Psychoneuroimmunology (PNI), Health, and Spirituality

Practical Application

What is Health?

- A state of complete physical, mental, and social well-being **and not merely the absence of disease or infirmity**." (The World Health Organization (WHO) in 1946)
- Where is spirituality?
  - We are a spirit being, we live in a body and we possess a soul. The real person inside of us is our spirit. Our soul consists of our mind, will and emotions. Our bodies are obviously what we live in while we are here on earth.
  - The soul and the spirit are connected, but separable (Hebrews 4:12).
- The soul is the essence of humanity's being; **it is who we are**.
- The spirit is the aspect of humanity that connects with God.

What is Health?

- Four aspects of our being that are **intimately connected**
  - Body
  - Mind - Soul
  - Spirit
  - Emotion -Soul
- Health and Well-Being – **keeping all four aspects in balance** and running like a well-oiled machine
  - If we ignore or neglect one aspect, the others are weakened
  - If we strengthen one aspect, the others are strengthened
- Currently basic healthcare for "healthy" individuals predominantly focuses on the body and the mind

Qualities Linked to the Four Aspects of Health

Energy (Cyclic, Exercise, Nutrition, Rest)
Physical Wellness
Presence
Made of the World

Self-Concept
Intellect
Wisdom
Logic
Beliefs
Self –Will
Eternal

Not of this World
Vision
Inspiration
Enlightenment
Meaning/Purpose
Service
Values
Eternal

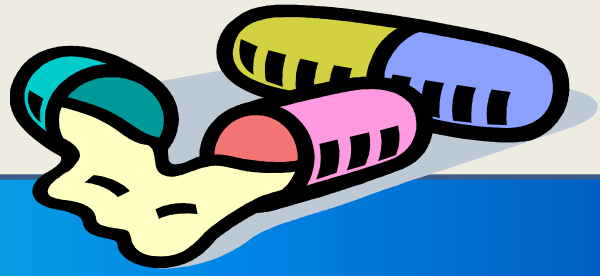
Health – is not simply the absence of disease

- The study of health is a new field and we know very little about
- Limited tools to evaluate health
- Validity of control groups

Clinical Implications of Balance between the Four Aspects of Health

- Whole person care should involve an integrated approach strengthening all 4 aspects of health
- There is no perfect drug – All drugs have side effects that effect one or more of the four aspects of health
- Chronic prescription drug use will not make you healthy – they may strengthen some component within the four aspects of health, but at the expense of balance
- Treatment strategies for maintaining/restoring health is through healthful behaviors, mindfulness approaches, and spiritual practices

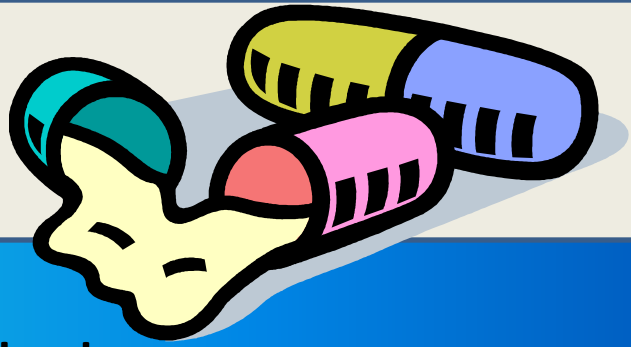
What about Prescription Drugs? The Good



- Effective pharmaceutical development has revolutionized medical care
- Offers treatments for a vast array of acute and chronic illnesses:
  - Some pharmaceuticals prevent or cure illnesses, especially those that historically resulted in premature death and disability (antibiotics, vaccines)
  - Most pharmaceuticals focus on alleviating the symptoms or side effects of chronic disease

What about Prescription Drugs?

The not-so-good news



- Growth in prescription drugs has led to an explosion of polypharmacy
  - Average # of prescriptions filled by each person in the US increased from 8.9 per year in 1997 to 12.6 per year in 2012
  - Often causes negative health outcomes from drug-drug interactions and adverse drug events
- Rising prescription drug costs are a significant factor in the rise of overall health care costs in the U.S.A. – retail prices of Rx drugs have more than doubled over the past decade
- Direct-to-consumer advertising has fueled consumer demand for drug therapy for many conditions that can be improved by life-style modification

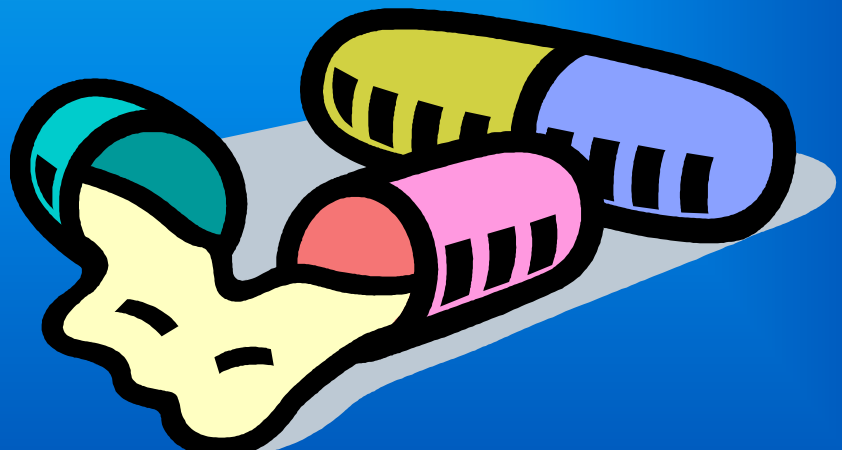
Growth of Rx Drugs

- Prescription drug use is the highest ever among insured Americans*
  - More than half of all insured Americans (51%) are taking Rx meds regularly for chronic health problems
  - Americans buy much more medicine per person than another country
  - Most widely used drugs:
    - Anti-hypertensives
    - Lipid-lowering
  - Among seniors, 28% of women and 22% of men take $\geq$ 5 meds
  - Largest increase in 20–44 year olds primarily due to more drugs for depression, diabetes, asthma ADD, seizures

*Data from Medco Health Solutions Inc, May 2008

Growing Use of Pharmaceuticals in Humans and Animals: New Issues of Concern

- Growing pro-industry bias that has eroded the objectivity of scientists, physicians and regulators
  - Promotion of off-label use* to expand market share
  - Rx overuse and resistance
  - "Medicalization" of non-illness
  - Unintended consequences of newer technologies (genetic engineering)
  - Cross-species effects
  - Environmental impact



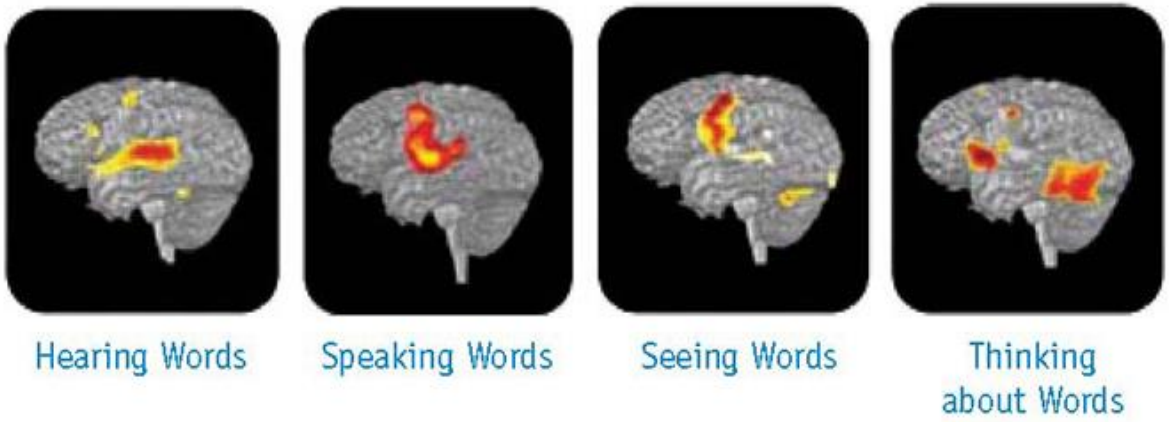
*unapproved indication, age group, dose, or form of administration

What's the Truth about Psychoneuroimmunology (PNI)?

- What do we know? How do the systems connect? How does this impact health? What's wishful thinking?
- What about stress and the immune system – can it cause disease?
- Do your thoughts matter to your immune system?
- Can your mind contribute to disease?
- Can your social world and your perceptions of it influence your immune system?
- Can the immune system influence the brain and changes your thoughts and feelings?
- What is health? How does spirituality influence health?
- What do we do with all this? Interventions – do they work?

On The Brain Side of PNI

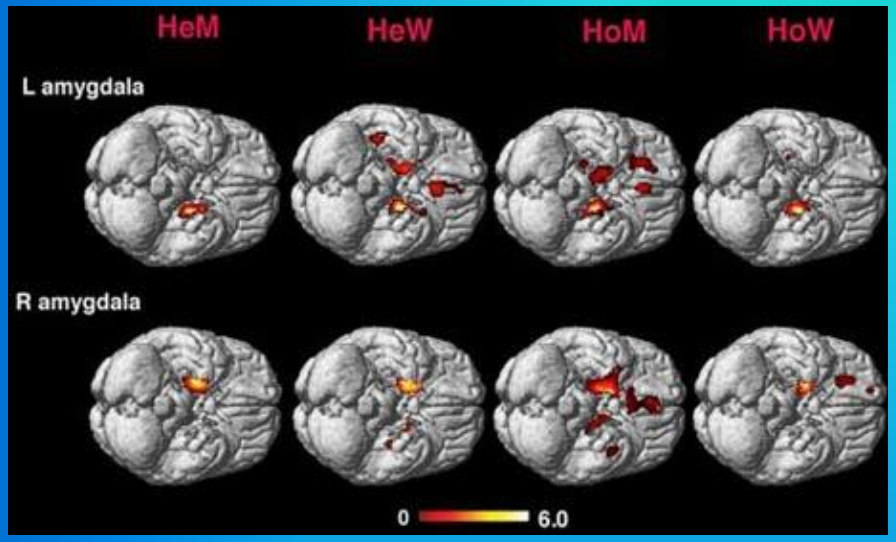
- The nervous system is responsible for interpreting our external and internal world
- Affective/cognitive neuroscience and PNI are an exploding fields of research
- Perceived stress and emotions are registered in the brain and localize to specific brain regions collectively called the limbic system, and create activation patterns when we experiences them (anger, fear, passion, love, thoughts)
- Regions activated by stress or are turned on due to our emotional interpretation overlap with the circuits that influence the immune system



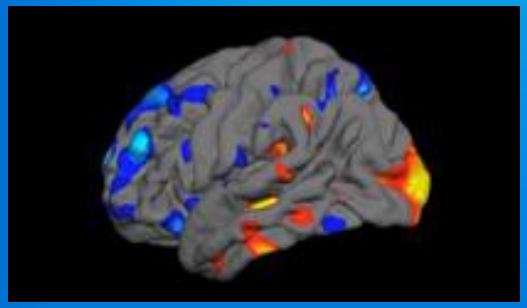
Our Brains Are Wired Differently and Adapt to our Environment Across Time

- Genetics
- Epigenetics
- Internal and External Environment
  - Drugs/toxins/hormones
  - Maternal care
  - **Immune activation/infections/vaccines**
  - Nutrition
  - Socioeconomic status
  - Deprivation/Enrichment
  - Psychosocial and familial influences

Brains Can be Wired Differently



Sexual orientation is hardwired into our neural circuitry. Homosexual men and heterosexual women have symmetrical brains, with the right and left hemispheres almost exactly the same size. Conversely, lesbians and straight men have asymmetrical brains, with the right hemisphere significantly larger than the left.



Regions of the brain are known to differ in people with autism. Red and orange show cortical areas that are thicker or larger, while the blue shows a reduction in size compared with a non-autistic brain.

Clinical Implications

New Technologies to Evaluate Brain Functioning:

Diagnostic tool for health as well as disease
(spirituality, trauma, emotional well-being, allostatic load, depression)
Early Intervention/Preventive Care
Better evaluate treatment strategies and/or monitor efficacy
May lead to reform: Social Stigma/Public Policies/Religious Views

Social Reform?

How does imaging data influence thinking about homosexuality?

How will we interpret these biological findings? Is homosexuality on the spectrum of normal? a disease/disorder? a disability?
How do these findings affect our views on social and political policies ?

Do our current social/religious beliefs and practices promote health and well-being in this population?

Two Main Stress Pathways Regulate Stem Cells and Immune Cells to Affect Immune Function

- Hypothalamic-Pituitary-Adrenal (HPA) Axis (cortisol)
- Sympathetic Nervous System (SNS) (norepinephrine/ epinephrine)
- Signaling mediators from these pathways act on receptors in immune cells altering their behavior
  - Development
  - Proliferation
  - Distribution
  - Migration in the body
  - Regulates immune response

Clinical Implication

Abnormal functioning of these pathways that occur with immune-mediated diseases may limit the effects of mind-body interventions

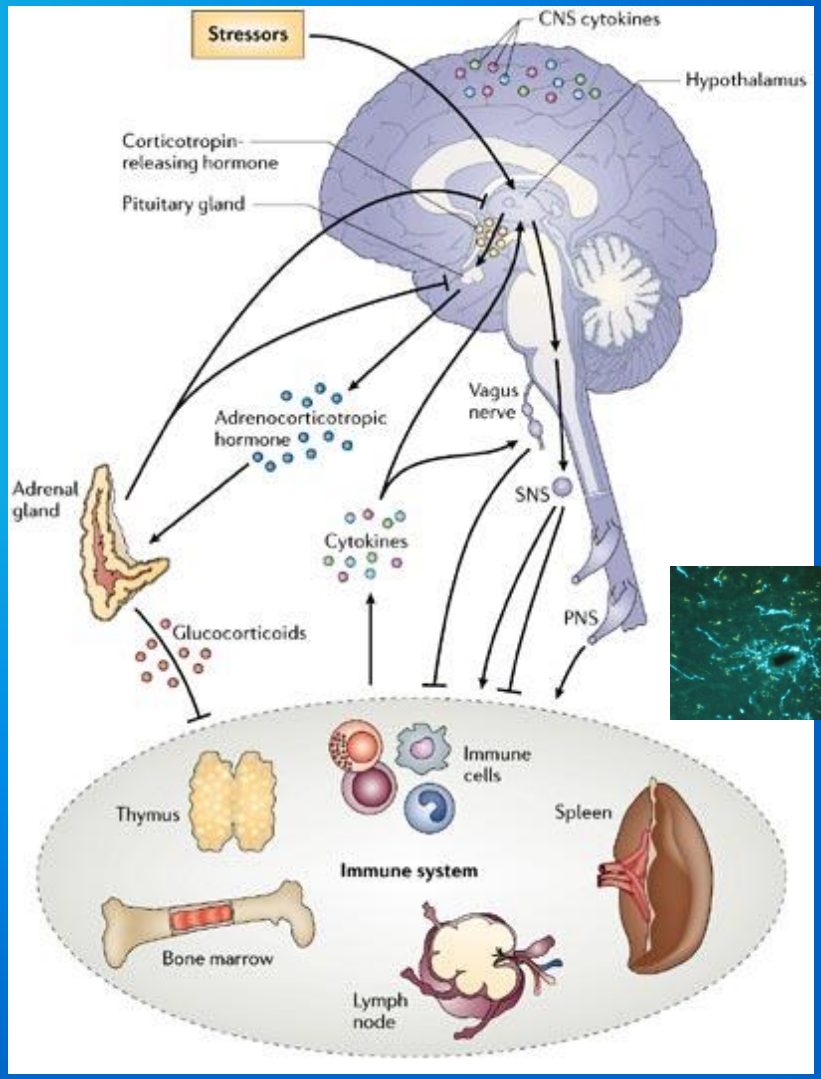
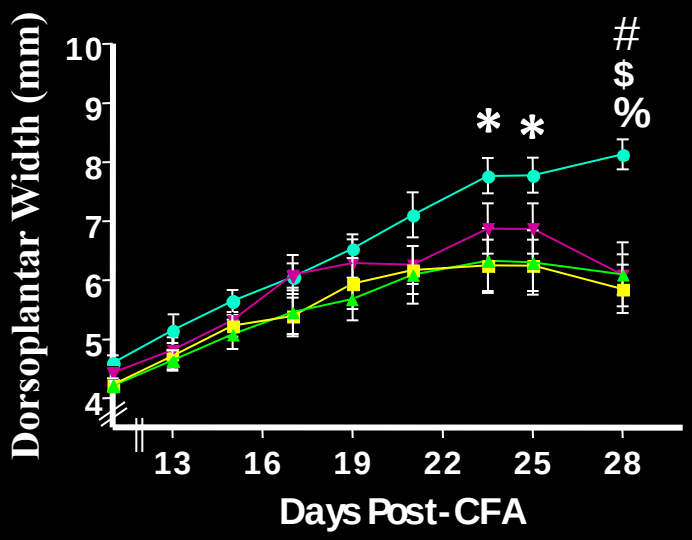
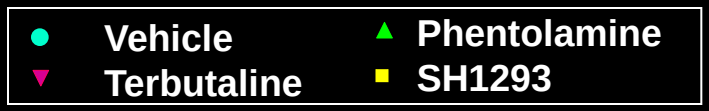
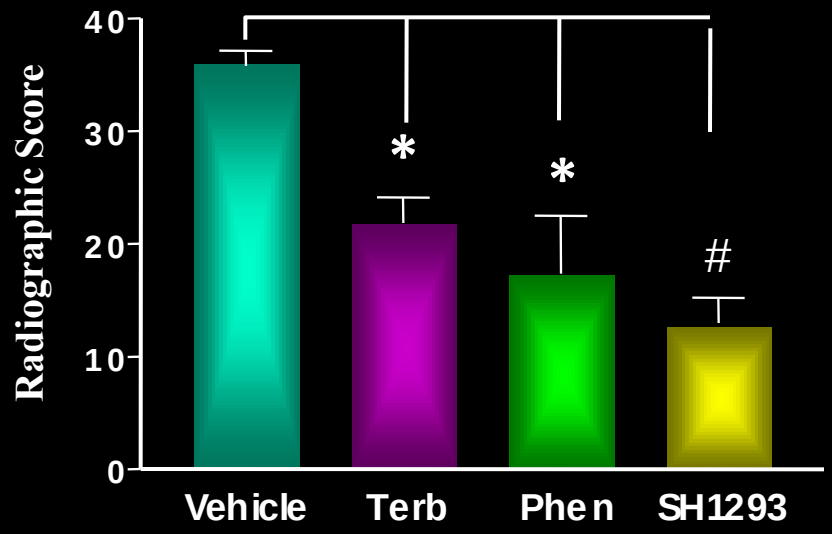


Image from Sternberg EM Nature Reviews Immunology 6, 318-328.

Adrenergic Drugs Reduce Inflammation and Joint Destruction when Administered from Disease Onset

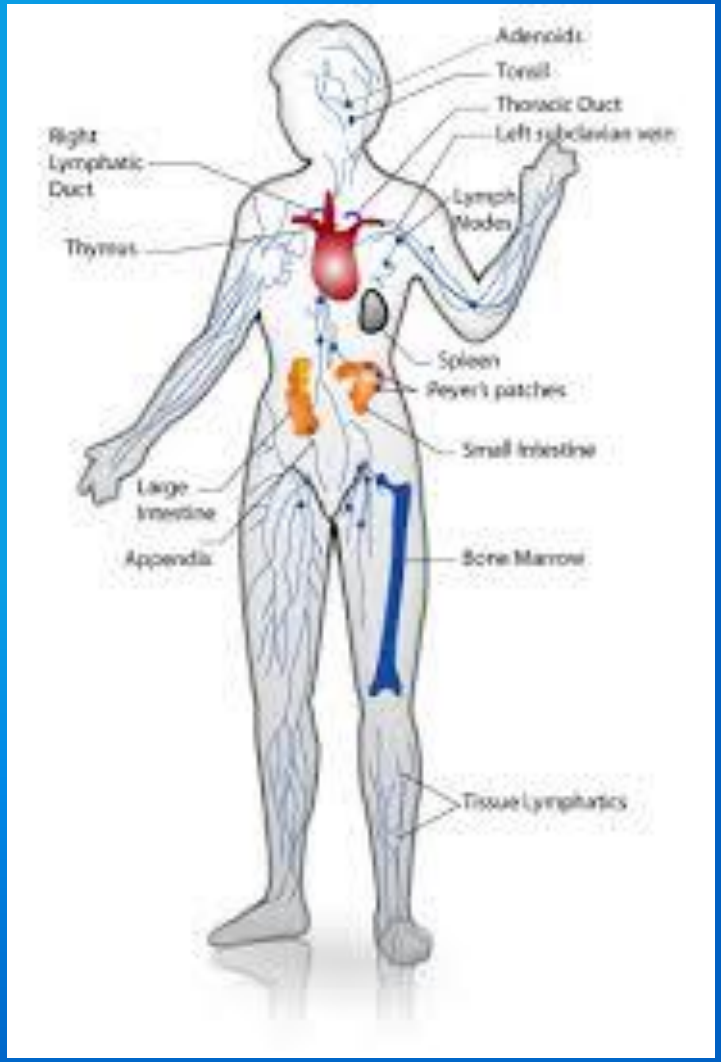






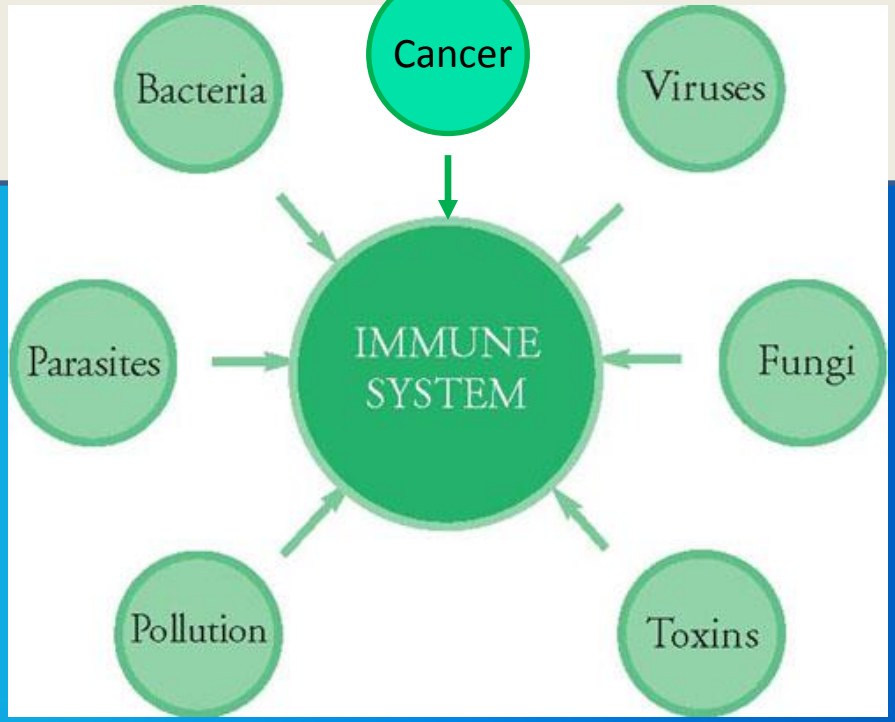
The Immune System

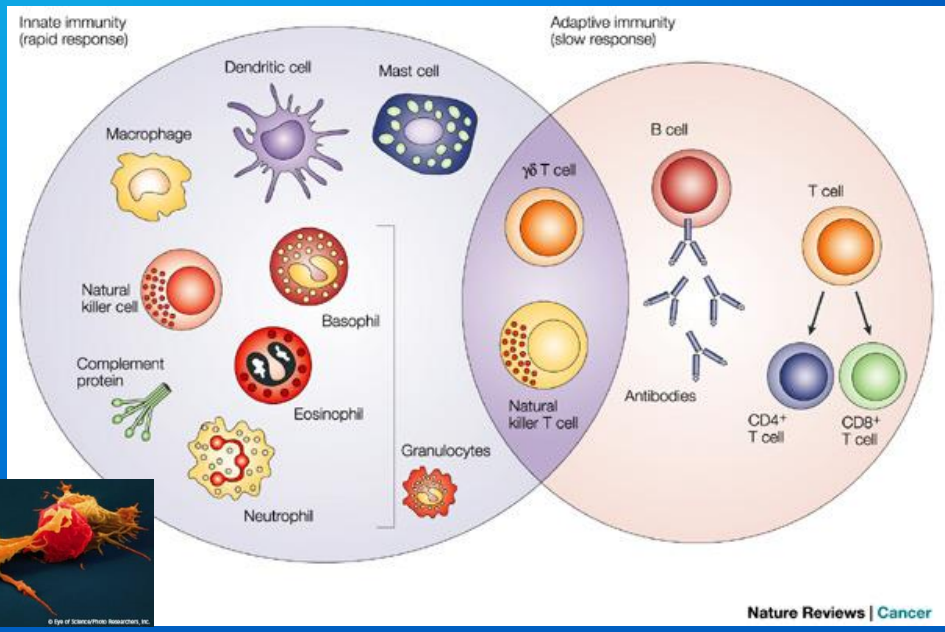
- Cells of the immune system distributed all over the body either in organs or as diffuse tissue
  - Primary and secondary lymphoid Organs
  - Diffuse lymphoid tissue
  - In blood vessels
  - In lymphatic vessels
  - Run along side of BV in connective tissue
  - Certain types of immune cells are in all tissues/organs



The Immune System

- The bodies armed forces
- Two arms of immunity that work together to provide host defense
  - Innate - first line of defense, is non-specific, important for detection, initiates inflammation, early response
  - Adaptive – second line of defense, driven by innate response, have specificity for foreign substances, late response
- Specificity: T cells – kill infected cells and help B cells produce specific types of antibodies – small number of T cell programmed to respond to a specific type of antigen – therefore they need to divide to create an army needed to fight off infection
- Effects of the immune system are mediated by cell-to-cell contacts and the production and secretion of signaling molecules called chemokines and cytokines





The Immune System Regulates Brain Function

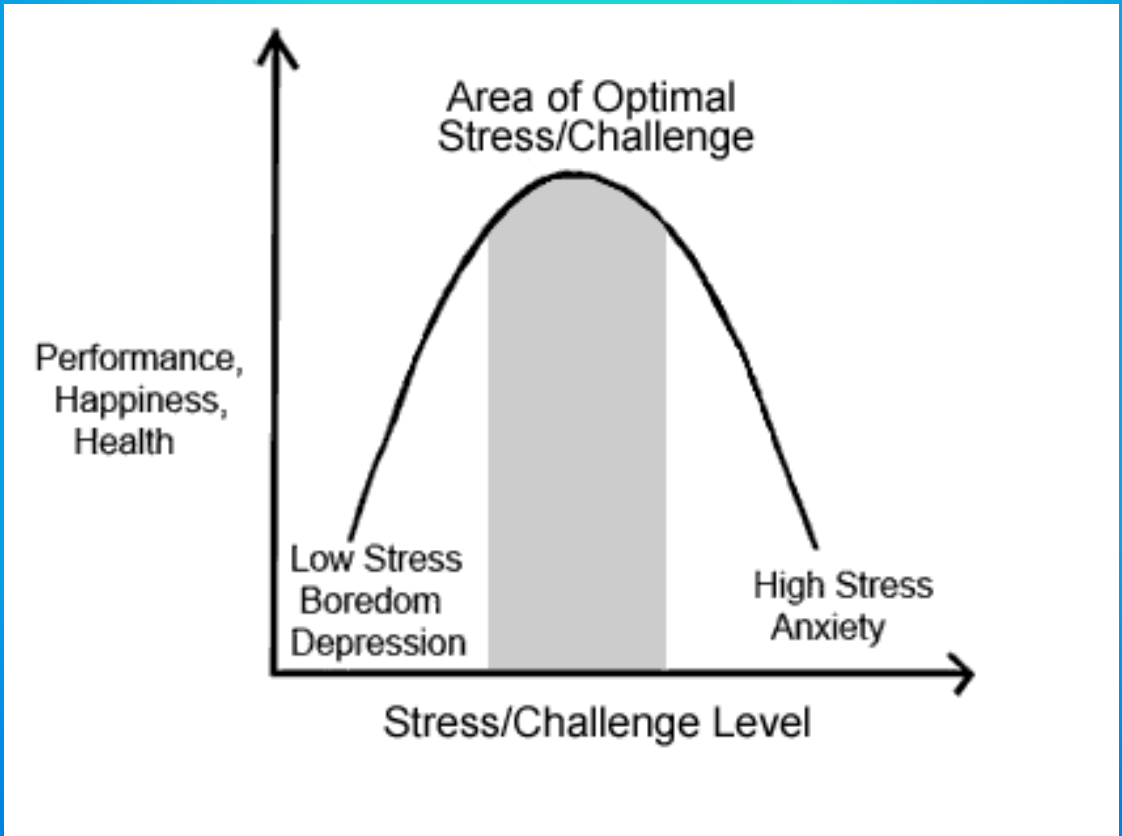
- Immune cells are reside in the brain
  - Microglia and dendritic cells
- The immune system immunosurveys the brain for foreign substance
- Regulates brain functions via the release of cytokines/chemokines
- The immune system can affect behavior
- Sickness behavior – Sickness behavior is a motivational state that reorganizes the organism's priorities to cope with infectious pathogens - survival benefit
  - Fever
  - Lethargy
  - Depression
  - Anxiety
  - Loss of appetite
  - Sleepiness
  - Hyperalgesia
  - Reduction in grooming
  - Failure to concentrate

- May be relevant to understanding depression and other mental health disorders, and some aspects of the suffering that occurs in cancer
- Sickness behavior is mediated by cytokines/chemokines that drive inflammation

Stress Pathways Regulates Immunity

- Functions of all immune cells
  - Both immunosuppression and immunoenhancing
  - Intensity (acute, subacute, chronic), timing relative to challenge
- Energy resources
- Homeostasis/Allostasis – Circadian rhythms of all cells
- Stem cells (turnover, activity and mobility)
- Development of red blood cells and all types of immune cells
- Mobility/migration of immune cells (via lymphatic and blood vessels)

Stress Can be Good or Bad



- This model focuses on the period of the day when we are awake. Models have not been developed for sleep although sleep is important for performance, happiness and health, and sleep is affected by stress, disease and by mind-body interventions

Chronic Stress

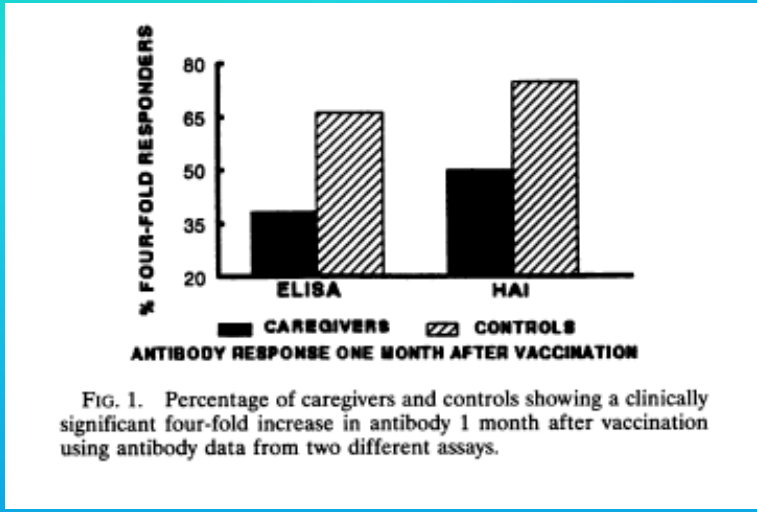


FIG. 1. Percentage of caregivers and controls showing a clinically significant four-fold increase in antibody 1 month after vaccination using antibody data from two different assays.

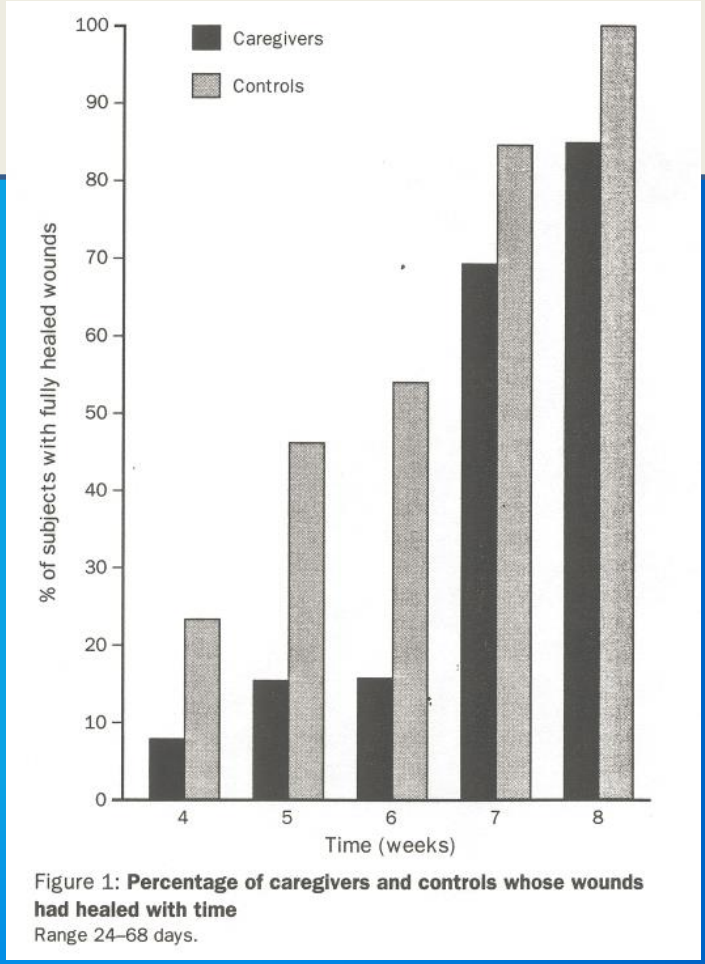


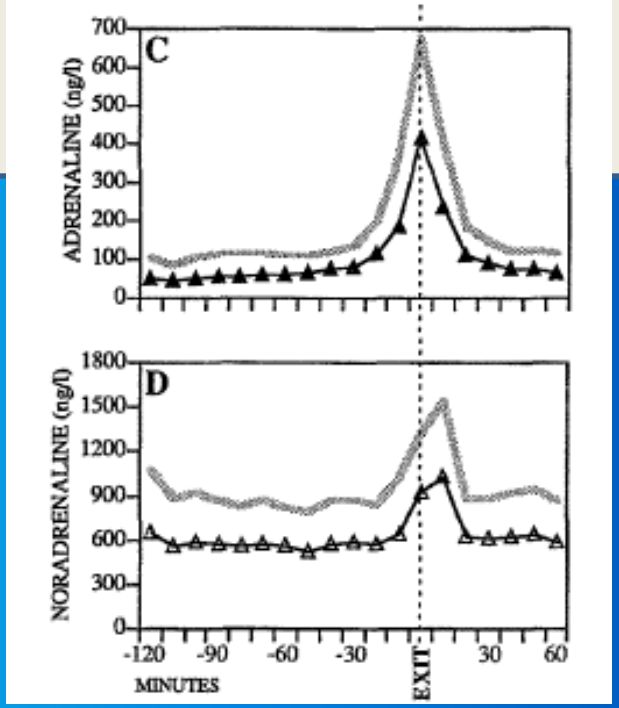
Figure 1: **Percentage of caregivers and controls whose wounds had healed with time**
Range 24–68 days.

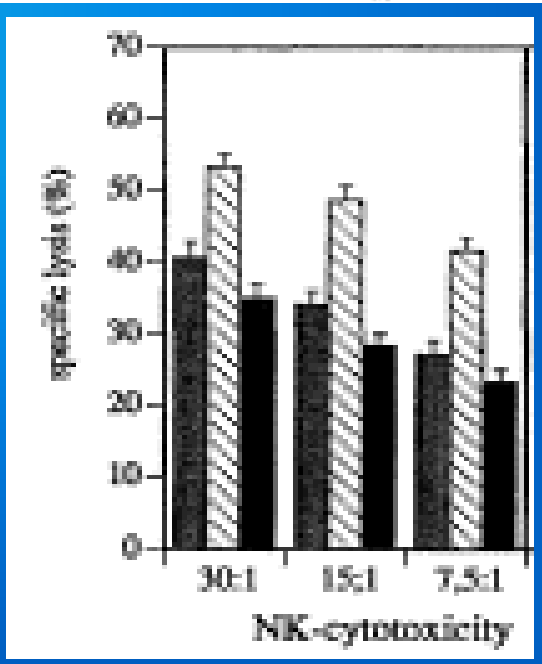
- Caregiver stress is profoundly stressful
  - Demand of caregiving
  - Devastating to witness slowly decline
  - Caregiving is a chronic stressor
- Caregiver stress interferes with protection from the flu by vaccination
- Caregiving stress and exam stress delays wound healing
- Important implications for vaccination programs and for surgery and may be targets for mind-body therapies

Kiecolt-Glaser et al., 1996. Proc. Natl. Acad. Sci. USA 93:3043-3047.

Acute Stress

- Jumping from an airplane for the first time enhances circulating NK cell number and NK cell activity
- Mediated via the sympathetic nervous system
- Circulating norepinephrine/epinephrine levels rise just prior to the jump–goes up and return to baseline 1 hr post -drop
- Acute stress increased immune function (NK cells are better at killing tumor cells) consistent with a eustressor





Collectively, most studies demonstrate stress-induced immunosuppression; however, direction of immune response is dependent on the duration of stressor, type of cells examined and the measure assessed

The magnitude of the stress effects are sometimes small

The Common Cold

- Studies by Sheldon Cohen's group have provided strong support that negative life events, perceived stress, and negative affect increase susceptibility to the common cold
- Individuals completed questionnaires assessing stressful life events, perceived stress and negative affect.
- Mucus weight and viral shedding in mucus were measured after nasally inoculation with cold or flu virus in a controlled environment
- Those individuals with severe chronic stress, negative affect or stressful life events in their lives were more likely to develop a cold or flu; those with more social support were less likely to develop a cold/flu
- Recent findings suggest prolonged stressor cause glucocorticoid resistance , which interferes with appropriate regulation of inflammation

- This would be a good model to tests the effects of mind-body interventions, with particular aim of determining their effects on glucocorticoid resistance (which occurs in a number of diseases) as well as their efficacy compared with flu vaccines

Cohen et al. 1993. J Pers Soc Psychol. 64(1):131-40; Cohen et al. 1998. Health Psychol. 17(3):214-23. Cohen et al. Psychol Sci. 2003 Sep;14(5):389-95. Cohen et al. 2012. Proc Natl Acad Sci U S A. Apr 17;109(16):5995-9.

Do your thoughts matter to your immune system?

Behavioral Conditioning Immune Responses

- Behavioral conditioning can alter a number of different types of immune responses
  - Prolongs heart allograft survival in rats[1]
  - Effects of immunosuppressive drugs[2]
  - Enhance an antibody response[3]
  - Delay the course of autoimmune disease in lupus-prone mice[4]
  - Increase pulmonary function in asthmatic children[5]
  - reduce the severity of adjuvant-induced arthritis in rats[5]

[1]Grochowitz, et al. 1991. Brain Behav Immun. 5, 349-56; [2]Ader & Cohen, 1975. Psychosom. Med., 37, 333–40; Goebel et al. 2002. FASEB J. 16, 1869–73; Exton et al. 1998. J. Neuroimmunol., 88, 182–91; [3]Ader et al. 1993. Brain Behav. Immun. 7, 334–43; Alvarez-Borda et al. 1995. Neurobiol. Learn. Mem., 64, 103–5; [4]Ader & Cohen, 1982. Science, 215, 1534–6; [5]Castes et al. 1998. Neuroimmunomodulation, 5, 70; Klosterhalfen et al. 1990. Behav. Neurosci., 104, 716–24; Klosterhalfen & Klosterhalfen. 1983. Behav. Neurosci., 97, 663–6; Lysle et al. 1992. Brain Behav. Immun. 6, 64–73.

Clinical Implications

"Can re-exposure to a symbolic stimulus previously associated with an immunomodulating agent or stressful life experiences—in biologically vulnerable individuals, immunocompromised hosts, or in the presence of a pathogen or a latent infection precipitate or reactivate manifest disease?'' Yes.

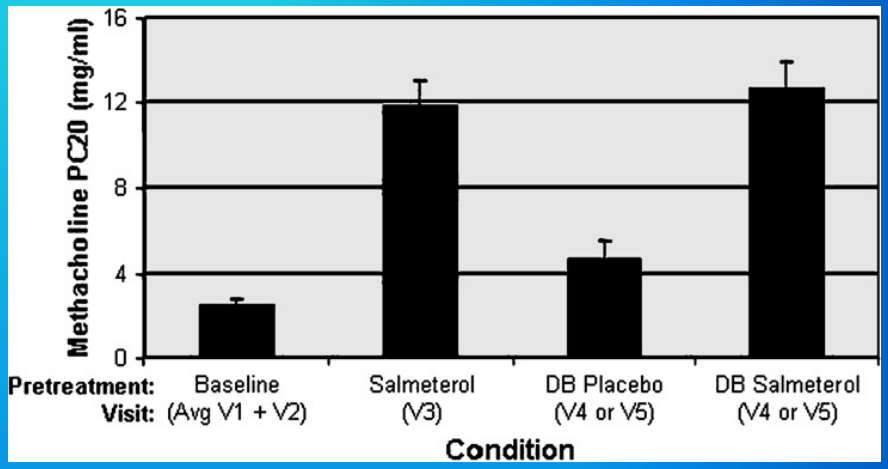
"Can re-exposure to a symbolic stimulus previously associated with immunomodulating circumstances contribute to the resistance to or recovery from disease?" Again, in consideration of relevant host factors. Yes.

Inadvertent conditioning of wanted or unwanted outcomes?

Pacebo

Placebo effects may not be experienced under conditions of learned-helplessness may explain why some antidepressants are not effective. If so, then spiritual and/or humor-based approaches may be beneficial

- Kemeny et al. 2007: Randomized, double-blind study investigating the effect of placebo on suppressing airway hyper-reactivity in asthmatic subjects
  - All subjects displayed bronchial hyperresponsiveness at baseline (average of Visits 1 and 2)
  - Pretreatment with (single-blind) salmeterol at Visit 3 significantly reversed the bronchoconstriction.
  - Pretreatment with either (double-blind [DB]) placebo or salmeterol (Visits 4 and 5) reduced bronchoconstriction
  - Double-blind placebo induced a significant effect

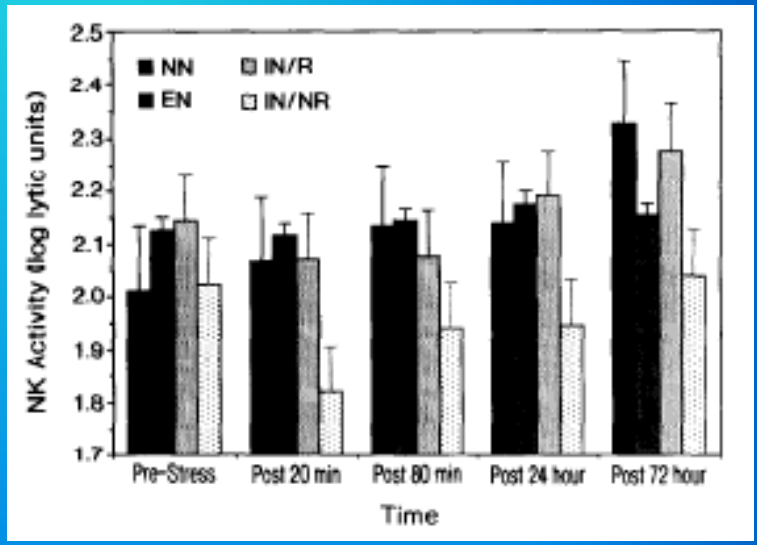


- So placebo was twice as good as doing nothing suggesting a significant benefit from believing and 1/3 of benefit of giving a real drug.

Kemeny et al. 2007. J Allergy Clin Immunol. 119: 1375-81

Illusion of Control over Stress

- In a study assessing natural killer (NK) cell activity in adult males exposed to controllable or uncontrollable erratic noise stress
  - No noise
  - Inescapable noise (No control)
  - Escapable noise (By switching a lever)
  - Inescapable noise but with perception of control (Illusion of control)



- Suppression of NK cell activity only in the group exposed to inescapable noise compared with the no noise control group
- These findings support that your perception of control is important and suggests that your thoughts matter

Sieber et al. 1992. Brain Behav Immun. 6(2):141-56.

Clinical Implications

- Illusion of control may be beneficial to health
- How much do our thoughts/ perceptions influence our health?
- How do we promote health under situations that are out of control?
- How do religious and healthcare practices influence our perception of control over stress and/or our health?

Navigating the social world and its affect on health

- Negative consequences on stress (increased stress pathway activation) and immune systems, and for health
  - Subordinate behavior/lower social status or power/esteem by others
  - Bereavement – Loss of persons or things in which a bond is formed
  - Stigmatized groups (obese, race, disability, disfigurement; homosexuality, certain illnesses)
  - Lower socioeconomic status
  - Loss of social status
- Social supports – predict better health, better function of stress and immune systems, and longer life

Perception of the Social World

- Acute social threat (social threat)
  - Acute situations where you feel demeaned, ashamed, less than others, or feel negatively evaluated can have long lasting consequences for self esteem, can profoundly affect behavior (e.g., sports, art, music), lead to risky behaviors (smoking, alcoholism) that negatively affect health
  - Creates misperception about how you are being treated that drive physiological responses

Perceived Stigma and ANS Reactivity

- Females randomly assigned to a group who believed that they would have a port wine stain birthmark placed on their face but instead translucent make-up was applies (illusion of a stigma) and then asked to do public speaking
- Those who thought they had a facial stigma showed
  - More embarrassment/sham type of behaviors (gaze avoidance, cover face)
  - Greater sympathetic reactivity during task with consequences for immune reactivity
  - Perceive more negative behaviors directed towards themselves
- Similarly, rejection sensitive men with HIV infection had more ANS reactivity to a variety of stimuli including social threats, and their the HIV virus was less well controlled after receiving anti-viral therapy; concealing homosexuality was protective
  - Adding the ANS neurotransmitter/hormone NE to HIV virus particles increases viral replication

Cole et al. 1997. J Pers Soc Psychol. 72(2):320-35; Medes et al., 2003

Clinical Implications

- **Assessment:** Knowing how your patient navigates the social world is important for providing quality health care
- **Early interventions** that teach strategies for coping and resilience to social stress **in safe environments** will likely promote health
- Awareness/educational resources for individuals and family members to work through bereavement
- Creating emotionally/socially safe medical facilities, school and work environments should have health benefits
- Preventative care using mind-body-spiritual based interventions may be important strategies to reduce the incidence of stress-related diseases and promote good mental and physical health

Clinical Implications Specific for Bullying

- Bullying (verbal, physical, psychologically aggressive behavior) is a widespread problem in our communities and schools
- Bullying can have short- and long-term academic, physical and emotional consequences on both the bully and the victim
  - Increased health-related problems including headaches, abdominal pain, anxiety, depression, sleeping problems, poor appetite, feelings of tension or tiredness, homicidal/suicidal thought
  - Increased behavioral problems - bed-wetting, school avoidance, a decline in academic performance, poor relationships with peers, poor self-esteem, and loneliness; bullying is associated with vandalism, shoplifting dropping out of school, fighting, drug and alcohol use

Reviewed by Hensley. 2013. Nurs Clin North Am. 48(2):203-13.

Clinical Implications Specific for Bullying

- Approximately 25-30% of children are affected by childhood bullying, either as a bully or as a victim
- There are some common characteristics of bullies and victims
- Knowing these characteristics will allow the health care providers to identify children at risk for or involved with bullying
- Both bullies and victims have short- and long-term consequences of bullying that negatively affect health
- It is imperative that health care providers have knowledge about bullying
- Health care providers need to take a pivotal role in assessing their parents for bullying and provide interventions

Clinical Implications Specific for Bullying

- **Assessment** and familiarity with characteristic of bullies and victims
- **Intervention** – take time to ask patients if they are being bullied or if they are bullying others
- **Prevention** – best addressed by comprehensive approach and health care professionals can play a large role by wellness exams and assessment
- **Promote** strong parenting skills and recognition, screening and appropriate referrals of patients involved in bullying behaviors
- **Training** – Nurses and other healthcare professionals need to learn the skills to assess students for bullying behavior and to identify characteristics of both victims and bullies and intervene with effective bullying prevention strategies
- Clergy can work with the schools as spiritual counselors and help to create effective programs that teach and develop spirituality principles (e.g., Spirituality for Kids program currently being used Los Angeles school district)

What we don't know

- Can we purposefully direct our immune system to cure diseases by our thoughts?
  - Claims on internet sites indicating that mind-body self hypnosis in cancer patients can direct their immune cells to more efficiently kill tumor cells
- This has not been demonstrated, although spiritual texts suggests this is possible

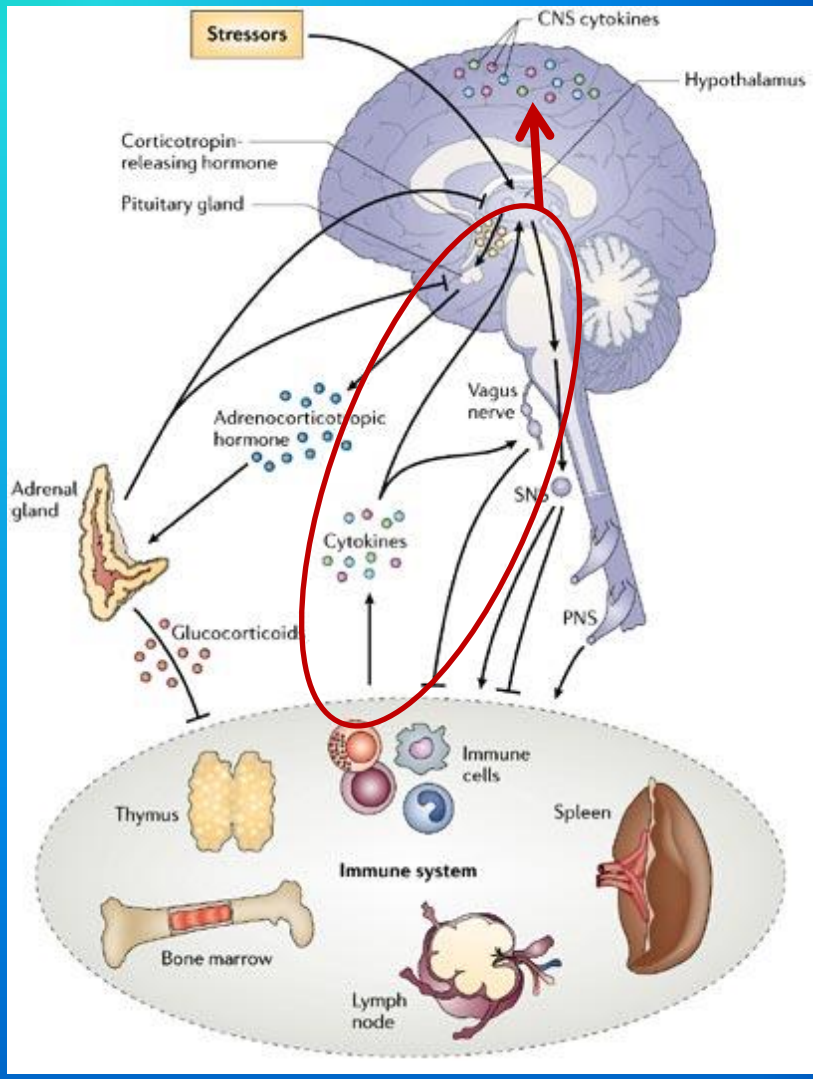
Possible problem – The functioning of stress pathways changes with disease states, so if mind-body interventions work through these pathways then their dysfunction may dampen or prevent their beneficial effects. That be said: there is redundancy in the nervous system alternative pathways may be able to "kick in"

What we don't know: stress and cancer

- In mice with ovarian cancer that are stressed
  - tumors grow and spread more quickly
  - Sympathetic mediator, NE, stimulate new blood vessel growth leading to faster and more aggressive tumors
- Human cancer studies are less clear
  - Stress not reliably associated with onset or course of cancer
  - Psychological states of mind also not reliably predictive
  - Newer work shows that stress hormones can influence cancer cell growth, suggestive of in influence of stress

Is there a link between inflammation and depression?

- Proinflammatory cytokines (IL-1β, TNF-α, IL-6) are important for coordinating the innate and adaptive responses, and regulate the brain for adaptive behaviors.
- Cytokines produced by the brain may also be contributory
- Aging, chronic stress, and chronic immune-mediated illnesses are conditions of chronic inflammation
- In these conditions, the incidence of depression is high
- Depressive symptoms overlap with sickness behavior
- The same pathways through which peripheral cytokines activate the brain are believed to play a role in depression, and possibly other affective disorders
- Cytokine-mediated activation of the brain induces cytokines centrally and suppresses the activity of the stress pathways



Depression and Proinflammatory Cytokines

- Depressed patients have increased levels of proinflammatory cytokines
- Inflammatory disease are often associated with depression
- Injections of proinflammatory cytokines in humans and animals can increase depressive symptoms

Depressive and Sickness Behavior

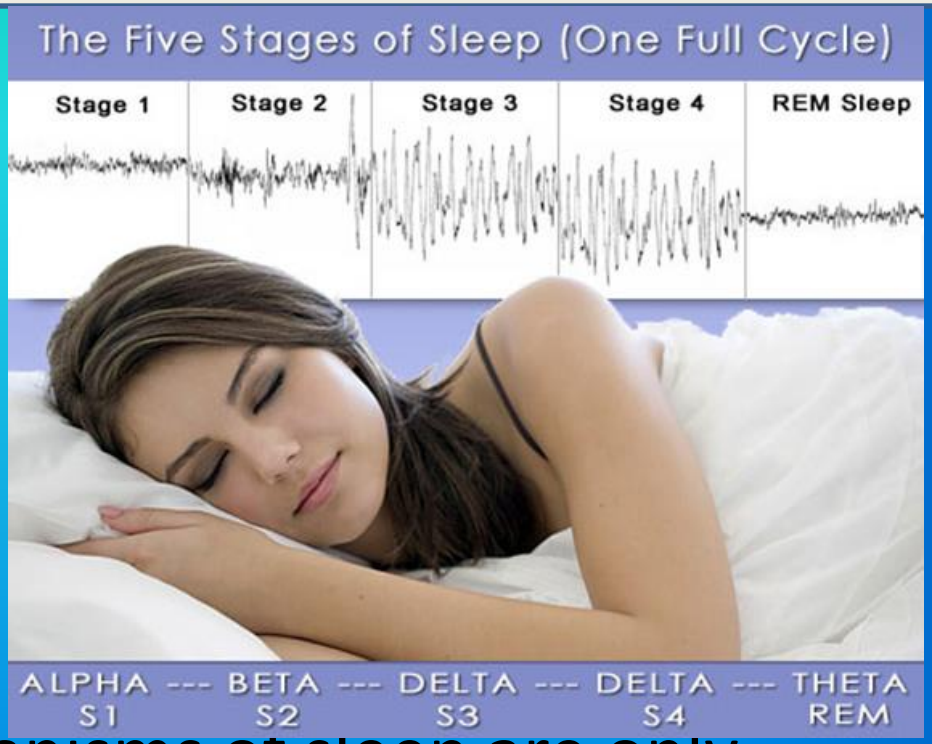
- Fever
- Decreased social, sexual, aggressive, and grooming behavior
- Decreased food and water intake
- Decreased exploration
- Deficits in learning and memory
- **Altered sleep (less sleep in depression)**
- Anhedonia – inability to experience pleasure
- **Greater sensitivity to pain – cytokines activate sensory nerves**
- **Allodynia** – sensations that are not normally painful become painful

Mind-Body Based Interventions

- Thoughts and feelings seem to be important mediating factors in health and disease
- So what about mind-body-spiritual interventions – Can these types of interventions:
  - Reduce stress pathway activation?
  - Restore appropriate immune system responses?
  - Heal immune-mediated diseases?
- These are some of the major questions asked by researchers and healthcare professionals
- Religious/spiritual texts like the Bible indicate that spirit and mind can have great healing power

Sleep, the Immune System and Health

- The importance of adequate and appropriate sleep for health maintenance is recognized in the Bible and other spiritual texts
- Essential to physical, spiritual, and emotional health



- The purposes and mechanisms of sleep are only partially clear and the subject of substantial ongoing research
  - Rejuvenation/Restoration, Ontogenesis, Learning and Memory Processing , Preservation

Sleep Deprivation Linked to Stress-Related Diseases

- Short sleep duration is a risk factor for obesity, which means greater risk for hypertension, CVD, and Type 2 diabetes, and doubles the risk of death from CVD
- Sleep disorders closely associated with psychiatric disorders (depression, alcoholism, bipolar disorder, anxiety, ADHD)
- Repeated stress in animal models causes brain regions involved in memory and emotions (hippocampus, amygdala, prefrontal cortex) to undergo structural remodeling, which impairs memory and increases anxiety and aggression

McEwen. 2006. Metabolism Clinical and Experimental 55 (Suppl 2), S20–S23; Majde & Krueger, 2005. J Allergy Clin Immunol. 116(6):1188-98.

Sleep Deprivation is a Form of Allostatic Load

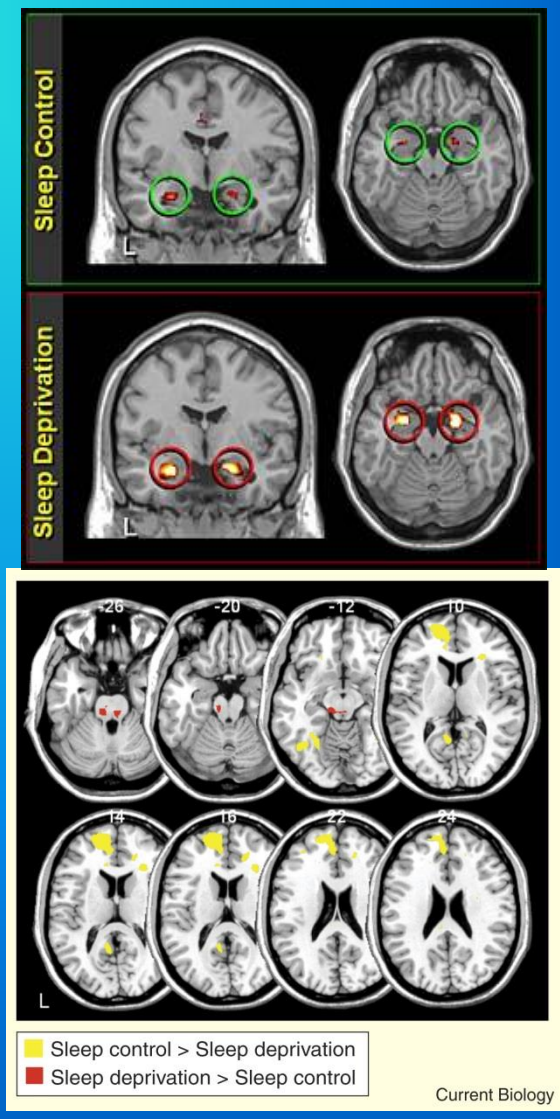
- Sleep deprivation overlaps with diseases that are linked with excessive stress, and with the dysregulation of the systems that normally promote allostasis or adaptation

- Suppresses immune function
- Slows wound healing
- Reduces parasympathetic tone
- Increases sympathetic tone
- Increases oxidative stress
- Raises insulin and blood glucose
- Elevates proinflammatory cytokines
- Increases evening cortisol
- Increases blood pressure
- Raises energy expenditures
- Increases appetite
- Impairs cognition, judgment
- Increases irritability and ADHD-like symptoms
- Causes depressive-like symptoms

McEwen. 2006. Metabolism Clinical and Experimental 55 (Suppl 2), S20–S23.

Hyperlimbic Activity and Changes Functional in Connectivity with Sleep Deprivation

- In 35-hour sleep-deprived participants who viewed negative images, the amygdala (emotional interpretation area) was hyperactive
- Hyperlimbic activity was linked to a functional loss in medial prefrontal cortex (MPFC) connectivity and greater connectivity with more primitive lower autonomic brainstem regions
- Suggests a failure of top-down, prefrontal control
- Also suggests that a night of sleep may 'reset' the correct brain reactivity to next-day emotional challenges by maintaining functional integrity of this MPFC-amygdala circuit to govern appropriate behavioral repertoires.
- Strongly suggests a relationship between sleep disruption and mood disorders; offers a neural foundation for hostility, poor decision-making, and emotional irrationality in our sleep-deprived society.



Yoo et al. 2007. Curr Biol. 2007 Oct 23;17(20):R877-8.

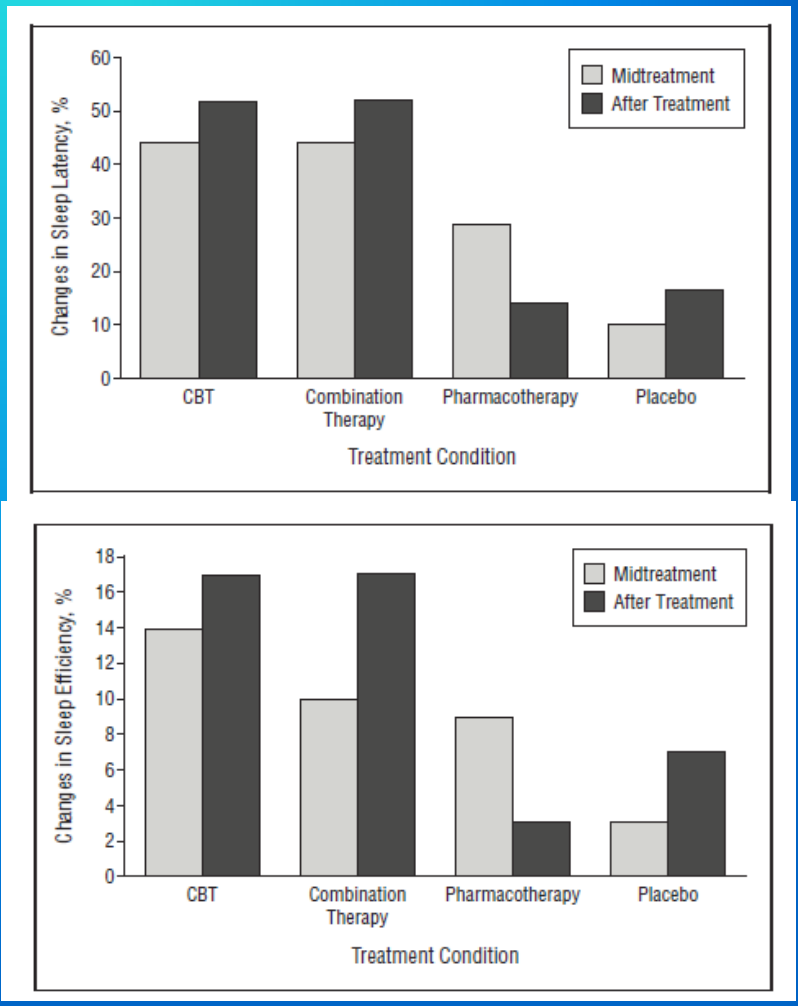
Sleeping Medications and Insomnia

- Ambien and Lunesta (nonbenzodiazepine medications) are an increasingly popular treatment for insomnia
  - Generally believed to be better and safer than earlier generations of sedatives, but still generating controversy and discussion regarding side-effects
  - Patients taking prescription sleep aids on a regular basis were nearly five times as likely as non-users to die over a period of two and a half years, according to a recent study.
  - Even those prescribed fewer than 20 pills a year were at risk, the researchers found; heavy users also were more likely to develop cancer (Kripke et al., 2012)

Kripke et al. 2012. BMJ Open Feb 27;2(1):e000850.

CBT: More Effective in Treating Insomnia and Sleep Meds

- Middle-age patients with sleep-onset insomnia
- Better at producing the greatest positive changes in sleep-onset latency and sleep efficiency
- Yielded the largest number of normal sleepers after treatment
- Maintained therapeutic gains at long-term (12 months) follow-up compared with sleeping pills (Morin et al. 2009. JAMA. 301(19):2005-15).
- Sleep duration in long-term experienced meditators is lower than in general population norms and non-meditators, with no apparent decrease in vigilance (Kaul et al. 2010. Behav Brain Funct. 6:47)



Clinical Implications

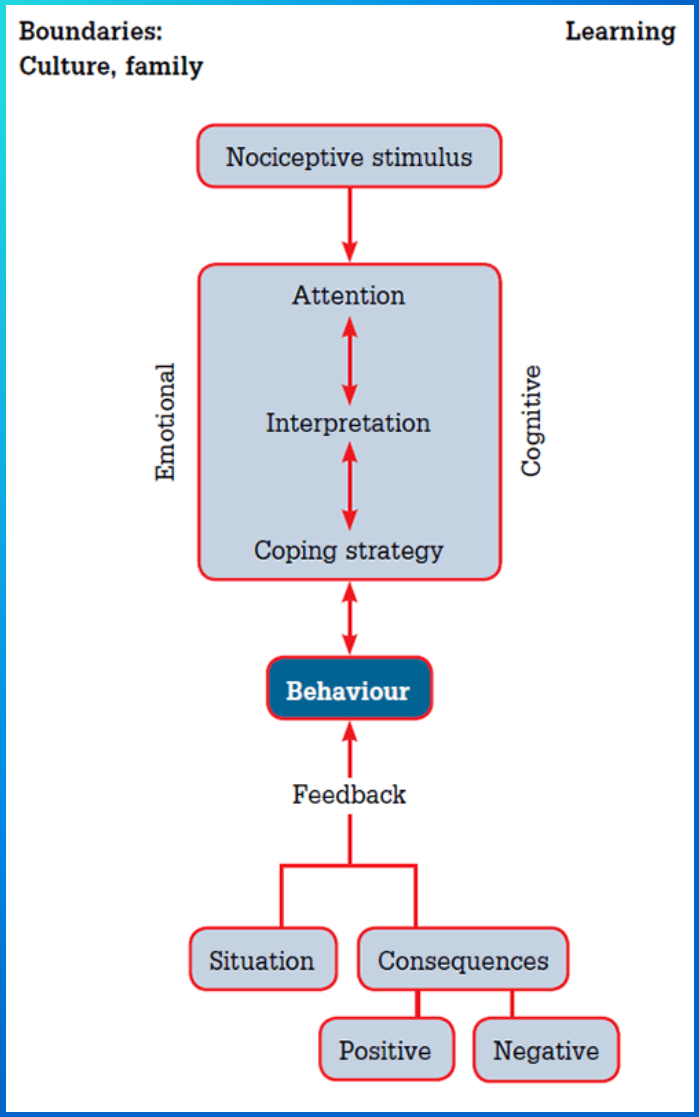
- Proinflammatory cytokines provides a link between depression and vulnerability to medical diseases (CVD, autoimmune); we need to find provide a way of understanding depression in medical conditions involving inflammation
- Too early for cytokine detection as diagnostic tests, but awareness that proinflammatory cytokines can contribute to depression is important (underlying inflammatory condition) – also we may be looking in the wrong place for cytokines
- **Awareness and Early Detection -** Increase patient awareness about how critically important sleep is to health and implement early detection strategies for sleep deprivation/disorders and chronic pain
- **Assessment** - Take a history of sleep time, quality, habits, and environment, and discuss behavioral strategies to improve sleep time and quality with patients
- New imaging and brain functional assessments may lead to better tools for evaluating and understanding depression and the role of inflammatory mediators and their relationship to sleep and pain, as well as monitor the efficacy of therapies, including mind-body and spiritual approaches
- **Intervention** - There is growing evidence that mind-body and spiritual based approaches are effective in treating chronic sleep onset insomnia, depression and other mood disorders – CBT should be considered a first-line intervention for chronic insomnia, and for treating depression and pain.
- Evidence-based data suggest that light therapy, yoga, acupuncture, mindfulness therapies, exercise, may also be effective treatments for mood disorders

Chronic Pain

- Associated with burnout, depression, chronic fatigue syndrome and fibromyalgia
- In many of these conditions, the brain is registering pain messages even in the absence of demonstrable tissue damage – difficult to assess or, in some cases, even believe their patients' stories.
- Neural loops in the brain are sensitized and maintained by 'sustained attention and arousal' (Eriksen & Ursin, 2004; Ursin & Eriksen, 2001)
  - Become hypervigilant around and preoccupied with the pain and very emotionally reactive to it when it is noticed. As a result,
  - Over time the same stimulus produces more suffering and a vicious cycle begins
- Existential or spiritual issue (e.g., fear of death in cancer patients) can potentially aggravate pain issues - need to be recognized and addressed.
- Some pain conditions (eg., chronic back pain) may be complicated by socioeconomic factors, such as worker's compensation or employment issues

Chronic Pain: Not Merely Somatic

- The mind, emotions and attention play an important role in the experience of pain.
- Stress, fear and depression can amplify the perception of pain
- Pain perception involves many brain centers
  - Register and modify pain signals
  - Involved with attention, beliefs, conditioning, mood, emotion, stress and cognition
- Mind-body approaches work at one or more of these levels in altering pain perception
- Change a person's mental or emotional state or utilize physical movement to train attention or produce mental relaxation.
- Importantly, they often work via similar mechanisms and have synergistic effects.



Caregivers of Patients with Chronic Pain

- Interestingly, working with empathy, which can involve vicariously experiencing another's pain, has been shown to produce similar changes in brain activation of the amygdala (indicating stress and arousal) as the person actually experiencing the pain (Singer et al., 2004). There are significant implications for vicarious stress, because when it is prolonged it can predispose to caregiver fatigue or caregiver burnout. Relaxation or mindfulness techniques may be a useful strategy for general practitioners to help caregiver avoid this outcome (Main & Spanswick, 2001).

Attention to the Pain

- Attention to pain is linked to activation of the 'fight or flight' (stress) response and the consequent need to take action, such as escaping or avoiding it.
- Hypervigilance involves an amplification of this response, resulting in an abnormal focus on, or preoccupation about, possible signals of pain or injury. This explains why a relatively small injury can result in the perception of intense pain and suffering.
- There is a close links between emotional and cognitive processes, attention and the perception of pain (Linton, 2005, Leeuw et al., 2007; Villemure & Bushnell, 2002).
- Despite importance of psychological factors in chronic pain syndromes
  - not always routinely assessed in general practice or physical therapy clinics
  - Sometimes not utilized to enhance treatment outcomes (Linton & Shaw, 2011).

Managing chronic pain

- Psychological and emotional issues can amplify the health problem
- Merely increasing the drug dosage (i.e., analgesics, depression) rather than improving the outcome can commonly add to the problem by leading to drug dependence or addiction.
- A combined approach where emotional, social and/or existential issues are being dealt with, as well as the physical problem, is far more likely to produce long-term benefits to the patient

Mind-body-spirit approaches in chronic pain

- Studies have shown that mind-body approaches can be effective in various conditions associated with chronic pain, however levels of evidence vary.
- Group delivered courses with healthcare professional input may have more beneficial effects than individual therapy
- General practitioners are well placed to recommend or learn and provide a range of mind-body approaches to improve outcomes for patients with chronic pain

Linton et al[10] reviewed the scientific evidence and laid out 10 principles that have likely implications for pain management in the clinical setting.

Guiding Principle	Clinical Implications
• Psychological factors that may affect pain outcomes are not routinely assessed by many treating clinicians	• Better methods of screening and early intervention are needed to improve feasibility and utility in usual care settings
• Persistent pain naturally leads to emotional and behavioral consequences for the majority of individuals	• Psychological concepts of learning can be useful to provide empathy and support without reinforcing pain behavior
• Clients who are more depressed or have a history of depression may have more difficulty dealing with pain	• A brief assessment of mood symptoms should be part of routine screening and intake procedures for pain conditions
• Persistent pain problems can lead to hypervigilance and avoidance, but simple distraction techniques are not enough to counter these behaviors	• Clinicians should avoid inadvertent messages that escape or avoidance from pain is necessary in order to preserve function
• Individuals hold very different attitudes and beliefs about the origins of pain, the seriousness of pain, and how to react to pain	• Assessment and treatment planning should take into account individual differences in pain beliefs and attitudes

Guiding Principle	Clinical Implications
• Personal expectations about the course of pain recovery and treatment benefits are associated with pain outcomes	• Providing realistic expectation (positive, but frank and not overly reassuring) may be a very important aspect of treatment
• Catastrophic thinking about pain is an important marker for the development of long term pain problems as well as for poor treatment outcome	• Clinicians should listen for expression of catastrophic thoughts and offer less exaggerated beliefs as an alternative. A brief assessment might be part of routine intake procedures
• Personal acceptance and commitment to self manage pain problems are associated with better pain outcomes	• Over attention to diagnostic details and biomedical explanations may reinforce futile searches for a cure and delay pain self management

Guiding Principle	Clinical Implications
• Psychosocial aspects of the workplace may represent barriers for returning to work while pain problems linger	• Return to work planning should include attention to aspects of organizational support, job stress, and workplace communication
• With proper instruction and support, psychological interventions can improve pain management outcomes	• Psychological approaches can be incorporated into conventional treatment methods, but require special training and support

Mind-body approaches can be effective in conditions associated with chronic pain

- Progressive muscle relaxation
- Meditation
- Laughter
- Mindfulness based approaches
- Hypnosis
- Guided imagery
- Yoga
- Biofeedback
- Cognitive behavioral therapy

Occasionally the sole treatment; more commonly adjuncts to other therapies.

Summary and Conclusions

- Health and Well-Being is more than the absence of disease – **it's keeping all four aspects of health in balance**
- Thoughts and feelings and religious/spiritual beliefs and practices are important mediating factors in health and disease via there influence on psychoneuroimmunology (PNI)
- Many different mind-body-spirit approaches and therapies have demonstrated to affect health and disease states
- Mind-body-spirit approaches work by at one or more of levels of the PNI axes to affect the balance between the four aspects of health
- These approaches work via similar mechanisms and therefore can have synergistic effects
- There are many clinical implications for mind-body-spirit interactions that will lead to exciting new avenues for health professionals and clergy to provide whole person care across a variety of community settings

Questions?