Herbs and Formulas for Chronic Pain

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Speaker

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Disclosure

• No financial interests
• No conflicting affiliation

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Pain

• Aching, burning, throbbing, sharp, and dull are common terms used to describe an all too familiar concept... pain

The concept of pain is multi-faceted:

• Physical
• Psychological
• Spiritual
• Psycho-social
• Cultural
• Environmental
Background

• Chronic pain is becoming an increasing problem
• According to the CDC & National Center for Health Statistics the United States is experiencing a trend in increased healthcare utilization
  – This increase is a direct result of the aging population
    • Special Populations (Geriatric, Veterans, Homeless)
    • Cost and Access Barriers

• Management Difficulties:
  • Co-morbid pathologies
  • Polypharmacy, compounds the picture
    • drug-drug interactions (DDI), side effects (SE), drug-herb interactions (DHI), nutritional status and elimination patterns, Tolerance and dependence
Background

• 1 in 5 people suffer from moderate to severe chronic pain
• 1 in 3 people are unable to maintain an independent lifestyle due to pain
• Chronic pain is one of the most underestimated health problems in the world
• “Chronic Pain is the leading cause of disability in the USA” (Porth, 2007)
  – The most common types of pain include arthritis, lower back, bone/joint pain, headaches, muscle pain and fibromyalgia (American Academy of Pain Management)
  – Pain is the second leading cause of work absenteeism
  (American Pain Society)
The current model of medical diagnosis and treatment to successfully address the chronic disease burden in our society is failing. (Hyman, (2004). The end of “Normal Science” in medicine. *Alternative Therapies, 10*(5).)
Pain Medications are #1 Rx

- Vicodin (hydrocodone/acetaminophen)
  - Opioid analgesic combination
  - Schedule III controlled substance (DEA)
  - Exceeds next most common Rx by almost 40 million (www.theatlantic.com, April 2011)
Clinical Experience Vicodin

• Vicodin in the Community:
  – Easily available
  – Given by Primary Care
    • Time
    • Address 5\textsuperscript{th} Vital sign
    • Considered low risk

• What I see...:
  – Used but not controlling symptoms
    • Promotes excess use/Misuse
  – Hidden addiction
  – Used for stress, sleep, anxiety
  – Subclinical toxicity
    • Fatty Liver
Definition

• **International Association for the Study of Pain**
  – “unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (IASP, 1979)

• **Clinical Definition** coined by McCaffery, 1968
  – “whatever the experiencing person says it is, existing whenever he/she says it does”

• **American Academy of Pain Management** statement
  – “Pain is complex and defies our ability to establish a clear definition”
  – More than neural transmission and sensory transduction
  – “Pain is a complex melange of emotions, culture, experience, spirit and sensation”.
Chronic Pain

- Chronic pain is more than a symptom... *An illness unto itself*
Chronic Pain

• Acute pain is a physiological response that warns us of danger (protective)

• Chronic Pain has lasted greater than 3-6 months (maladaptive)
  • Does not improve with time
  • Can potentially continue for years

• Can affect a specific part of the body, or involve many regions

• Multi-factorial causes:
  – Structural/mechanical
  – neurological
  – Vascular
  – Central Sensitization
  – Disease process
Physiology of Pain

- **Nociception** describes the normal processing of pain and responses to noxious stimuli (typically acute)
  - Afferent (sensory) from distal receptor to cns
  - Efferent (motor) from cns to distal site
Four basic processes

- Transduction
- Transmission
- Modulation
- Perception
- Interpretation
- Behavior
Physiology Theories of Pain

Mechanisms of chronic pain are complex and unclear (Central and Peripheral):

• Rapid and long-term changes occur in parts of the CNS that are involved in the transmission and modulation of pain (nociceptive information) (Ko, S.M., Zhou, M. (2004) Central plasticity and persistent pain; Drug Discovery Today: Disease Models; Pain and Anaesthesia; 1: 2, 101-106)
  • Nociceptive response without stimuli

• Central “wind-up” = repeated, prolonged, noxious stimulation causes the dorsal horn neurons to transmit progressively increasing numbers of pain impulses
  • Direct and indirect > Increased sympathetic tone

• Neuroplasticity = generation of, and increased transmission of pain impulses
  • What fires together wires together
Role of the Brain

- **Reticular system:**
  - Autonomic & motor response to pain
    - Automatically responds to hand in fire
  - Role in the affective-motivational response to pain
    - Assessing the injury-processing

- **Somatosensory cortex:**
  - Involved with the perception and interpretation of sensations
    - It identifies the intensity, type and location of the pain
  - **Relates** sensation to past experiences, and memory

- **Limbic system:**
  - Responsible for the emotional and behavioral responses
    - Attention, mood, and motivation.

- **All Neurotransmitters involved in Pain** (Signaling, Processing, Perception)
Neurotransmitters

Serotonin
- Anxiety/OCD
- Depression
- Peristaltic reflex
- Circadian rhythm
- Decreased memory

Dopamine
- Motor control
- Pain
- Fatigue
- Memory

Norepinephrine
- Hyper-alertness
- Increased pain signaling
- Anxiety/Panic
- Decreased Focus
Neurotransmitters

- Gamma-Aminobutyric acid (GABA):
  - Chief inhibitory neurotransmitter in the CNS.
  - Important role in regulating neuronal excitability.
  - Also directly responsible for the regulation of muscle tone.

- Glutamate:
  - Most common neurotransmitter in the brain.
  - Always excitatory.

- Substance P:
  - Substance P tells your brain that you are experiencing pain.
  - Signaling molecule.
  - Opens Calcium ion channel.

- Histamine:
  - Wakefulness.
  - Cognition.
Excitatory (Pain) Neurotransmitters

- Synaptic cleft between the terminal ends of the C fiber and A-delta fibers and the nociceptive dorsal horn neurons (NDHN) require excitatory neurotransmitters
  - glutamate
  - adenosine triphosphate
  - calcitonin = gene-related peptide
  - bradykinin
  - nitrous oxide
  - substance P
Inhibitory Neurotransmitters

• Inhibitory neurotransmitters involved with the modulation of pain include:
  – endogenous opioids (enkephalins and endorphins)
  – serotonin (5-HT)
  – norepinephrine (noradrenalin)
  – gamma-aminobutyric acid (GABA)
  – neurotensin
  – acetylcholine
  – oxytocin
Traditional Model of Pain

• Basic mechanism of pain viewed in relation to stagnation
  – Stagnation is a concept of impediment: Flow of energy is blocked
    • Described as blockage of Qi and Blood
      – Activate, nourish, warm, defense
    • Multiple causes: i.e. Cold, Damp, deficiency

• Long term stagnation is referred to as “Bi Syndromes”
  – Categorized by the total symptom picture (S/Sx)

• Majority of Chronic Pain is a mixed pattern
  – Multi- factorial etiology
    • Mind, Body, Spirit
Contributing Mechanisms to Pain

ANYTHING CAN CONTRIBUTE TO PAIN

- Diet and Hydration
- Posture/Ergonomics
- Time
- Stress/Depression/Anxiety
- Sleep & Rest
- Lifestyle
- Money & Access to care
- Relationships & Support
Types of Pain

- **Mechanical** damage/trauma = nociceptive/acute
  - Joint (capsule stretch); Ligaments (sprain, tear); Muscle (strain, tear, spasm); Tendon (strain, tear)
  - Radicular (impingement) from spine to distal site and cns

- **Inflammation-”itis”**
  - Systemic disease: auto-immune, metabolic etc.

- vs. degeneration “osis” = chronic
  - Repetitive trauma/injury
  - Overuse/degeneration and disease process

- Vascular = claudication
  - Can be internal i.e. SMAS
Types of Pain

• Nerve (central vs peripheral)
  – Neuropathy originating distally
    • Damage, lesion or dysfunction in the nervous system
      – Demylination/lesions
    – Surgery (CRPS II), ischemia (diabetes), chemical, infection
      • Nutrient Deficiency (B12, methylfolate, Mg, EFA, etc)

• Central Sensitization: *Directly increases pain perception & response*
  – Central pain involves “**wind-up**” and **neuroplasticity**: Fibro & CRPS
    • Substance P can be sustained & propagated > Increased **NMDA** activity via **glutamate release**
      – Glutamate transporters move glutamate into the extra-cellular space > allows Ca+ to accumulate Intra-cellularly
    – Increased **FOS** expression > increased pain processing
      • Inhibition of descending **serotonergic** path and 5-HT receptors
    – Altered spinal a2 adrenergic receptors
Types of Pain

- **Cancer** (Multiple mechanisms)
  - Location
  - Type
  - Extent

- **Bone**

- **Psychogenic**
  - Somatization/Conversion
    - Metabolic Correction?
Identifying source of pain

- History and description of pain
- Exam finding
  - Imaging results
  - Laboratory and other diagnostics
- Reviewing what has helped and what has not
- Recognizing and treating the source
- Step-wise approach
- Treating contributing layers
- Establishing Therapeutic order
- Individualize treatment
  - multiple modalities
Biochemical Origin of Pain

- All pain involves an inflammatory component
- Biochemical mediators cause inflammation and an inflammatory response
  - “It is” & “Osis”= cytokines (IL-1, IL-6, TNF-a, TIMP-metalloproteinas, NO)
  - Central= NMDA receptors and Neurotransmitters
    - Sub P, Glutamate, NO
    - NMDA, calcitonin gene-related peptide
- Migraine= gene peptides (Neurokinin, somatatostatin, cholecystokinin)
- Nerve= receptor & signaling alteration and Inflammatory mediators
  - A-delta, & C fibers
  - Histamine, bradykinin, Sub P
  - TNF-a, IL-6

Classes of Medication

• Anti-inflammatory
  – NSAID (COX 1-2)
  – Steroid (hormone analog, immune suppressant)

• Muscle relaxants
  – GABA, anticholinergic, decrease motor neuron activity

• Analgesics (Centrally Acting)
  – Acetaminophen
  – Opioids
  – Marijuana

• Neuropathic (GABA, Ca+ or NA+)
  – Anti-convulsant/Nerve - a2 ligand
  – Antiarrhythmic

• Antidepressants (serotonin/norepi/dopamine)
  – SSRI, SNRI, Tricyclic

• Sleep
  – Sedative /Hypnotic, and dopamine agonist
Target Mechanisms

- **Pain**
  - Opioid and Cannabinoid receptor system
  - Direct acting: Analgesic, inflammation (COX, LOX, bradykinin)
- **Excitatory** Neurotransmitters (CNS)
  - Antagonist (i.e. Glutamate)
- **Inhibitory** Neurotransmitters (CNS)
  - Agonists (i.e. GABA, serotonin)
- **Topical**
  - DNIC (i.e. substance P)
- **Hormonal**- HPA(GO) axis
  - Cortisol agonist or potentiator
  - Catecholamine antagonist
  - Metabolic (i.e. insulin)
- **Immune**
  - Up vs. Down regulation (T1/T2 Modulation)
  - Tolerance (IgA)
- **Traditional** categories
Herbs for Chronic Pain

• **Why?:**
  – Large pharmacopeia to chose from
    • Adaptive approach
  – Act on multiple pathway
    • More with less
  – Majority are low risk
    • Generally a low SE profile
  – Often can combine with existing treatment or address new concern without additional pharmacologic or DDI burden
    • Augment, complement, synergy or reduce SE

• **Considerations:**
  – Role
  – Dose & delivery
  – DDI?
  – Cost & compliance
Low Risk DHI

• A review of the literature demonstrated that beliefs about herb–drug interactions are mainly theoretical considerations, and not clinically observed facts.
  – Herb–drug interactions do occur but, equally, common foods such as broccoli, grapefruit juice, alcohol, and cigarette smoking may cause interactions (Butterweck V, Derendorf H, Gaus W, Nahrstedt A, Schulz V, Unger M. Pharmacokinetic herb-drug interactions: are preventive screenings necessary and appropriate? Planta Med2004;70:784–91)

• A review of devil’s claw, ginkgo, and garlic RE: antiplatelet or anticoagulant effects, potentially exacerbating the risk of gastrointestinal bleeding from non-steroidal anti-inflammatory drugs or corticosteroids.
  – No direct evidence supports these claims (Ann Rheum Dis 2005;64:1527-1528)
Reasonable start- Clinical Basics

- Initiate **dietary** discussion
  - Modified Anti-inflammatory
    - Increased veggies
    - Low CHO/Low glycemic, Grains vs. Gluten free???
    - Non-GMO
    - Animal Protein???
    - Intermittent fasting
- Initiate **exercise** or activity program / discussion
  - Mitochondria
- **Evaluate** for common nutrient deficiencies & drug induced depletions
  - 27,000 calories to meet all of the RDIs for micronutrients (http://www.jissn.com/content/pdf/1550-2783-7-24.pdf Research article Prevalence of micronutrient deficiency in popular diet plans -Jayson B Calton)
  - Metformin inhibits B12, Statins deplete CoQ10
Reasonable start- clinical Basics

- **Supplements:**
  - Whole Food **Multi-vitamin** daily or Medical Food shake
  - Vit **D3** 4000IU daily
  - Mixed **fatty Acids** (EPA/DHA/GLA)
  - **Probiotics**
    - Kombucha etc.
  - **B-complex** (active forms)
  - **Magnesium**
  - **CoQ10**
  - **Green Tea**
  - **Bitters**- healing begins with the Gut / Broad systemic effect
  - **Urine alkalinization**- Standard for toxicity treatment
    - concentrated greens with minerals
Building a Formula

- Use adaptive model (specific paradigm) to determine primary condition
  - Underlying cause
    - Inflammatory type
    - Contributing mechanisms
    - XS, def, Hot, cold, Qi, Blood, Constitutional etc.
- Identify specific target pathway
  - Inflammation
  - Nerve
  - Neurotransmitter
- Choose Base formula
- Add evidenced based herbs
- Choose secondary targets
- Add supportive interventions
Clinical Approach

- Underlying - Root
- Primary Formula
- Inflammation
- Pain Receptors
- Target Mechanism
- Contributing mechanism
- Secondary Target
- Support
- Damage
Example of Clinical Approach

- Osteoarthritis
- Du Huo Ji Sheng Tang
- Inflammation & Pain
  - Curcumin
  - Corydalis
  - Salix & Devils’ club
  - Petasites
- Circulation
  - Gingko
  - Sleep
  - Depression
- Secondary Target-
- Support
  - Gelatin
  - Glucosamine & SAMe
  - Sleep
  - Depression
Formula

Du Huo Ji Sheng Tang

- Curcumin: Evidence based anti-inflammatory
- Corydalis: Anodyne 1% morphine equiv. Blood mover
- E Jiao-Gelatin: Collagen joint support
- Other

Yin support
Increased warmth
Anxiolytic - shen

Note: This formula contains multiple supportive herbs
- Adaptagens- Ginseng, Licorice
- Circulation Support, Blood tonic/mover- Angelica
- Moving/Warming- cinnamon
Anodyne & Analgesics

- **Salix spp.**: Willow family-Willow (S. alba), Black Willow or American Willow (S. nigra), European willow
  - Modern Aspirin is derived from Willow bark
  - Converted into its active form, salicylic acid (via oxidation process in liver).
    - Salicylic acid is an analgesic & antiplatelet agent.
    - The analgesic actions of willow are typically slow-acting but last longer than standard aspirin products.
    - Salicylic acid also has antipyretic, anti-inflammatory & antiseptic qualities-inhibits cyclooxygenase.

**Evidence:**
- German E commission approved
- Grade A osteoarthritis pain (Natural Standards)
- Grade B Low Back Pain (Natural Standards)
- 3 Star (Healthnotes)

Anodyne & Analgesics

- Yan Hu Suo: Corydalis
  - Traditional Properties: warm, acrid, bitter; enters H, LR, LU, ST
  - Anodyne, Moves Blood and Qi
    - Useful for all pain conditions – central and peripheral
      - Calms nervous tone and decreases spasticity (Neeb, G. Blood Stasis, 2007)
    - Multiple Effects: analgesic, anti-inflammatory, decreases blood resistance, sedative, muscle relaxant, adaptagenic

- Evidence: strong traditional, limited EBP/meta-analysis
  - 1% equivalent to Morphine
    - Analgesic properties enhanced by vinegar
  - Grade C (Natural Standards)
  - 2 Star (Healthnotes)

(Chen & Chen. Chinese Medicinal Herbology and Pharmacology, 2001)
Anodyne & Analgesics

- *Commiphora molmol*: **Myrrh** (Mo Yao)
  - Traditional Properties: neutral, bitter; enters-H, LR, SP
  - Anodyne, Moves Blood and Qi
    - Useful for all pain conditions
      - Synergistic when combined with *Boswellia Spp.* (Ru Xiang)
    - Internal and Topical use
      - Mo Yao- stronger internally, particularly GI & Gyn
        » Small doses promote digestion and prove antiseptic to the intestinal canal
        » Boswellia- stronger externally
  - Myrrh is a stimulant to mucous tissues – menstrual disorders
  - C/I in active inflammatory conditions

Anodyne & Analgesics

- **Boswellia Spp.**: Frankincense or Olibanum (Ru Xiang)
  - Traditional Properties: neutral, bitter; enters H, LR, SP
  - Anodyne, Moves Blood and Qi
    - Useful for all pain conditions
      - Moves Blood, moistens/relaxes sinew & muscle
      - Synergistic when combined with Boswellia Spp. (Ru Xiang)
    - Internal and Topical use: 3 star evidence (Healthnotes)
      - Stronger for external use- promotes healing-Vinegar enhances effect
  - Boswellic acids: biologically active ingredients
    - Noncompetitive inhibitors of 5-lipoxygenase
    - Boswellia inhibits pro-inflammatory -inhibits the synthesis of leukotrienes
    - Administration of a non-phenolic crude herb produced analgesia in 60% of rats
      - 60.0 mg/kg bw. A dose of 150.0 mg/kg bw induced analgesia in 70%
      - *The degree of analgesia was comparable to a dose of 3–4.5 mg/kg bw of morphine.*

Anodyne & Analgesics

- *Piscidia piscipula* - Jamaican Dogwood

- **Use**: Piscidia is indicated for many types of severe and acute pain
  - can be applied topically

- **Medicinal Action**: Hypnotic, anodyne (pain-killing), sedative, antispasmodic, analgesic, diaphoretic, sialogogue, diuretic, antitussive, insecticidal, anti-dermatophyte

- **Mechanism**: Glycosides, Flavones, Acids, Tannins
  - Appears to be an antispasmodic

- **Note**: Excess doses are toxic
  - **Recommended Range**:
    - Take 1 to 4 ml of the tincture three times per day. Tincture (1:5 extract) 90 drops (~3ml).
    - 5-10g Bark in Decoction

(Natural Medicine Comprehensive Database, Bastyr Monograph- Welliver & ABC)
Anodyne & Analgesics

Cannabis Spp.

- Cannabis used medicinally for possibly greater than 5,000 years
  - Evolutionary adaptation
    - use for neuropathic pain has been documented as early as the mid-1800s (Haroutunian, Rosen, Shouval, & Davidson, 2008; Perez & Ribera, 2008)

- Effects multiple parameters of pain: Centrally and Peripherally acting
  - Tetrahydrocannabinol (THC) most recognizable, most psychoactive
  - Cannabidiol (CBD) reduces the psychoactive side effects of THC, and also offers anti-inflammatory & immune modulating effects

- 2 primary cannabinoid receptors CB1/CB2

- Anti-inflammatory
- Sedative
- Immune Modulating
Anti-inflammatory

• *Curcuma* Spp.: *Tumeric* (Yu Jin, Jiang Huang, E Zhu)
  – Long history of use in TCM, and Aryuveda
    • Type differentiates use- different properties

• Wide variety of uses / high safety index

• Anti-inflammatory activity of curcumin has been demonstrated in cell culture and animal studies

Curcumin Spp. Evidence

- A preliminary intervention trial that compared curcumin with a nonsteroidal anti-inflammatory drug (NSAID) in 18 RA patients found improvements in morning stiffness, walking time, and joint swelling after two weeks of curcumin supplementation (1,200 mg/day).

- *Placebo controlled* trial in 40 men who had surgery to repair an inguinal hernia or hydrocele found that oral curcumin supplementation (1,200 mg/day) for five days was more effective than placebo in reducing post-surgical edema, tenderness and pain, and was comparable to phenylbutazone therapy (300 mg/day).

- Curcumin in conjunction with NSAIDs has **synergistic effect**
  - used an adjuvant model of rat inflammation to demonstrate that curcumin and ibuprofen modulate inflammatory biomarkers such as reactive protein when used in combination;
  - Curcumin synergistically potentiates the growth-inhibitory and pro-apoptotic effects of the NSAID celecoxib in OA-derived synovial adherent cells (Int J Mol Sci. 2012; 13(4): 4202–4232.)
The Arachidonic Acid Cascade
Curcumin Inhibits Pain and Inflammation and Supports Homeostasis

Stimulus

Phospholipids

Phospholipase A-2

Arachidonic Acid

COX-1 and COX-2

LIP OXYGENASE

CYCLO OXYGENASE

Curcumin INHIBITS Both SELECTIVELY

Leukotrienes
LTB4, LTC4, LTD4
LTE4, 5-HPETE, 5-HETE

Prostaglandins
Thromboxanes
Anti-inflammatory

• *Harpagophytum procumbens*: Devils’ Claw
• Dual Anti-inflammatory and anodyne actions

• Action though to be due to the presence of a glycoside
  – harpagoside that reduces inflammation in the joints

• **Evidence:**
  – Cochrane Database review - Strong evidence for use in chronic back pain demonstrated (with Salix, Cayenne and Devil’s Claw)
  – Grade B (Natural Standards)
  – 2 Star (Healthnotes)
  – Commission E approved for loss of motor function & coordination

Anti-inflammatory

• **Bromelain:**
  – Proteolytic enzyme contained in pineapple.
  – Reduces leukocyte activation and migration
    • “Digests” inflammatory proteins (Take on empty stomach)
      – Extract taken three times daily, is comparable to diclofenac 50 mg three times daily for reducing pain
  
• **C/I** anti-coagulation (research inconclusive)

• **Evidence:**
  – Grade B (Natural Standards)
  – 2 Star (Healthnotes)
  – B1 (Rakel-Integrative Medicine)

(Natural Medicine Comprehensive Database, and Rakel. *Integrative Medicine*, 2006)
Anti-inflammatory

- **Propolis**
  - Processed resin derived from honey bees (*Apis mellifera*)
    - Red and Green
  - Long history of traditional use: Lung-Large Intestine (Metal) in TCM
    - Egypt- mummification / Sterile
  - Wide range of internal and topical applications
  - Moderate to strong effect on GI and Pulmonary system
    - Activation of gut associated lymphoid tissue (GALT)
      - leading to reflex increases of IgA in the lung mucosa

DNIC

- Increased **Substance P** signaling
  - Can be overridden by activating neurons located in the spinal column or medullary dorsal horn
  - Distally applied noxious stimuli
- Effect is variable in terms of length of efficacy since Substance P does not easily naturally degrade
Topical

*Capsicum annuum* - *cayenne* pepper

- Capsicum peppers contain the constituent "capsaicin."

- **Medical Action:** Circulatory stimulant, tonic, carminative, spasmolytic, diaphoretic, antiseptic, rubefacient, vasodilator, counter-irritant.
  - Considered pure stimulant by King & Cook

- **Capsicum** works as a counterirritant via DNIC activation
  - Depletes Substance P
    - Without the neurotransmitters, pain signals can no longer be sent.
    - Depletion takes approximately three to ten days
      - Administration 4 times per day for 7 days.

- Activates vanilloid receptor TRPV-1 (nociceptive)

(Comprehensive Natural Medicine Database & Welliver. Bastyr Monograph, 2005)
Capsaicin

- **Evidence:**
  - 3 Stars (Health Notes)
  - Commission E Approved- muscle spasms
  - FDA-approved OTC preparation for topical use - analgesic and anesthetic
    - Concentrations of 3% to 11%
    - Effective for temporary symptom relief of pain r/t osteoarthritis & some evidence for decreased back pain and pain in fibromyalgia
Topical

- **Other** herbs that deplete substance P:
  - Ginger
  - **white mustard** seed - *Sinapis albae semen*
    - Commission E Approved
  - Curcuma

(Bastyr Materia Medica Ref- Yarnell)
Neuropathic Herbs

- *Tanacetum parthenium*: **Feverfew**
  - Most well-known natural medicine used to prevent migraine
    - Grade A Evidence (Natural Standard)
    - 3 Star Evidence (Healthnotes)
    - Not Commission E Approved
    - Most evidence - reduces the frequency of migraines, and severity of symptoms: nausea, vomiting, and sensitivity to light and noise
      - Not effective for treating an acute attack.
  - Mechanism unclear:
    - Inhibits platelet aggregation
    - Serotonin release
    - Leukotrienes, and prostaglandin synthesis (Parthenolide)
    - Inhibit COX-2, TNF-alpha and IL-1 (Parthenolide)
    - Inhibition of vascular muscle contraction (Chrysanthenyl acetate)
    - Might have analgesic properties (Chrysanthenyl acetate)
    - Contains melatonin

(Comprehensive Natural Medicine Database)
Neuropathic Herbs

• *Petasites hybridus*: **Butterbur**

• **Mechanism:**
  – Directly inhibits Calcium ion channel (Petasins):
    • Ca(2+) antagonism of L-type voltage-dependent Ca(2+) channel (VDCC)
  – Anti-inflammatory effects by inhibiting leukotriene synthesis
  – Antispasmodic effects on smooth muscle and vascular walls
  – Decreases priming of mast cells

• **Note**: Raw contains PA’s- C/I Liver Disease

(Comprehensive Natural Medicine Database & Memorial Sloan Kettering Database)
Neuropathic Herbs

• **Valarian** - *Valarian officinalis*

• **Medicinal actions**: Tonic Sedative, hypnotic, nerve, hypotensive, antispasmodic, carminative, sedative (paradoxical stimulant)
  - Primarily a sedative
    • Valerenic acid - binds to GABA-A receptors
  - Has some Calcium ion channel binding action
    • Theoretically useful pain - No Evidence / Overall conflicting-unclear

• **Evidence** (Sleep):
  - Natural Standards Grade C
  - Health Notes 3 Star
  - German E Commission Approved
  - **C/I**: MAO inhibitors

Bee Venom
Bee Venom

• Apitherapy was known to many ancient cultures going back 6000 years
  – It was practiced by three of the Great Civilizations known for their highly
devolved medical systems:
    • ancient Egypt, China, and Greece, as well as by the Aztec and Maya in the
      New World (American Apitherapy Society, 2010)

• Venom is administered either by direct sting from the bee itself, or by manual
  injection of venom, via syringe (Apitoxin)
  – Combined mechanical and pharmacological action
  – Acts synergistically
    • Elicits both central and peripheral pain inhibition

• Therapeutic use of venom is not an unheard of clinically
  – The FDA approved drug, Prialt (Zoconitide) is a non-narcotic pain medication
    derived from the conotoxin of the Conus magus snail and is now available in
    many pain clinics
Traditional Property of Venom

- **Energetic Nature of Venom: Characteristics of Both Yin and Yang**
- **Energy**: Yang, Toxic, Hot
- **Flavor**: Pungent-Moving
- **Channels Entered**: Yin (Based on the effects venom enters all the Yin organs)
  - Lung: *Wei Qi* = Immune response, antigenic
  - Spleen: *Qi Trans/Muscle* = HPAA, Enzymes, Muscle
  - Liver: *Sp Qi/Blood/Sinew* = Circulation, anti-inflammatory, Muscle
  - Kidney: *Marrow/Brain*: CNS, HPAA, Antioxidant, immune stimulation
  - Heart/PC: *Shen/Sovereign Blood* = Neurotransmitters, + inotropic action, Circulation, coagulopathy

- **Movement**:
  - Inward- affects organs: Yin
  - Outward- Treats the superficial layers (skin, muscle, tendon): Yang
Bee Venom

• Bee venom is a complex molecule, consisting of several compounds that directly contribute to its anti-nociceptive effect
  – *Apis* venom has direct analgesic and pain modulating effect:
    • Gating Mechanism
    • DNIC
    • Activation endogenous opioids
    • Serotonergic and noradrenergic pathway activation – pain modulation
    • Decreases *FOS* expression- decreasing nociceptive response
  – Indirect effect on contributory mechanisms:
    • Inflammation: 100x potency endogenous cortisol
    • oxidation : inhibits nitric oxide synthase (iNOS) expression
    • histamine release
    • Immune response
      – directly influenced immune T-cell response *without* being activated by antigen presenting cells
      – Influenced CD4+ T-helper cells to selectively differentiate to a Th-1 path
Sarapin

- **Pitcher Plant** extract - *Sarracenia purpurea* (Injectable)

- **Uses**: Trigger points, Sciatica, Neuropathic Pain

- **Mechanism**:
  - Leaf & root contain sarracenia acid, tannin, resin, & the alkaloid sarracenin
    - Effect on sensory nerves without changing sensation or affecting motor
    - Affects only C nerve fibers, perhaps containing a biological antagonist that potentiates the action of the ammonium ion

- **Evidence**:
  - Inconclusive overall
  - Considered likely safe without evidence harm

(Natural Medicine Comprehensive Database & Sarapin.com)
Circulation Support

- Circulation support: Herbs that Move Blood, Improve Microcirculation
  - *Angelica sinensis*: **Dang Gui**
    - Primary blood tonic TCM
  - Salvia: **Dan Shen**
    - Blood Mover—cardiovascular specific: HTN, Angina
  - *Rosmarinus officinalis*: **Rosemary**
  - *Crataegus laevigata*: **Hawthorn**
    - Primary Cardiovascular Tonic: CHF, Cor Pulmonal
    - ACE inhibitor
  - *Ginkgo biloba*: **Gingko**
    - Cerbrovascular specific & promotes motor neuron growth
    - Distal microcirculation

Adaptogens

• Very useful clinically for multiple targets- system modulation
  – Metabolic, HPA(Go) axis, immune etc.

• Variety/Choices
  – *Panax ginseng*: Ginseng (Ren Shen)
  – *Panax quinquefolius*: American Ginseng (Xi Yang Shen)
  – *Eleutherococcus senticosus*: Siberian Ginseng
  – *Astragalus membranaceus* (Huang Qi)
  – *Withania somnifera* (Ashwagandha)
  – *Bupleurum falcatum*: Hare’s ear /Thorowax (Chai Hu)
  – Glycerrhiza glabra: Licorice (Gan Cao)
  – *Schizandra sinensis*: 5 flavor fruit (Wu-wei-zi)

(Winston & Maimes. *Adaptogens*, 2007)
Addiction Herbs

• Addiction control agent, anti-addiction
  – **Alcoholism** (antidipsotropic)
    • hyperforin, *Hypericum perforatum* (St. John’s wort)
    • *Pueraria lobata* (kuzu, kudzu)
    • *Salvia miltiorrhiza* (Chinese sage)
  – **Narcotics**, opioids
    • *Panax ginseng* (Asian ginseng)
    • *Piper methysticum* (kava)
    • *Withania somnifera* (ashwagandha)
    • *Passiflora incarnata* (passion flower)
  – **Nicotine**
    • *Avena sativa* (oats)
    • *Lobelia inflata* (lobelia)
    • *Piper longum* (long pepper)
Nutrients

• L-tryptophan 2-4g daily (mixed results in double-blind trials)
  – Works best on empty stomach or with small amount CHO
• Phenylalanine DL 500-750mg 2-3x daily (mixed results across trials)
  – 2 primary forms L & DL
  • DL preferable as analgesia thought to be associated with D isomer
• Glucosamine 500mg 3x daily (strong + results in multiple double-blind trials)
  – Sulfate form best
  – Improvements typical 1 month- 12 weeks.
  • Decrease joint space lost (knees) over 2 years
• Chondroitin sulfate 800-1200mg daily (suggestive results)
• S-Adenosyl-L-methionine (SAME) 400mg 3x daily (strong + results in multiple double-blind trials)
  – As effective as typical NSAID doses- better tolerated

• Note- no current data on combined products but common practice

(Gaby and Wright. Nutritional Therapy in Medical Practice, 2011. Nutritional Seminars)
Clinical Considerations

- Diet / Nutrition & Supps
- Physical Medicine
- Hydrotherapy
- Rehabilitation
- Psychotherapy
- Interventional
- Medications
Questions, Comments, Arguments

That's all Folks!