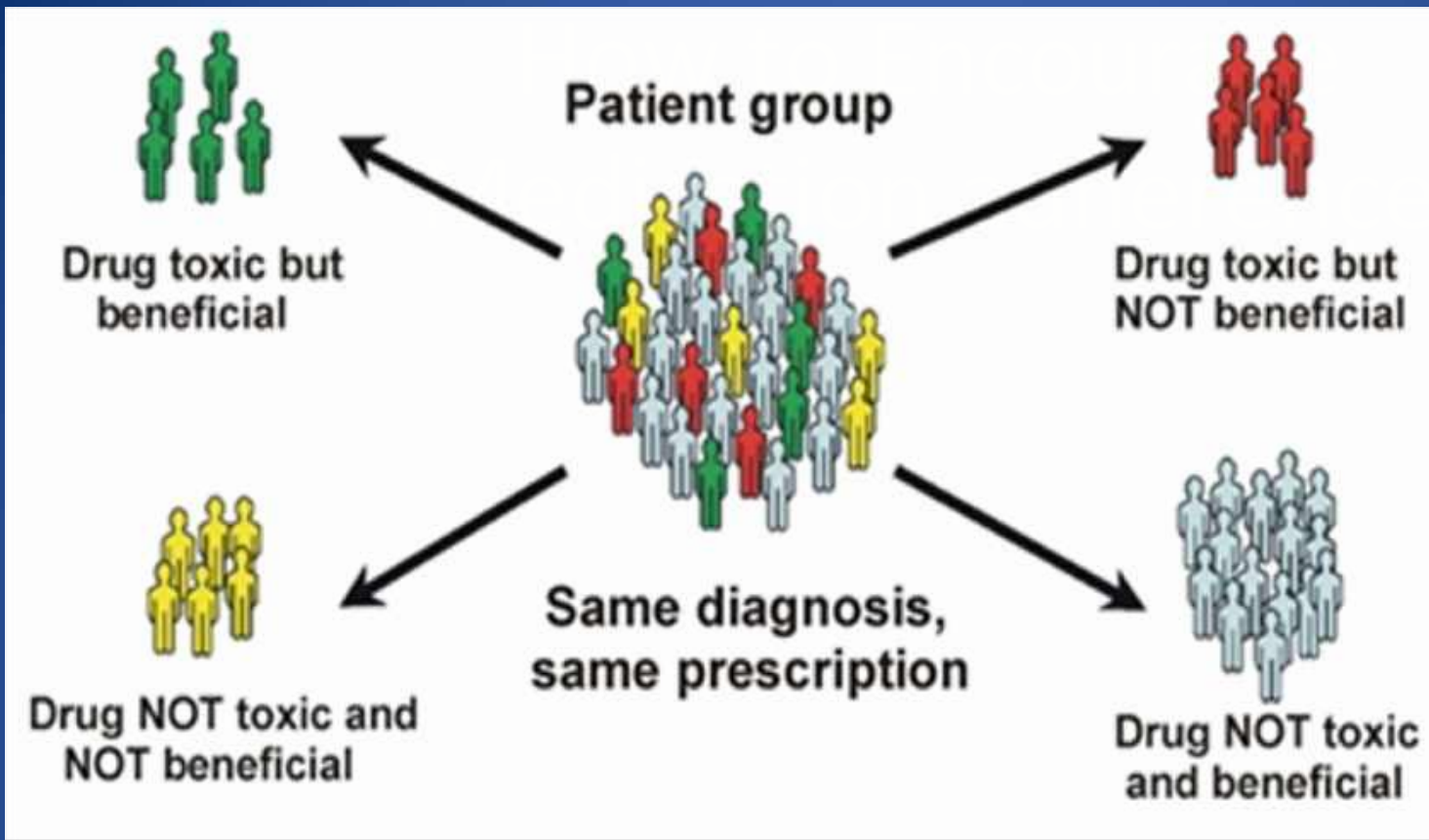


Personalized Medicine



“Personalized Medicine” refers to the use of genetic or other molecular biomarker information to improve the safety, efficacy, and health outcomes of patients by risk stratification, prevention, and tailored management approaches.”

Geneva C. Briggs, PharmD, BCPS



How genetics can affect medication response



EXTENSIVE (NORMAL)
METABOLIZER

Breaks down medications normally. Has normal amounts of medication at normal doses.



ULTRARAPID
METABOLIZER

Breaks down medications rapidly. May not get enough medication at normal doses.



INTERMEDIATE
METABOLIZER

Breaks down medications slowly. May have too much medication at normal doses.



POOR
METABOLIZER

Breaks down medications very slowly. May experience side effects at normal doses.

CYP450 Metabolizer Phenotypes

Ultrarapid (UM) : Rapid rate of metabolism

Extensive (EM) : Normal metabolism

Intermediate (IM) : Reduced rate
of metabolism

Poor (PM) : Slow
rate of metabolism

ANTIDEPRESSANTS

USE AS DIRECTED	MODERATE GENE-DRUG INTERACTION	SIGNIFICANT GENE-DRUG INTERACTION
desvenlafaxine (Pristiq®)	trazodone (Desyrel®) 1	bupropion (Wellbutrin®) 1,6
levomilnacipran (Fetzima®)	venlafaxine (Effexor®) 1	mirtazapine (Remeron®) 1,6
vilazodone (Viibryd®)	selegiline (Emsam®) 2	amitriptyline (Elavil®) 3,8
	fluoxetine (Prozac®) 1,4	clomipramine (Anafranil®) 1,6,8
	citalopram (Celexa®) 3,4	desipramine (Norpramin®) 1,6,8
	escitalopram (Lexapro®) 3,4	doxepin (Sinequan®) 1,6,8
	sertraline (Zoloft®) 3,4	duloxetine (Cymbalta®) 1,6,8
		imipramine (Tofranil®) 1,6,8
		nortriptyline (Pamelor®) 1,6,8
		vortioxetine (Brintellix®) 1,6,8
		fluvoxamine (Luvox®) 1,4,6,8
		paroxetine (Paxil®) 1,4,6,8

CLINICAL CONSIDERATIONS

- 1: Serum level may be too high, lower doses may be required.
- 2: Serum level may be too low, higher doses may be required.
- 3: Difficult to predict dose adjustments due to conflicting variations in metabolism.
- 4: Genotype may impact drug mechanism of action and result in reduced efficacy.
- 6: Use of this drug may increase risk of side effects.

Drug Interactions with Marijuana

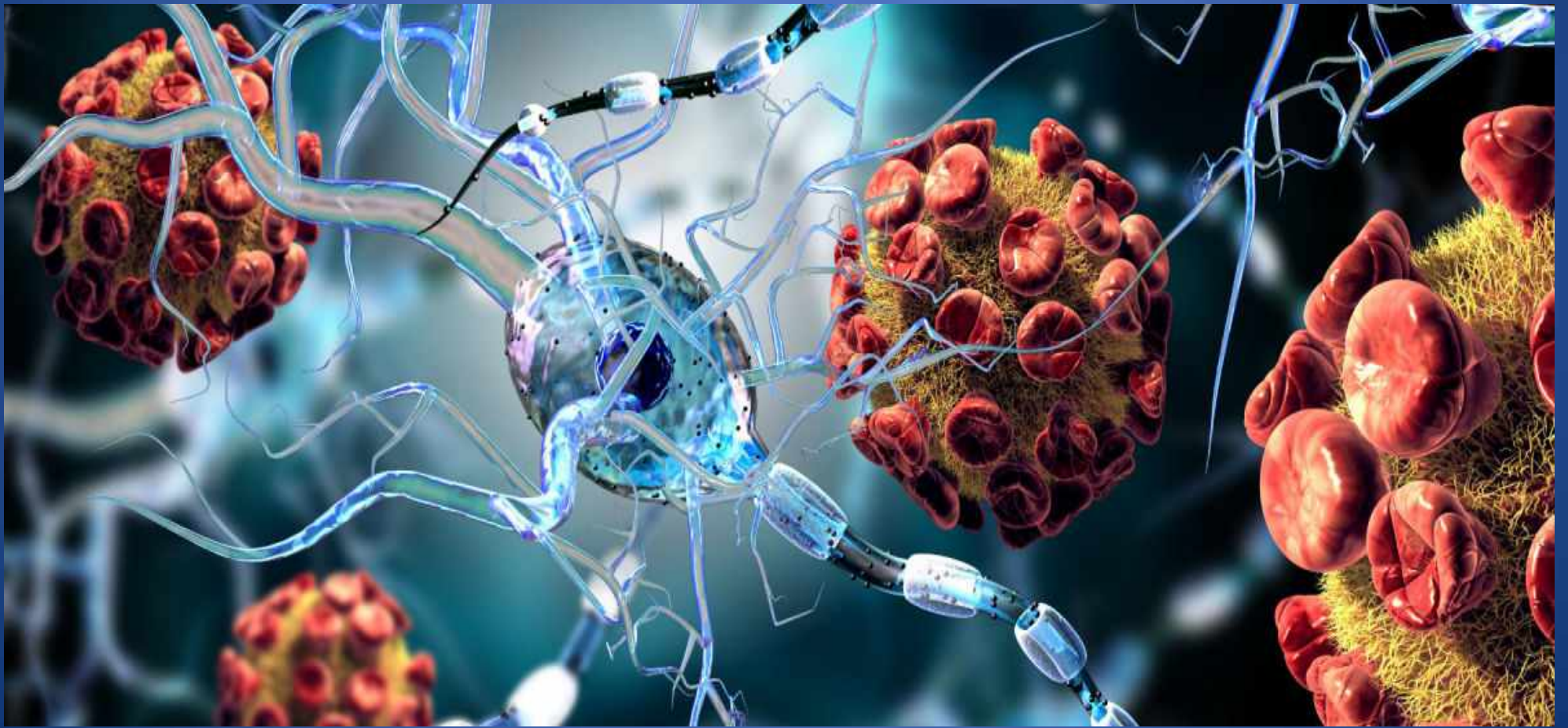
Potential Drug Interactions

Tetrahydrocannabinol (THC)

- **THC is metabolized by CYP2C9 and CYP3A4.3**
- **Patients who are poor metabolizers of CYP2C9 have been shown to have THC concentrations that are about 3-fold higher than those of extensive metabolizers of CYP2C9.4**
- **We are unaware of any studies examining the effect of CYP2C9 inhibitors on the elimination of THC. Based on genetic studies, inhibitors of CYP2C9 would be expected to increase the plasma concentration of THC.**
- **CYP2C9 inhibitors that would be expected to inhibit THC elimination include amiodarone, cimetidine, cotrimoxazole, metronidazole, fluoxetine, fluvoxamine, fluconazole, and voriconazole.**



The Neuropsychiatric Manifestations of Covid – 19



THE FACES OF COVID





The Spanish Flu 1918

“We have long known about a link between pandemics and neuropsychiatric disease.”

“Dating back over a hundred years ago, this was referred to then as “influenza psychosis.”

“Many of my colleagues and I believe that after this worldwide COVID 19 pandemic, we potentially are going to see a tremendous rise in post-infectious neuropsychiatric presentations.”

Dr. Suzanne Gazada,

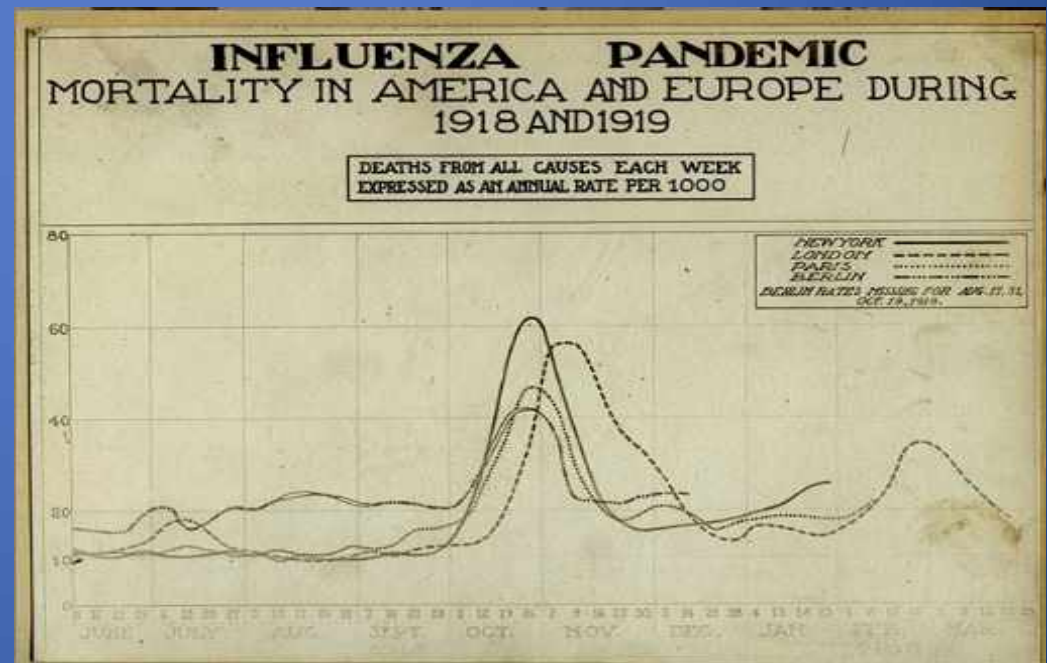
Integrative Neurology



Spanish Flu 1918 - 1919

- “After observing 100 cases during the Spanish Flu, Dr. Karl Menniger described manifestations of extreme mental disturbances; in fact, over half of his patients had some sort of psychosis and almost two-thirds had hallucinations.”
- The Spanish Flu also taught us about a post-viral form of Parkinson’s as a late-presenting feature of “encephalitis lethargica” with widely varying acute manifestations including:
 - ✓ Extrapyrmidal disorders
 - ✓ Myoclonus
 - ✓ Eye Movement Disorders
 - ✓ Paralyzes
 - ✓ Delirium
 - ✓ Mood Changes
 - ✓ Inverted Diurnal rhythms
 - ✓ Catatonia

Dr. Suzanne Gazada,
Integrative Neurology



Spanish Flu 1918 - 1919

- **Major pathological changes involved:**
 - The Substantia Nigra (associated with dopamine production)**
 - Globus Pallidus (Basal Ganglia associated with Anxiety and Panic)**
 - Hypothalamus (the brain thermostat)**
- **A symptom-free recovery period was often followed by**
 - Post-encephalitic disturbances**
 - Diagnosed as Parkinsonism in Adults**
 - Conduct disorders in children.**

“Occurrence of depression, mania, obsessive-compulsive disorder, and hyperactivity in post-encephalitic patients anticipated current concepts of the role of the basal ganglia in mood, personality, and obsessional syndromes.”

Dr. Suzanne Gazada

Integrative Neurology

Immunopsychiatry

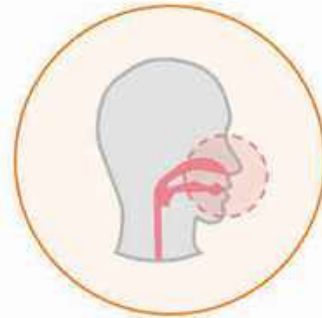
- “Viruses have now been linked to every neurodegenerative disease from autism to Alzheimer’s disease.”
- “A new field of “Immunopsychiatry” has emerged in the last few years where in a subset of patients where there is an inflammatory root to their brain disease.”
- “We see this clearly in PANS and PANDAS where an infectious trigger(s) [streptococcal (strep) infection, such as strep throat or scarlet fever] provokes an immune response in the brain.”

Dr. Suzanne Gazada
Integrative Neurology

Neuropsychiatric Manifestations in Covid-19



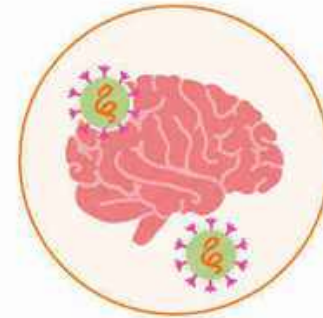
Encephalopathies
Meningoencephalitis
Neuromuscular disorders
Psychiatric disorders
? Neurodegenerative
disorders



Anosmia
and Ageusia



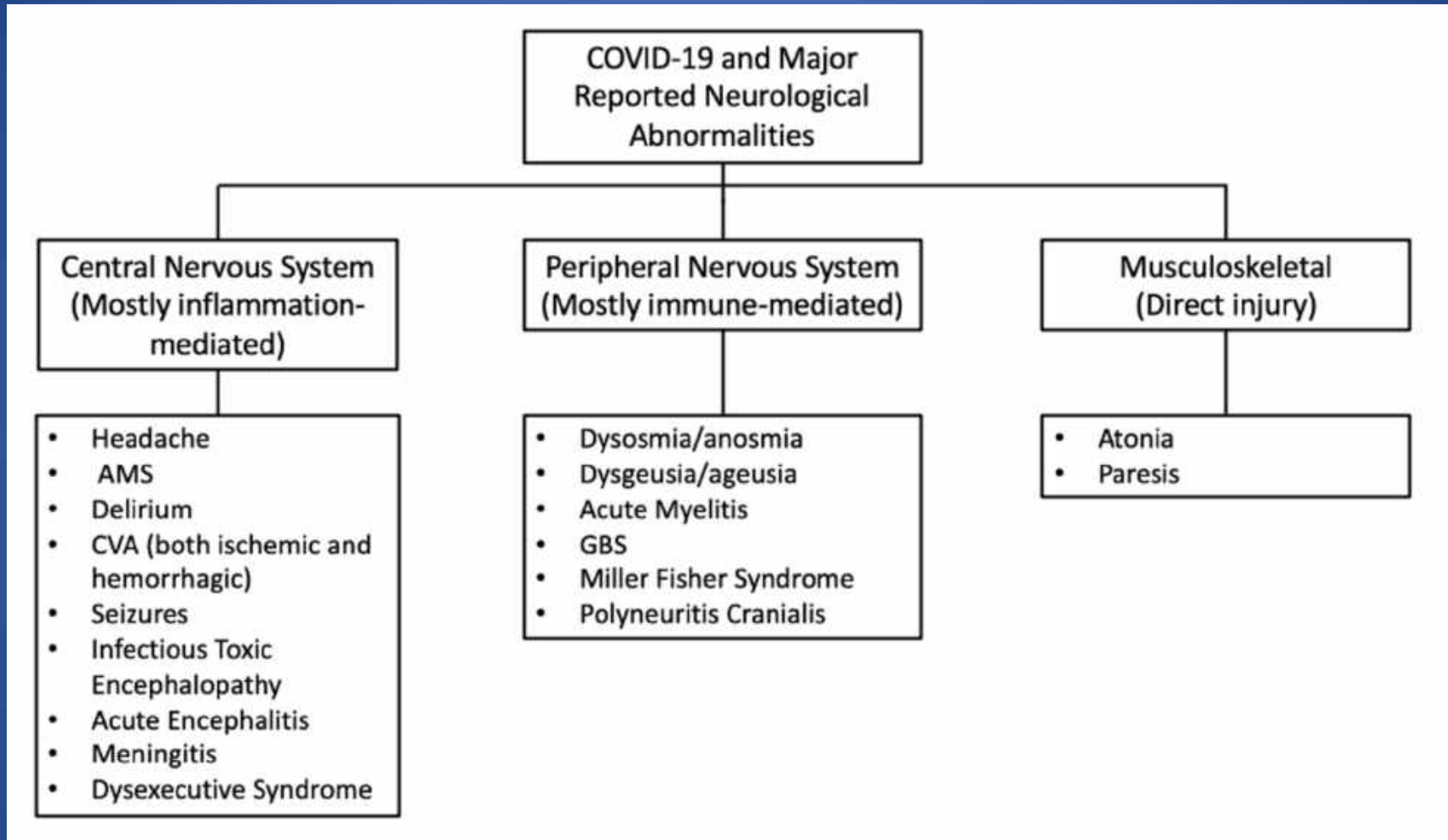
Acute Cerebrovascular
Disease



Infectious Toxic
Encephalopathies (Hypoxia,
metabolic disturbance and
systemic inflammation)

Wu, Y., Xu, X., Chen, Z., Duan, J., Hashimoto, K., Yang, L., ... & Yang, C. (2020). Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain, Behavior, and Immunity*.

Covi



Sheraton M, Deo N, Kashyap R, et al. (May 18, 2020) A Review of Neurological Complications of COVID-19. Cureus 12(5): e8192. doi:10.7759/cureus.8192

Neurologic Manifestations in Covid 19

- **Headache** - It is imperative to screen patients who present with headache for secondary causes if they **have had a change in their headache frequency or severity, develop systemic symptoms such as a fever, or are refractory to preliminary treatments.**
- **Anosmia and Ageusia** - **In COVID-19, anosmia is typically not accompanied by nasal swelling or rhinitis.** Given the reports of anosmia presenting as an early symptom of COVID-19, dedicated testing for anosmia may offer the potential for early detection of COVID-19 infection.
- **Stroke** - More specific viral mechanisms may also increase risk of stroke. Infection of the vascular endothelial cells and subsequent damage to vasculature may increase the risk of ischemic and hemorrhagic infarcts. **Autopsy in donors who had SARS-CoV-1 have demonstrated systemic vasculitis and vasculitis of venules in the brain.**
- **Impairment of consciousness** - There are several possible mechanisms of altered consciousness in patients with COVID-19, **including direct infection and damage of the parenchyma, toxic-metabolic encephalopathy, seizures, or demyelinating disease.**

Neurologic Manifestations in Covid-19

- Seizures - can also lead to impairment in consciousness and have been reported in other CoV infections. Additionally, **subclinical seizures are reported in roughly 10% of patients with critical illness and patients with primary seizure disorder are at higher risk of seizures and status epilepticus in the setting of severe infection**
- Toxic-Metabolic Encephalopathy - The hallmark of encephalopathy is impaired attention and arousal, presenting with confusion, lethargy, delirium, or coma. **Common risk factors that predispose patients to delirium are advanced age, underlying dementia or cognitive impairment, multiple comorbid diseases, infection, severe medical illness, poor functional baseline, and malnutrition. Patients hospitalized with COVID-19 may exhibit numerous toxic-metabolic derangements, including cytokine storm, severe inflammation, sepsis, and renal issues. High levels of proinflammatory cytokines in the CSF can cause breakdown and increased permeability of the BBB, which may in turn lead to viral invasion.**
- Encephalopathy - High levels of proinflammatory cytokines in the CSF can cause breakdown and increased permeability of the BBB, which may in turn lead to viral invasion.
- Guillain-Barré Syndrome and Peripheral Nerve Disorders - Reports of GBS in patients with COVID-19 are emerging. A case series⁸⁵ reported 5 cases of GBS in Italy after COVID-19 infection. In 4 cases, patients presented with lower-extremity weakness and paresthesias. **Patients developed symptoms a mean of 5 to 10 days after onset of viral symptoms.**

Psychopharmacology of COVID-19

Clinicians should be aware of the need to adjust existing psychotropics or avoid using certain medications in some patients with COVID-19.

COVID-19 is believed to impact multiple organs, including the liver, kidneys, lungs, and heart, as well as the immune and hematological systems.

Damage to these organs or systems by Covid 19 may lead to pharmacokinetic changes that impact absorption, distribution, metabolism, and/or excretion of psychotropic medications as well as increased sensitivity to certain psychotropic adverse effects.

As such, clinicians should be aware of the potential need to make adjustments to existing psychotropic regimens or avoid using certain psychotropic agents if such safety concerns arise

Psychopharmacology of COVID-19

Damage to these organs or systems by Covid 19 may lead to pharmacokinetic changes that impact absorption, distribution, metabolism, and/or excretion of psychotropic medications as well as increased sensitivity to certain psychotropic adverse effects. As such, clinicians should be aware of the potential need to make adjustments to existing psychotropic regimens or avoid using certain psychotropic agents if such safety concerns arise

Pearls

- Several psychotropics have been implicated in hematological adverse effects, including **leukopenia, neutropenia, and agranulocytosis**. The most commonly implicated psychotropics include **carbamazepine and clozapine**
- **Recognize potential for lowered seizure threshold**
- **Monitor CBC**
- **Baseline EKG for QTc; caution in patients with baseline prolonged QTc and/or other risk factors for drug-induced QT prolongation**
- **Monitor liver function tests**
- **Consider avoiding antipsychotics (especially clozapine, quetiapine, olanzapine, and first generation drugs) or adding antiepileptic drug (AED) in patients who have seizures**
- **COVID-19 with potential for acute kidney injury; gabapentin clearance dependent on intact renal function Adjust gabapentin dose based on renal function**
- **SSRI's and SNRI's - Monitor coagulation factors and platelet count; weigh risks and benefits for individual patient but consider avoiding SSRIs and SNRIs in patients with recent bleeding or high risk for bleeding (e.g., thrombocytopenia, concurrent anticoagulation therapy, history of hemorrhage) can instead use nonserotonin reuptake inhibitor antidepressant such as bupropion.**
- **Avoid bupropion in patients with seizures or lowered seizure threshold**

Psychopharmacology of COVID-19

Pearls

- Adjust lithium dose based on renal function; consider temporarily holding lithium until acute kidney injury resolves
- Avoid or taper existing benzodiazepines in patients with delirium if possible
- Weigh risks versus benefits in using benzodiazepines in patients with prominent respiratory symptoms; a low dose may be able to be used safely in nondelirious patients
- **Lopinavir/Ritonavir contraindicated with midazolam and triazolam** (and can raise levels of some other benzodiazepines) due to CYP450 inhibition
- Avoid midazolam and triazolam and consider using lorazepam, temazepam, or oxazepam in patients taking lopinavir/ritonavir

Consider avoiding medications that can negatively impact white blood cell production

- **Highest risk: carbamazepine, clozapine, olanzapine**
- Moderate risk: all first and second generation antipsychotics (especially low-potency conventionals)
- Rare reports: TCAs, benzodiazepines (chlordiazepoxide), gabapentin, and valproate
- Consider avoiding medications that can increase bleeding risk (via thrombocytopenia or impaired platelet aggregation): valproic acid, SSRIs, SNRIs

Psychopharmacology of COVID-19

Hematologic

- Consider avoiding medications that can negatively impact white blood cell production
 - **Highest risk: carbamazepine, clozapine, olanzapine**
 - Moderate risk: all first and second generation antipsychotics (especially low-potency conventionals)
 - Rare reports: TCAs, benzodiazepines (chlordiazepoxide), gabapentin, and valproate. Consider avoiding medications that can increase bleeding risk (via thrombocytopenia or impaired platelet aggregation): valproic acid, SSRIs, SNRIs

Cardiac

- **Several medications being used for COVID-19 (azithromycin, hydroxychloroquine, chloroquine, lopinavir/ritonavir) reported to prolong QT interval**
- Caution with psychotropics known to prolong QTc and in patients with other underlying risk factors for QT prolongation **Highest risk: antipsychotics, citalopram, tricyclic antidepressants**

Hepatic

- Consider avoiding psychotropics that can also cause serious drug induced liver injury: chlorpromazine, carbamazepine, valproate, duloxetine, and nefazodone. Refer to prescribing information to determine if dose adjustments are needed

Psychopharmacology of COVID-19

Renal

- Consider dose adjustment with some psychotropics (e.g., lithium, gabapentin, topiramate, pregabalin, paliperidone, and duloxetine)
- Consider avoiding potentially nephrotoxic drugs

Nervous System

- In patients with delirium, caution with deliriogenic medications: benzodiazepines, opioids, sedative-hypnotics, and those drugs with strong anticholinergic effects (tertiary amine tricyclic antidepressants, low-potency first-generation antipsychotics, some second-generation antipsychotics, benztropine, and diphenhydramine)
- Caution with medications that can lower seizure threshold: antipsychotics and certain antidepressants (bupropion, tricyclics)

Pulmonary

- In COVID-19 patients with anxiety or panic symptoms, weigh risks versus benefits in using benzodiazepines in patients with prominent respiratory symptoms, given potential to suppress respiratory drive

Goals of Treatment

(Health care providers are therapist -
Patients look to us as informed, wise, experts looking out for the patient and their families)

Mental

- Distinguish Organic vs Functional Psychiatric Illness
- Watch for Drug-Drug interactions between Psychiatric Medications and Medications used to treat Covid-19
- Prevention screening and early identification of treatment in mental health disorders
- Management of relapses in psychiatric illness in a vulnerable population
- Refer to higher level of psychiatric care if patient appears to be acutely decompensating to a dangerous level
- Consider use of Mobile Psychiatric Services

Suicide

Suicide rate projected to increase as unemployment jumps from coronavirus outbreak

BY ERIC W. DOLAN JULY 2, 2020

- **“The link between unemployment, economic shock and suicide is highly replicated in population health. The anxiety of the virus with the economic shock, along with the physical distancing, is an unprecedented assault on mental health.” –**

Roger S. McIntyre. MD Lead author of both studies and a professor of psychiatry and pharmacology at the University of Toronto

- **Based on previous suicide and unemployment data, the authors of the study were able to estimate the number of excess suicides likely to occur in the wake of increased unemployment amid the COVID-19 pandemic.**

- **Between 2020 to 2021:**

They project 418 to 2,114 excess suicides in Canada

They project 3,235 to 8,164 excess suicides in the United States.

In 2018, 48,344 Americans died by suicide

<https://afsp.org/suicide-statistics/>

The studies, “Projected increases in suicide in Canada as a consequence of COVID-19” and “Preventing suicide in the context of the COVID-19 pandemic”, were authored by Roger S. McIntyre and Yena Lee.

300-400 Physicians die by suicide in the USA each year

The New York Times

'I Couldn't Do Anything': The Virus and an E.R. Doctor's Suicide

Dr. Lorna Breen was unflappable — until she faced a new enemy.



[New York Times 'I Couldn't Do Anything': The Virus and an E.R. Doctor's Suicide](#)
[Dr. Lorna Breen was unflappable — until she faced a new enemy.](#)
[By CORINA KNOLL, ALI WATKINS AND MICHAEL ROTHFELD JUL 20 2020](#)



Dr. Breen during her residency at Long Island Jewish Medical Center. via the Feist family

If Dr. Breen is lionized along with the legions of other health care workers who gave so much — maybe too much — of themselves, then her shattered family also wants her to be saluted for exposing something more difficult to acknowledge: the culture within the medical community that makes suffering easy to overlook or hide; the trauma that doctors comfortably diagnose, but are reluctant to personally reveal, for fear of ruining their careers.

The pandemic intensified both the demands made of doctors and the pressure to endure those demands. Recent studies of medical workers in China, Canada and Italy who treated Covid-19 patients found increasing rates of anxiety, depression and insomnia.

[New York Times: 'I Couldn't Do Anything': The Virus and an E.R. Doctor's Suicide. Dr. Lorna Breen was unflappable — until she faced a new enemy.](#)
By CORINA KNOLL, ALI WATKINS AND MICHAEL ROTHFELD

Health Providers of all Kinds – Balance Yourself First

- We are products of “fear-based learning experiences” (i.e. medical school)
- We are usually afraid of failure, getting behind, not being up to date with current medical information.
- We are all suffering together
- “You can’t read everything” – patient remark
- Acknowledge your suffering – and self distress
- Return to the present moment – example (neurosurgeon during long surgeries > 8 hours)
- Do what you can do to finish the day – break it down into 15 minutes intervals if necessary.
- Schedule in exercise like a patient are you won’t get it done



[About](#) [PSL In The Media](#) [f](#)

Physician Support Line 1 (888) 409-0141

Psychiatrists helping our US physician colleagues
and medical students navigate the many intersections
of our personal and professional lives

Free & Confidential | No appointment necessary
Open 7 days a week | 8:00AM - 1:00AM ET

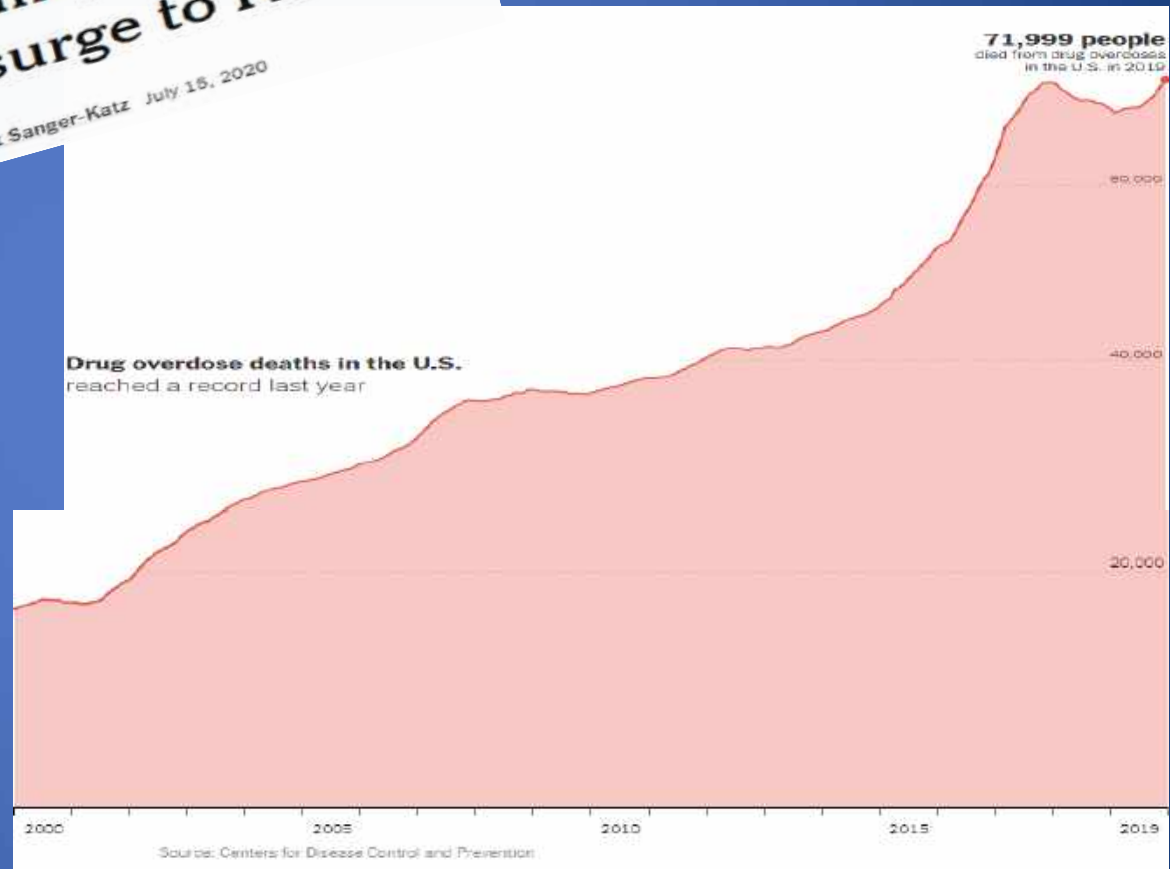
Anonymous service and not affiliated with any institution. Answered by volunteer Psychiatrist to help navigate an immediate stressor. No Medication is prescribed. Available to Physicians, Residents, Fellows, and Medical Students. No payment accepted.

The New York Times

In Shadow of Pandemic, U.S. Drug Overdose Deaths Resurge to Record

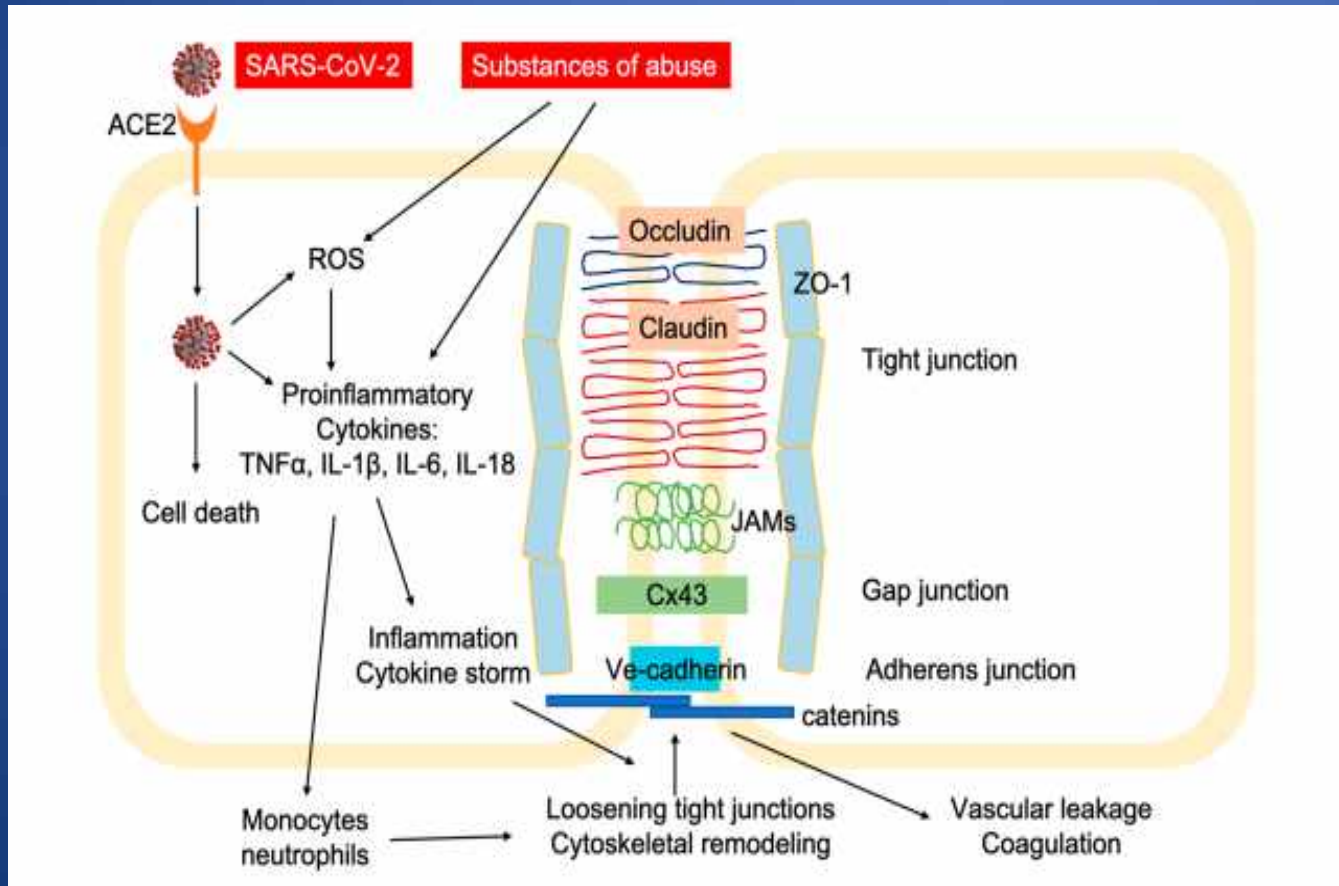
By Josh Katz, Abby Goodnough and Margot Sanger-Katz July 15, 2020

It looks as if 2020 will be even worse. Drug deaths have risen an average of 13 percent so far this year over last year, according to mortality data from local and state governments collected by The New York Times, covering 40 percent of the U.S. population. If this trend continues for the rest of the year, it will be the sharpest increase in annual drug deaths since 2016, when a class of synthetic opioids known as fentanyl first made significant inroads in the country's illicit drug supply.



Substance Abuse and Covid – 19

Substances of Abuse have been shown to severely compromise the endothelial barrier at the BBB, leading to increased BBB permeability and possibly intensified brain damage in Covid -19



SARS-CoV-2 infects vascular endothelial cells through the surface-expressed ACE2 receptor. Internalization of the virus can cause endothelial cell death, increase in reactive oxidative species (ROS) and the release of various pro-inflammatory cytokines.

Excessive inflammation, and potential cytokine storm, induce the loosening of the tight junction complex and cytoskeletal remodeling, leading to vascular leakage and coagulation

Various substances of abuse exert similar effects at the brain endothelial junctions disrupting the BBB and allowing viral infection in the CNS












Goals of Treatment

- Psychological First Aid if Needed
- Brief advice on management for short and long term isolation (exercise, no drugs and alcohol, use of vitamins and supplements)
- Long term management of psychosocial consequences of losses (i.e. Bereavement, financial loss, job loss) Anticipatory Grief
- Participate in post-pandemic screening and surveillance to address psychiatric disorders

Connect your patient to care or treatment even if you can't treat them directly

<https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/managing-stress-anxiety.html>

Get immediate help in a crisis

- Call 911
- [Disaster Distress Helpline](#)  : 1-800-985-5990 (press 2 for Spanish), or text TalkWithUs for English or Hablanos for Spanish to 66746. Spanish speakers from Puerto Rico can text Hablanos to 1-787-339-2663.
- [National Suicide Prevention Lifeline](#)  : 1-800-273-TALK (8255) for English, 1-888-628-9454 for Spanish, or [Lifeline Crisis Chat](#) .
- [National Domestic Violence Hotline](#)  : 1-800-799-7233 or text LOVEIS to 22522
- [National Child Abuse Hotline](#)  : 1-800-4AChild (1-800-422-4453) or text 1-800-422-4453
- [National Sexual Assault Hotline](#)  : 1-800-656-HOPE (4673) or [Online Chat](#) 
- [The Eldercare Locator](#)  : 1-800-677-1116 [TTY Instructions](#) 
- [Veteran's Crisis Line](#)  : 1-800-273-TALK (8255) or [Crisis Chat](#)  or text: 8388255

Find a health care provider or treatment for substance use disorder and mental health

- [SAMHSA's National Helpline](#)  : 1-800-662-HELP (4357) and TTY 1-800-487-4889
- [Treatment Services Locator Website](#) 
- [Interactive Map of Selected Federally Qualified Health Centers](#) 

Connect your patient to care or treatment even if you can't treat them directly

<https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/managing-stress-anxiety.html>

People who may respond more strongly to the stress of a crisis include:






- People who are at higher risk for severe illness from COVID-19 (for example, older people, and people of any age with certain underlying medical conditions).
- Children and teens.
- People caring for family members or loved ones.
- Frontline workers such as health care providers and first responders.
- Essential workers who work in the food industry.
- People who have existing mental health conditions.
- People who use substances or have a substance use disorder.
- People who have lost their jobs, had their work hours reduced, or had other major changes to their employment.
- People who have disabilities or developmental delay.
- People who are socially isolated from others, including people who live alone, and people in rural or frontier areas.
- People in some racial and ethnic minority groups.
- People who do not have access to information in their primary language.
- People experiencing homelessness.
- People who live in congregate (group) settings.

Connect your patient to care or treatment even if you can't treat them directly

<https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/managing-stress-anxiety.html>

Learn more about CDC's work in [suicide prevention](#).

Other Resources:



- [National Suicide Prevention Lifeline](#)  : 1-800-273-TALK (8255) for English, 1-888-628-9454 for Spanish, or [Lifeline Crisis Chat](#)  .
- [SAMHSA Suicide Prevention](#) 
- [Suicide Risk Factors and Warning Signs](#) 
- [Five Action Steps for Communicating with Someone Who May Be Suicidal](#) 

Connect your patient to care or treatment even if you can't treat them directly





<https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/managing-stress-anxiety.html>

Resources

For Everyone

- [Coping with a Disaster or Traumatic Event](#)
- [HHS ASPR TRACIE COVID-19 Behavioral Health Resources](#) 
- [Coronavirus Tax Relief and Economic Impact Payments](#) 

For Communities

- [Coping with Stress During an Infectious Disease Outbreak](#)  
- [Taking Care of Your Behavioral Health during an Infectious Disease Outbreak](#)  

For Families and Children

- [Helping Children Cope during an COVID-19 Outbreak](#)
- [Helping Children Cope with Emergencies](#)
- [Coping After a Disaster](#)  – A Ready Wrigley activity book for children age 3-10
- [Teen Depression](#) 

For People at Higher Risk for Serious Illness

- [Serious Illness Care Program COVID-19 Response Toolkit](#) 

For Healthcare Workers and First Responders

- [Healthcare Personnel and First Responders: How to Cope with Stress and Build Resilience During the COVID-19 Pandemic](#)
- [Emergency Responders: Tips for Taking Care of Yourself](#)
- [Disaster Technical Assistance Center](#)  (SAMHSA)

For Other Workers

- [Employees: How to Cope with Job Stress and Build Resilience During the COVID-19 Pandemic](#)

Connect your patient to care or treatment even if you can't treat them directly
<https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/managing-stress-anxiety.html>

- 🏠 Your Health
- Symptoms
- Testing
- Prevent Getting Sick
- If You Are Sick
- Daily Life & Going Out**
- At Home
- Going Out
- Caring for Children

- Stress & Coping**
- Coping with Stress**
- Helping Children Cope
- Reducing Stigma
- Stop the Spread of Rumors
- Grief & Loss
- Alcohol & Substance Use
- Support for People Experiencing Abuse
- Support for Veterans
- Support for Teens & Young Adults

- Funeral Guidance
- Contact Tracing
- People at Increased Risk
- Pets & Other Animals
- Travel
- Frequently Asked Questions

Boost Physical Immunity

Preventive Measures are also “a physical action to break the worry loop”

- Wash your Hands
- Wear your Mask

Diet

- The immune system relies on white blood cells that produce antibodies to combat bacteria, viruses, and other invaders.
- Vegetarians have been shown to have more effective white blood cells when compared to non - vegetarians, due to a high intake of vitamins and low intake of fat.
- Plant-based diets are effective for weight loss, because they are rich in fiber, which helps fill you up, without adding extra calories.
- A plant-based diet has also been shown to reduce inflammatory biomarkers.
- Fiber can also lower BMI, which is linked to improved immunity.

Exercise

- Maintaining a healthy weight can also benefit the immune system.
- Obesity and Diabetes has been linked to increased risk for influenza and other infections such as pneumonia.

Foods To Boost the Immune System



Photo: Getty Images

Give your immune system a **boost** with healthful, **plant-based foods**.

Vitamins, Minerals, and Antioxidants

- Studies have shown that fruits and vegetables provide nutrients—like beta-carotene, vitamin C, and vitamin E—that can boost immune function.
- Vegetables, fruits, and other plant-based foods are also rich in antioxidants, they help reduce oxidative stress.
- Beta-Carotene: Beta-carotene is a powerful antioxidant that can reduce inflammation and boost immune function by increasing disease-fighting cells in the body. Excellent sources include sweet potatoes, carrots, and green leafy vegetables.
- Vitamins C and E are antioxidants that help to destroy free radicals and support the body's natural immune response.
- Sources of Vitamin C include red peppers, oranges, strawberries, broccoli, mangoes, lemons, and other fruits and vegetables. Vitamin E sources include nuts, seeds, spinach, and broccoli.
- Vitamin D research shows vitamin D supplementation may reduce the risk for viral infections, including respiratory tract infections, by reducing production of proinflammatory compounds in the body.



Increased vitamin D in the blood has been linked to prevention of other chronic diseases including tuberculosis, hepatitis, and cardiovascular disease.

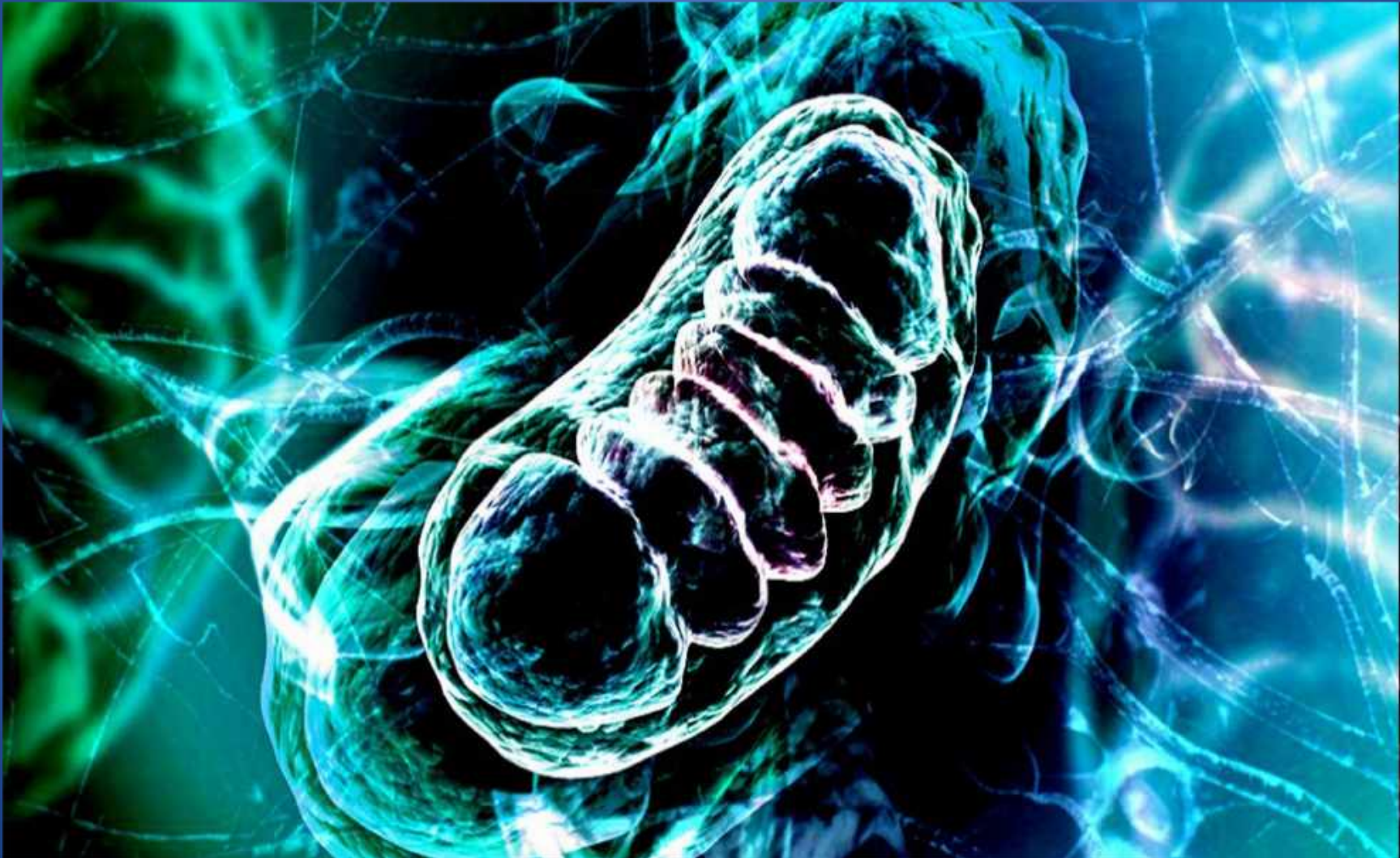
Zinc is a mineral that can help boost white blood cells, which defend against invaders.

Zinc sources include nuts, pumpkin seeds, sesame seeds, beans, and lentils.

“If the patient has been to more than four physicians, nutrition is probably the medical answer.”

-Dr. Abram Hoffer

Mitochondrial Resucitation
NAD⁺
Nicotinamide Adenine Dinculeotide

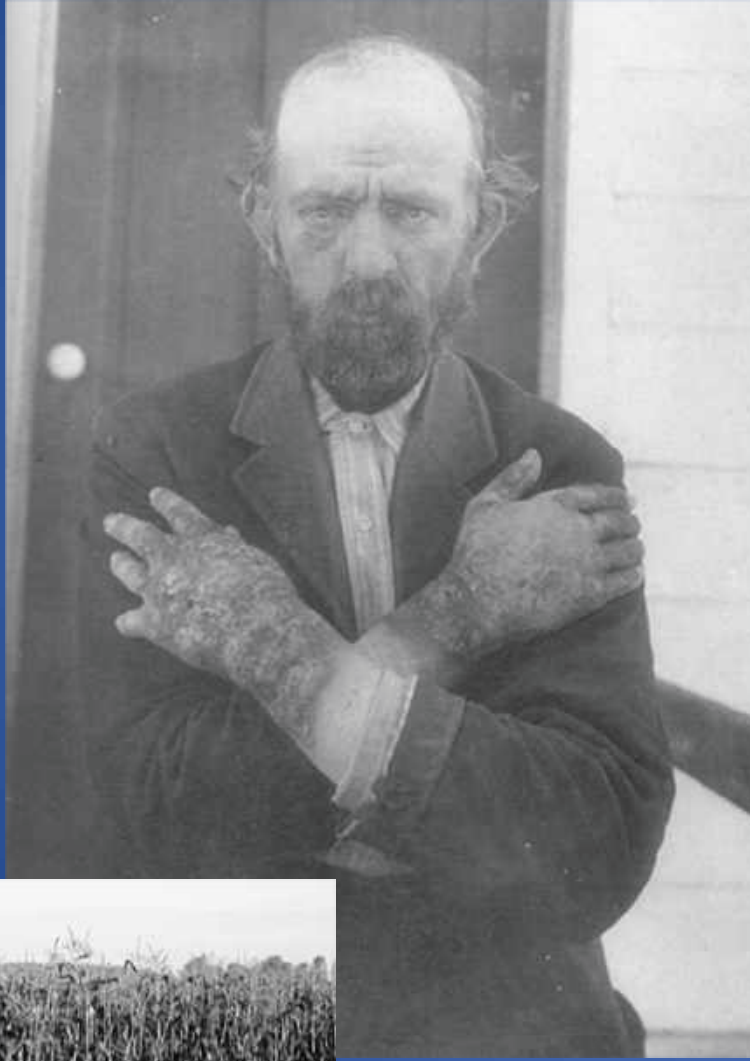




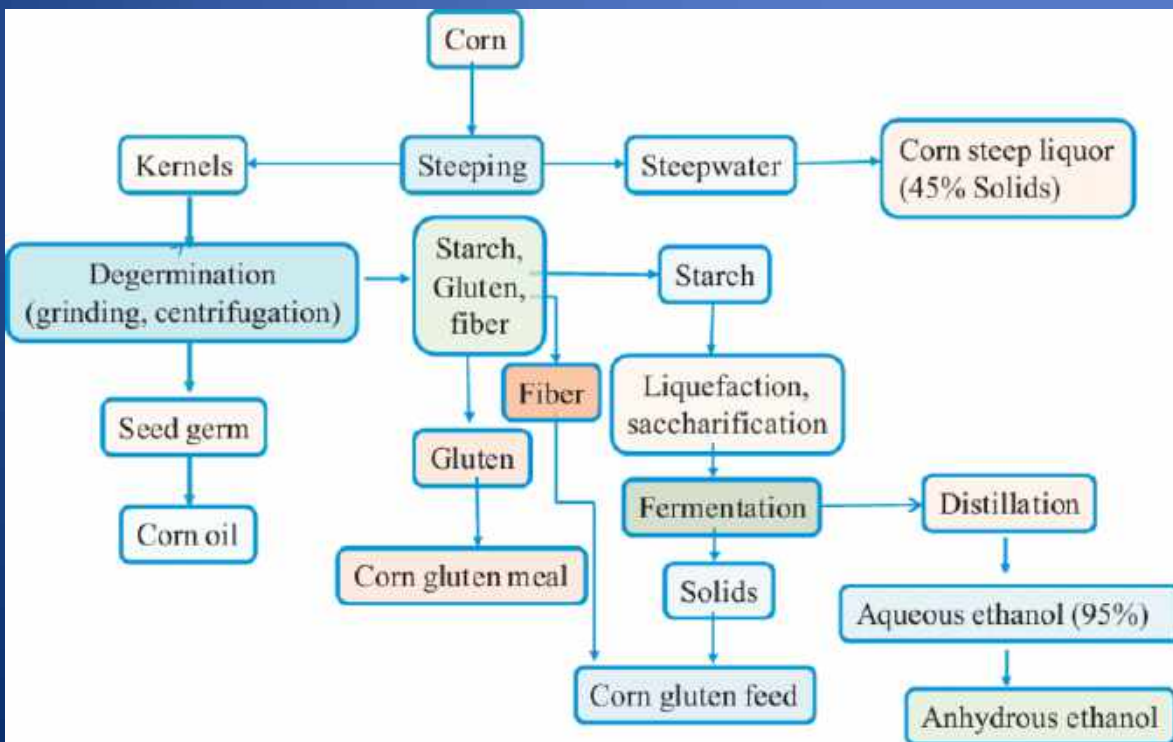
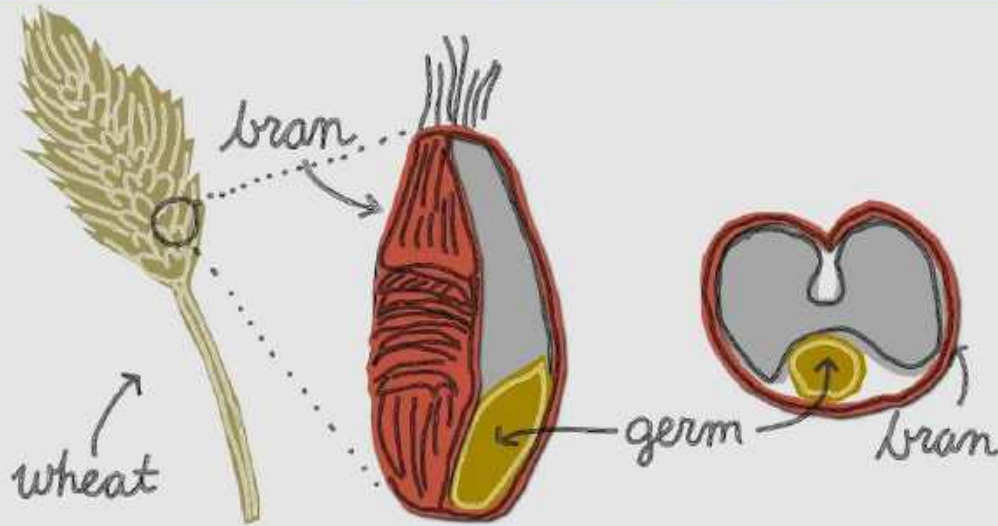
THUNDERBIRD – AKA BUM WINE

Pellagra

Old and New



WHEAT OR WHITE



Refined Grains



White Flour

- Enriched Flour
- All Purpose Flour



White Rice



Parboiled Rice



Cream of Wheat



Degermed Cornflour

Just the Facts

White Bread vs Whole-grain Bread

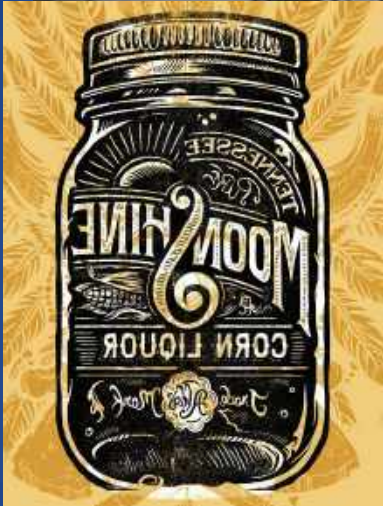


- Bran and germ are removed during the refinement process.
- Simple carbohydrate
- One slice has 0.5 grams of fiber.
- Although some vitamins and minerals are added back to refined grains after milling, they still lack nutrients found in whole grains.



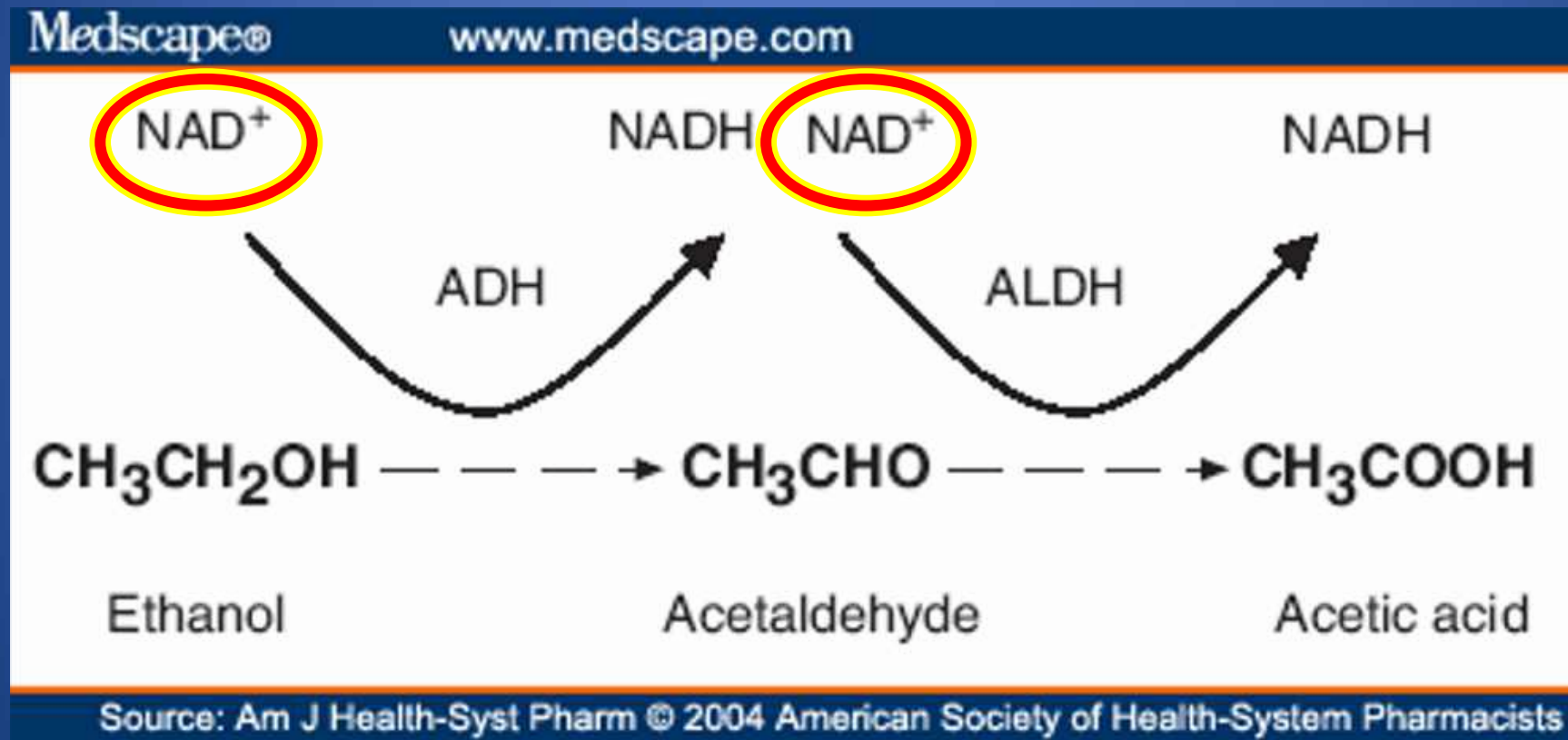
- Contain the entire grain (bran, germ, endosperm)
- Complex carbohydrate
- One slice has 3.6 grams of fiber.
- Whole grains contain large amounts of vitamins such as vitamin E, niacin, riboflavin, thiamin, and folate, as well as minerals such as iron, magnesium, potassium, copper and selenium. as minerals such as iron, magnesium, potassium, copper and selenium.

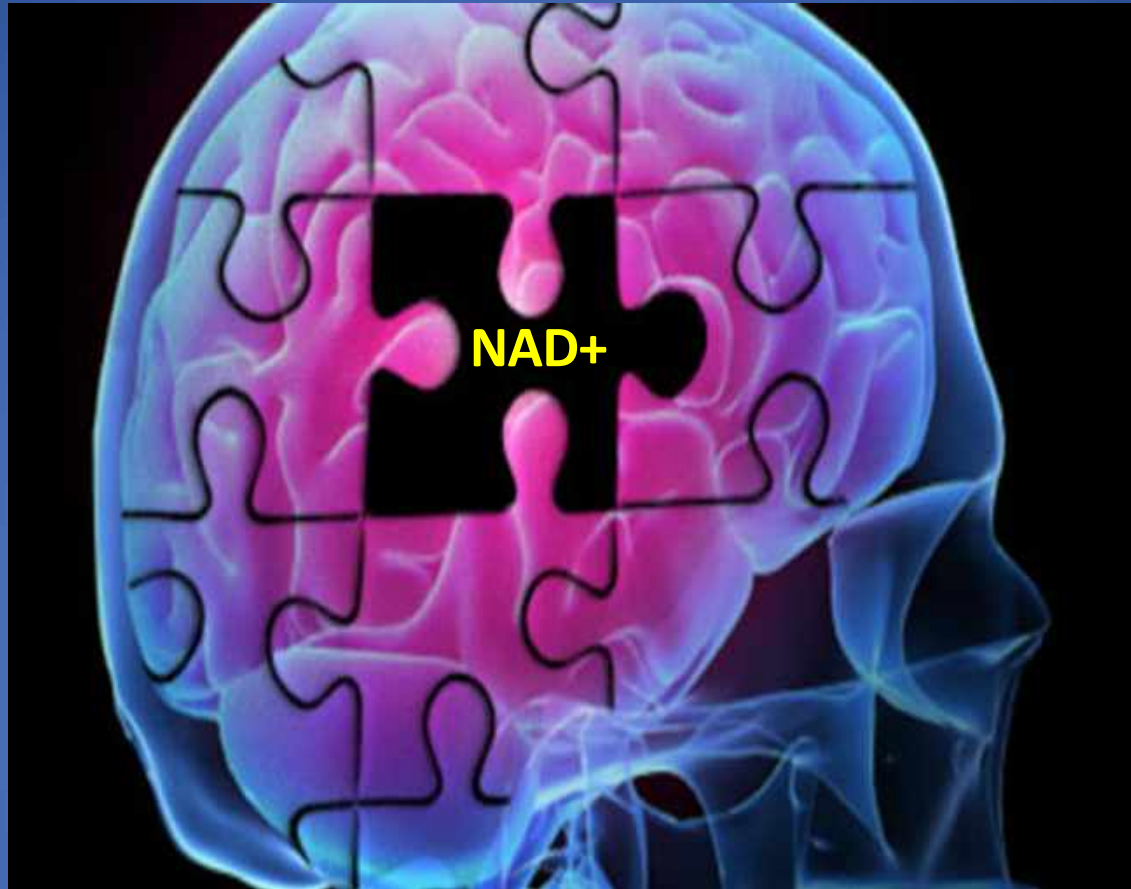
Moon Shine Madness



Alcohol Metabolism

Further expedites depletion of NAD⁺



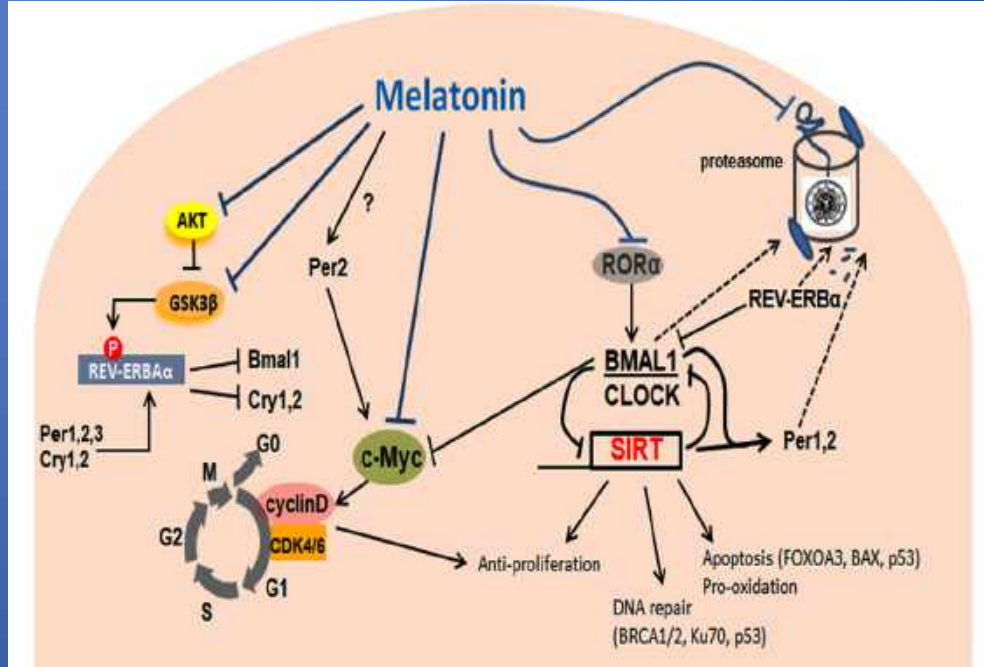
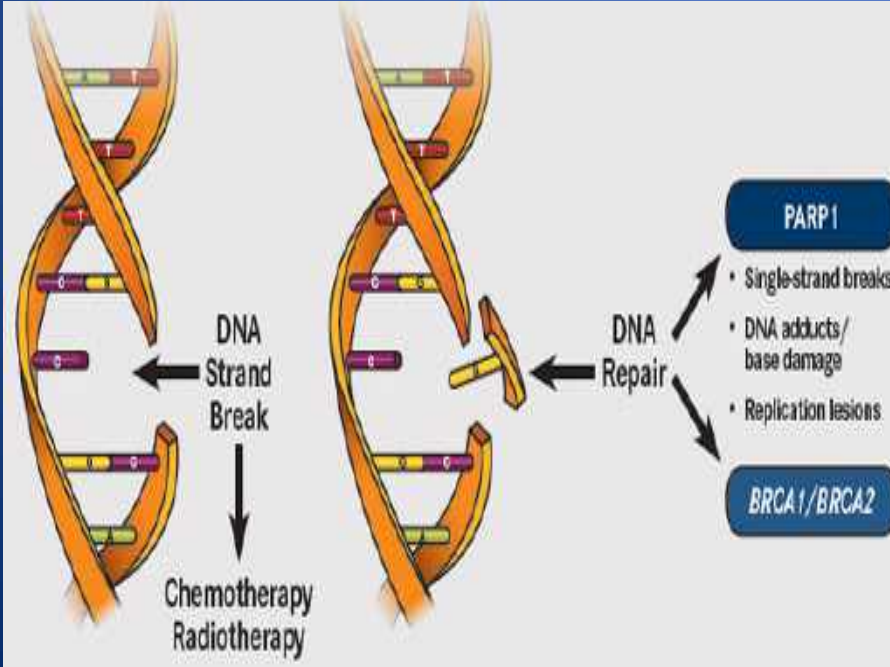
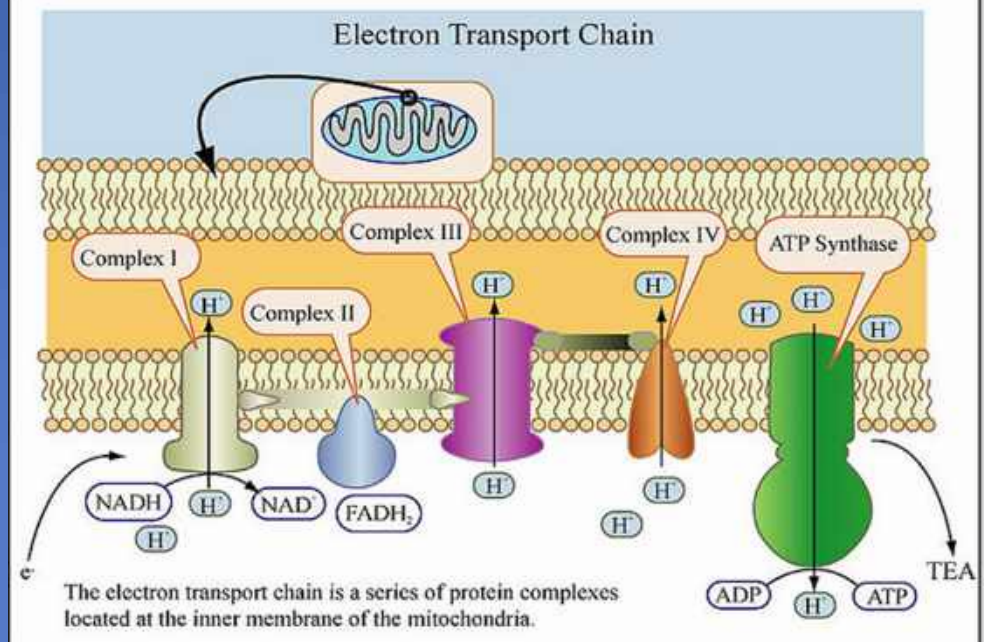
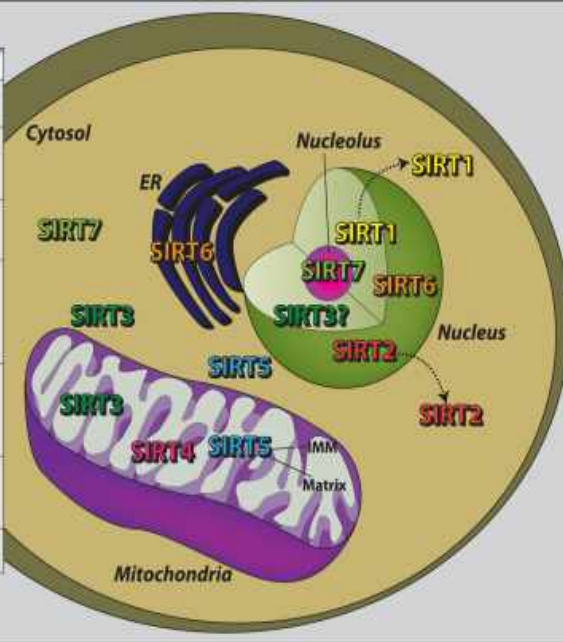


“NAD deficiency may be an unrecognized epidemic of cellular disease.”

- Dr. Abram Hoffer, MD, PhD

IV and Oral NAD+ - SIRT6, PARP1, BMAL1/ Clock Gene

Sirtuin	Enzyme Action
SIRT1	Deacetylase
SIRT2	Deacetylase ADP-ribosyltransferase Demyristoylase
SIRT3	Deacetylase Decrotonylase
SIRT4	ADP-ribosyltransferase Deacetylase Lipoamidase
SIRT5	Deacetylase Desuccinylase Deglutarylase Demalonylase
SIRT6	Deacetylase ADP-ribosyltransferase Demyristoylase
SIRT7	Deacetylase



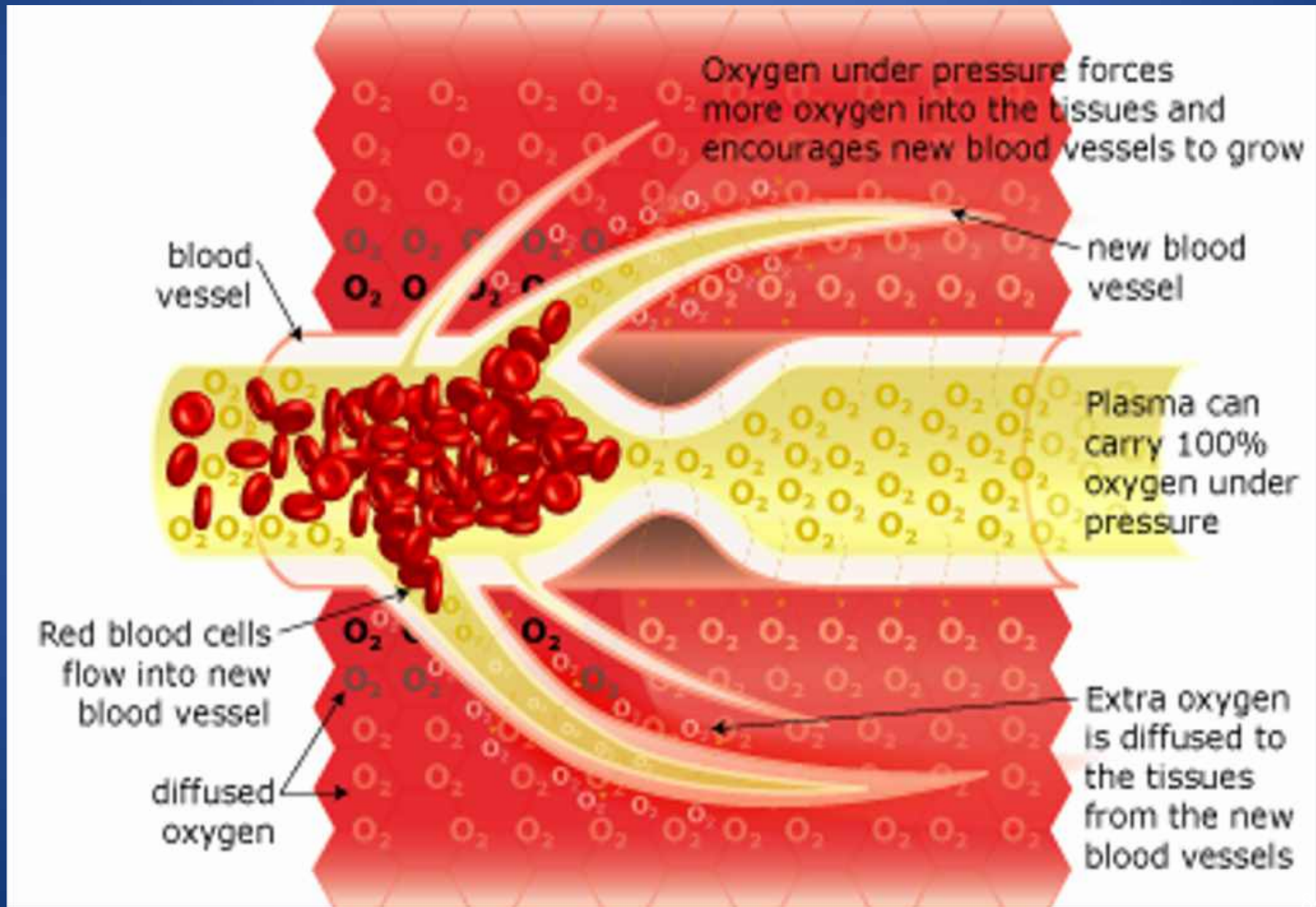
Hard 1.5 ATM Chamber with 100% Oxygen



Soft 1.3 ATM Chamber



How HBOT Works

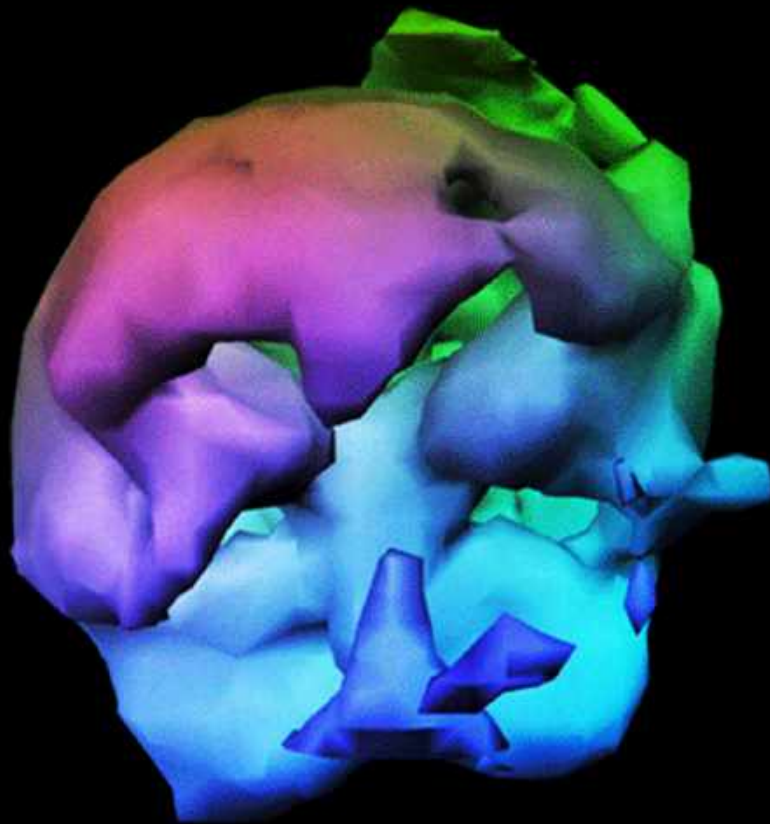




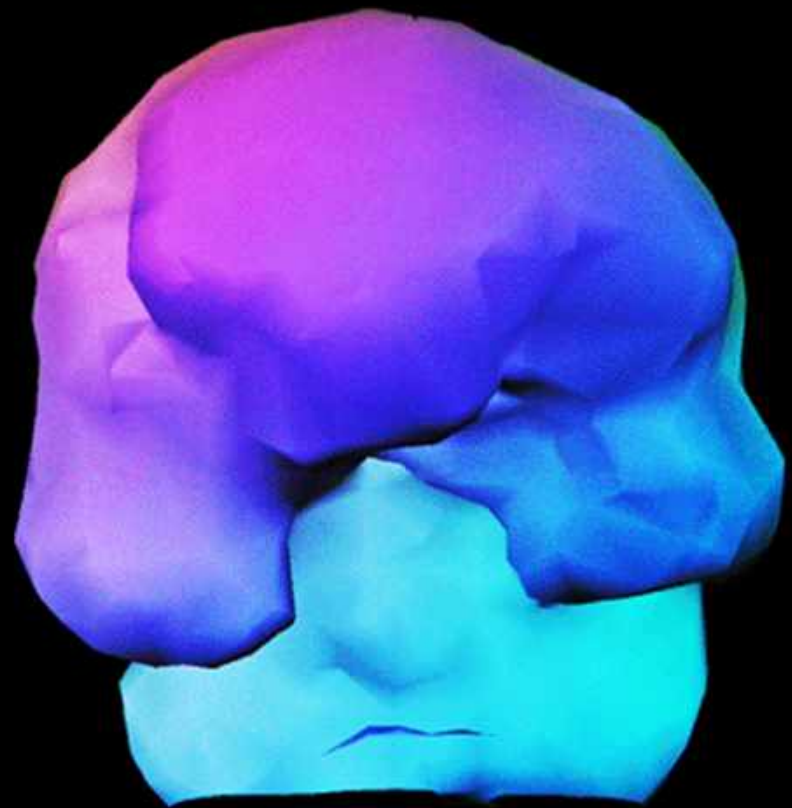
BEFORE



AFTER HBO



PRE-HBOT



POST-HBOT

FIGURE 2

GUARD YOUR SLEEP



Sleep Hygiene for Adults

Avoid electronics (computers, smartphones, tablets, video games) and bright light at least 60 minutes before bedtime.

Avoid daytime napping, if napping during the day, or have non-restorative sleep, get tested.

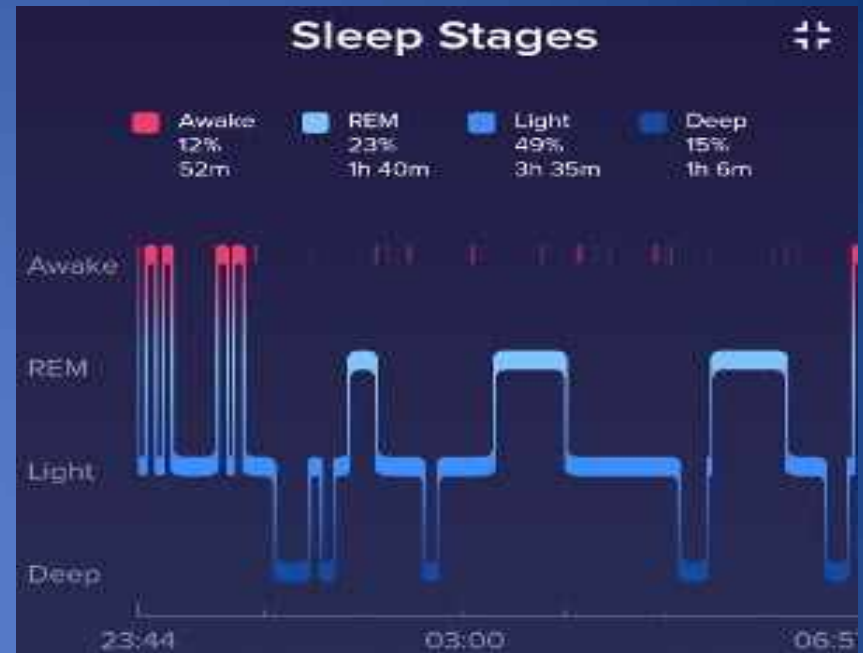
Actually use your CPAP or prescribed device. If your sleep partner has snoring or Central Apnea, get them treating to improve your health.

If you have pets and your sleep is disrupted, consider removing pets from the bedroom while you sleep.

Inadequate sleep has also been linked to suppressed immune function.



Home Sleep Testing and APP Monitoring



Sleep Hygiene for Children and Teens

Build a Bedtime Routine:

- Children need about 10-11 hours of sleep. Teens need about 9-10 hours.
- Set a regular time for bed each night and stick to it, even on weekends.
- Establish a relaxing bedtime routine, such as a warm bath, light reading, gentle stretching, or meditation (for example – imagining being on a beach) before bed

Make after-dinner time a relaxing time.

Avoid feeding children/teens big meals close to bedtime.

A small healthy snack can be helpful if they are hungry

Avoid giving children/teens anything with caffeine (soda, chocolate, energy drinks) within six hours of bedtime.

Keep the bedroom cool, noise low, and dark or small night light if needed

Exercise can promote good sleep

Ensure adequate exposure to natural light

Try to avoid emotionally upsetting conversations and activities before trying to go to sleep.

Don't dwell on, or bring your problems to bed.

Schedule a block of time for “worry time” earlier in the day if needed.

Associate bed with sleep.

Sleep Hygiene for Children and Teens

- Children/teens not have TVs, computers or cell phones in their bedrooms at night.
- Avoid the use of computers, TV/video games, cellphones or tablets/iPads 2 hours prior to bedtime.
- **“The Lost Hour”**
 - **“30 minutes of Sleep is the difference between and “A” and a “B” student.”**
 - Author Po Bronson - Nurture Shock

Teach Mental Resilience

Patients are suffering from national and international chaos, social anxiety, and social contagion panic.

People “fear – fear” – “fear of whether they will live or die.”

Interrupt the pattern of Automatic Negative Thoughts

Dr. Stuller Technique:

- ✓ “Hear my words when you feel yourself being anxious”
- ✓ (Most people feel anxious when they are too far into the future or too far into the past)
- ✓ “Raise a red flag in your mind”
- ✓ “Come back to the present moment which is all you can control”
- ✓ “All you need to do and can do is to get through today”
- ✓ “Acknowledge and Thank the Fear – Taking action relieves fear”
- ✓ “Action of any kind – Do one task, Clear one thing, Exercise or walk using the 5 minute rule”
- ✓ “Do what you can do in 10 minutes increments if necessary to make it do-able”
- ✓ “Practice daily for sustained endurance in conquering fears”



See yourself as a Medical S.E.A.L. – An Academic Athlete

See Yourself Fit and Centered with
Concentration and Focus

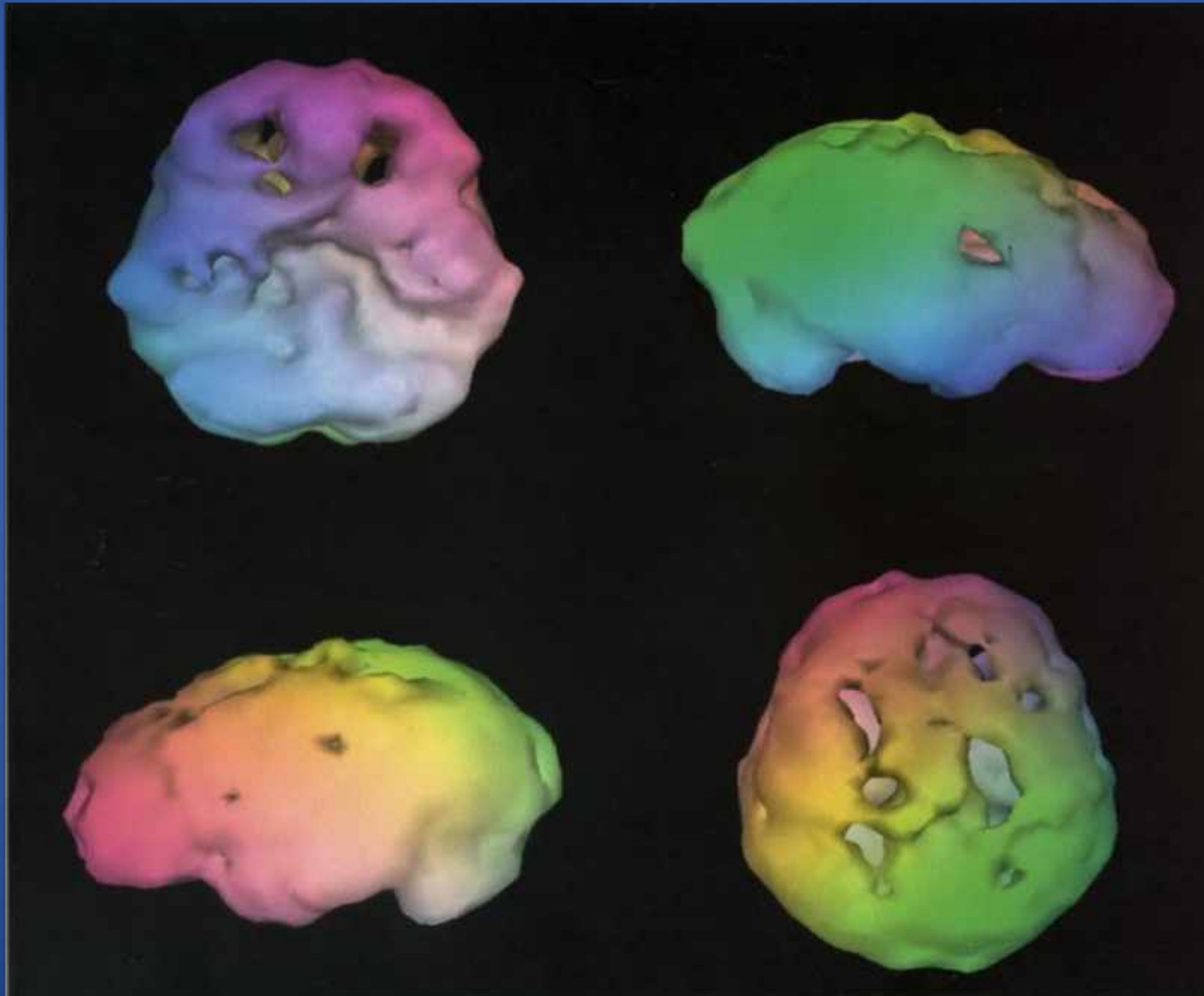


Brain Restoration

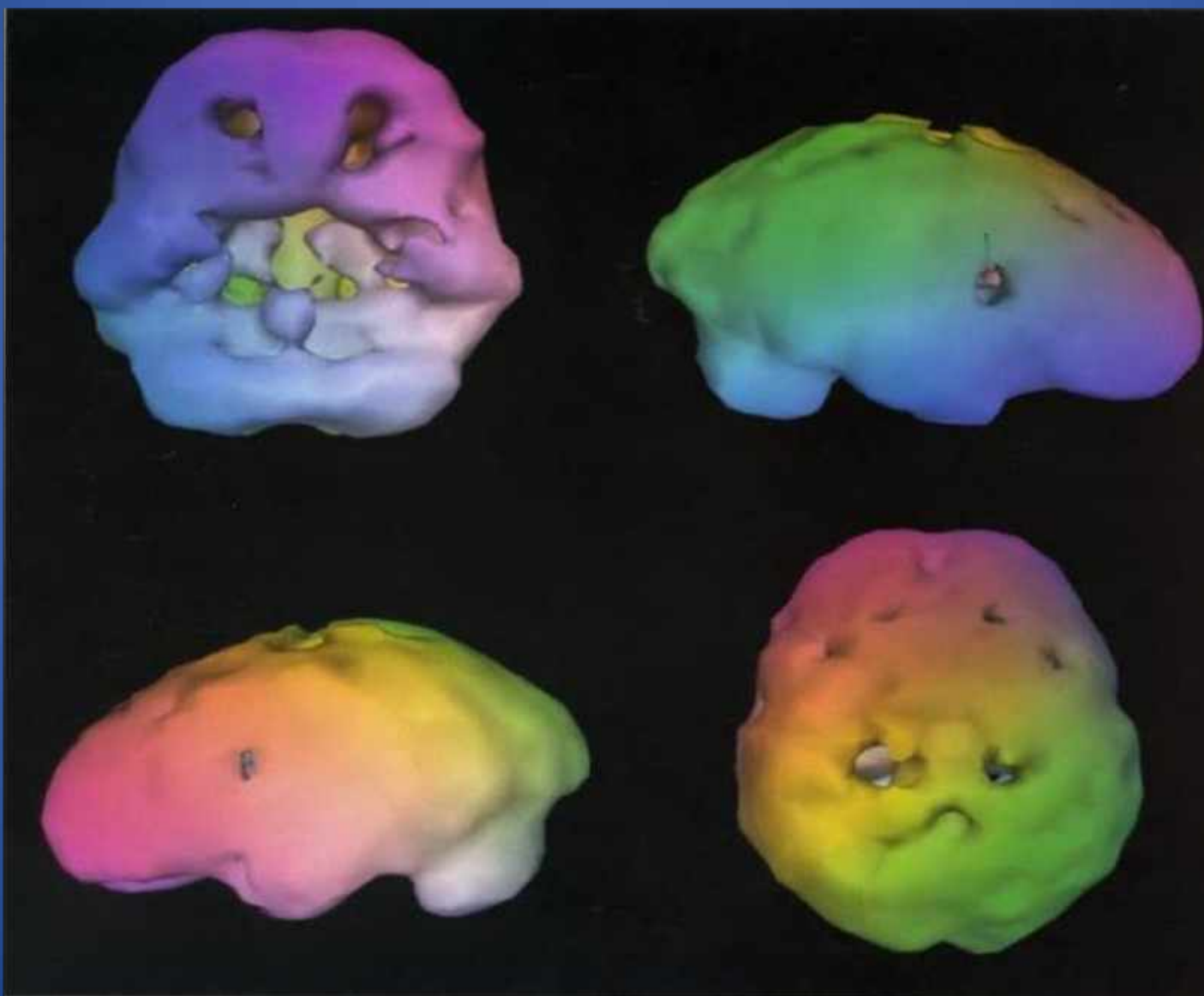
Beginning the upward spiral of recovery



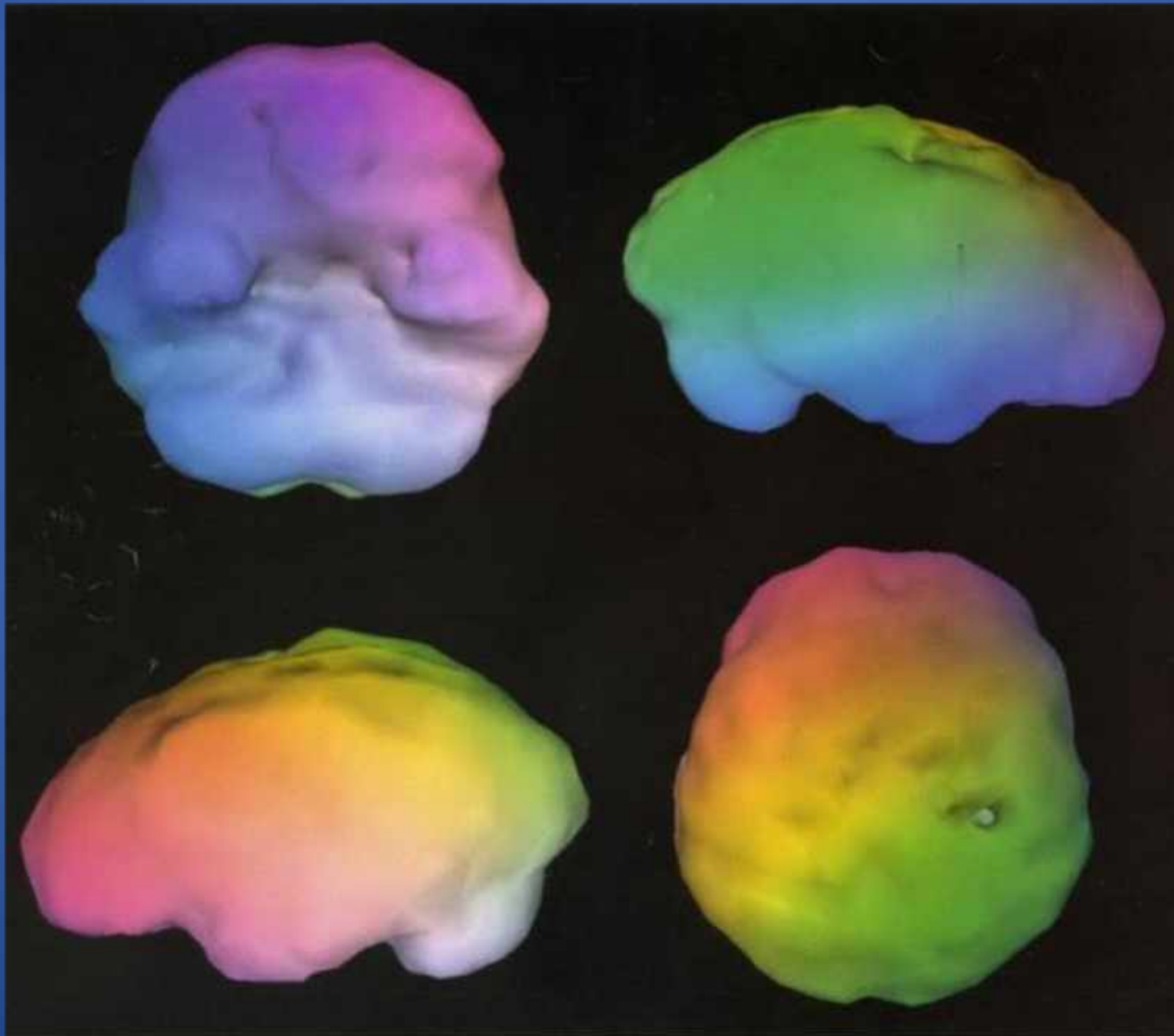
May 2007



October 2009



April 2012





Thank You!



Elizabeth A. Stuller, MD
ABPN Board Certified
Adult and Addiction Psychiatry
Fellow – American Psychiatric Association
Fellow – American Society of Addiction
Medicine

Stuller Resettings, LLC
Catonsville, Maryland

stullerresettings@gmail.com