Objectives

- This session will provide an overview of herbal medication usage patterns and discuss the most commonly used herb and supplements.
- Faculty will provide an update on the top 10 herbs and supplements used by children and adolescents, including Arnica, Butterbur, creatine, kava, probiotics, and St. John’s wort.
- Emphasis will be placed on the efficacy and safety of herbal medicines. Resources will be shared, including information on how to receive updates on herbal medicines and supplements.

2012 National Health Interview Survey (NHIS)

- 11.6 percent of the more than 10,000 children aged 4 to 17 included in the survey had used or been given some form of complementary health product or practice during the past year.
- The most frequently used complementary approaches for children were natural products such as fish oil, melatonin, or probiotics and chiropractic or osteopathic manipulation.
- For children, complementary approaches were most often used for back or neck pain, other musculoskeletal conditions, head or chest colds, anxiety or stress, attention-deficit hyperactivity disorder (ADHD), and insomnia or trouble sleeping.
- CAM users were more likely than non-CAM users to be: adolescents rather than infants or; live in the West, Northeast, or Midwest compared to the South; more likely to have a parent with a college education and more likely to use prescription medication.
- Use of CAM by a parent was strongly associated with the child's use of CAM.

Regulation: DEFINITION OF DSHEA 1994

Sec. 201(ff) The term dietary supplement --
(1) means a product (other than tobacco) intended to supplement the diet that bears or contains any of the following dietary ingredients:
(A) a vitamin
(B) a mineral
(C) an herb or other botanical
(D) an amino acid
(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake:
(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E)

What the law allows:

- Products can go on the market with no testing of efficacy.
- Companies do not have to prove that their products are safe only reasonable assurance.
- Supplements do not have to be manufactured according to any standards (the reputable manufacturers are in favor of standards).
- FDA approval is not needed for package or marketing claims.
Safety Messaging

- Raynor DK. Buyer beware? Does the information provided with herbal products available over the counter enable safe use? BMC Med. 2011
- 51 (75%) of 68 products contained none of the key safety messages.
- This included 4 of 12 St John’s wort products, 12 of 12 ginkgo products, 6 of 7 Asian ginseng products, 20 of 21 garlic products and 9 of 13 echinacea products.
- The two products purchased that are registered under the new European Union regulations (for St John’s wort) contained at least 85% of the safety messages.

Herb Drug Interactions


Herbal Use in Patients Undergoing Surgery

- Approximately 26% of patients scheduled for surgery use herbal products
- Cardiovascular instability
- Prolongation of anesthesia/sedation
- Bleeding
- Electrolyte disturbances
- Immunosuppression

Labeling and Manufacturing Standards Proposal

- Current good manufacturing practices (CGMPs)-manufacturing, packaging and holding standards
- Manufacturers required to evaluate the identity, purity, quality, strength and composition of their dietary ingredients and dietary supplements
- Required to report impurities, potency errors

United States Pharmacopeia (USP) Dietary Supplement Verification Program (DSVP)

ConsumerLab.com
### IBIDS Database

- **International Bibliographic Information on Dietary Supplements**
  - Office of Dietary Supplements (ODS) at the NIH
  - Published, international, scientific literature
    - Vitamins, minerals, and botanicals
  - Over 676,000 unique scientific citations abstracts
  - Three databases
    - Full IBIDS database
    - Peer-Reviewed Citations Only database
    - IBIDS Consumer database

### Natural Medicines Research Collaboration

- [https://naturalmedicines.therapeuticresearch.com/](https://naturalmedicines.therapeuticresearch.com/)

### Case Study

- 16 yo female with chronic fatigue syndrome after symptoms of a URI 18 months ago. She now has been diagnosed with fibromyalgia.
- She has been evaluated by
  - Her primary care physician
  - A Neurologist
  - Two rheumatologists
  - An otorhinolaryngologist
  - A nutritionist
  - A psychotherapist
- She has been treated with
  - Erythromycin twice
  - Cephalexin twice
  - Augmentin three times
  - Ciprofloxacin
  - Intravenous ceftriaxone
  - Oral nystatin
  - High doses of vitamins and a restriction diet

### Family wants to try turmeric, Coenzyme Q10 and cannabinoid oil.
- Is this ok?

### Turmeric (Curcumin)

- **Uses:** osteoarthritis, rheumatoid arthritis (RA), dyspepsia, abdominal pain, Crohn's disease and ulcerative colitis, coronary artery bypass graft (CABG) surgery, hemorrhage, diarrhea, flatulence, abdominal bloating, loss of appetite, jaundice, hepatitis, ... radiation mucositis, radiation dermatitis, fibromyalgia, fatigue, leprosy, ...
Turmeric (Curcumin)

- **Mechanism of Action:** anti-inflammatory
- **Dose:** 500 mg four times daily
- **Adverse Effects:** constipation, dyspepsia, diarrhea, distension, gastroesophageal reflux, nausea, vomiting, pruritus, urticaria
**Background**

Joint pain is a common and persistent problem affecting quality of life in community adults. The study aimed to assess the effect of a 74% boswellic acid extract and curcumin in alleviating joint pain severity in middle-aged and older adults, with mitigation of difficulty in daily activities, and improvement in health-related quality of life.

**Subjects**

A double-blind, placebo-controlled community trial involving 100 men and women, ages 50-75, with a history of joint pain for more than 3 months, was conducted. Participants agreed to avoid the use of non-steroidal anti-inflammatory drugs (NSAID) and all other medications and supplements during the study period.

**Methods**

Subjects were randomized to Instaflex™ or placebo (3 colored gel capsules per day for 8 weeks, double-blind administration). Subjects included health-related quality of life (Short Form 36 or SF-36), systemic inflammation (serum C-reactive protein and 9 indicators in rheumatoid arthritis patients: A randomized, double-blind, placebo-controlled, two-dose, three-arm, and parallel-group study. J Med. 2017;20(10):1022-1030.

**Results**

Curcumin 500 mg twice daily reduces RA symptoms more than diclofenac sodium 50 mg twice daily after 8 weeks of treatment.

**Chandran B. A randomized, pilot study to assess the efficacy and safety of curcumin in patients with active rheumatoid arthritis. Phytother Res 2012;26:1719-25.**

**Turmeric (Curcumin)**

- Might reduce some symptoms of rheumatoid arthritis (RA), including pain, morning stiffness, walking time, and joint swelling compared to baseline.
- Cannabidiol is a non-psychoactive constituent of Cannabis sativa, also known as marijuana.
- Over 80 constituents, known as cannabinoids, have been identified from the Cannabis sativa plant, of which delta-9-tetrahydrocannabinol (THC) is the major psychoactive compound.
- Cannabidiol makes up around 40% of cannabis extracts and has been investigated for a wide variety of therapeutic effects.

**CoEnzyme Q10**

- Uses: congestive heart failure (CHF), cardiotoxicity associated with doxorubicin chemotherapy, muscular dystrophy, increasing exercise tolerance, chronic fatigue syndrome (CFS), Lyme disease, autism, and chemotherapy-related fatigue.
- Mechanism of Action: Coenzyme Q10 is a fat-soluble compound with a chemical structure similar to vitamin K. Antioxidant.
- Clinical Studies:
- Coenzyme Q10 200 mg in conjunction with ginkgo 200 mg orally daily for 12 weeks improves measures of quality of life such as physical fitness levels, emotional feelings, social activities, overall health, and pain.
Cannabidiol

- **Uses**: anticonvulsant, antianxiety, antipsychotic, antinausea, and antirheumatoid arthritis
- **Dose**: Cannabidiol 160 mg - 300 mg daily
- **Adverse Effects**: dry mouth, hypotension, lightheadedness, orthostatic hypotension, psychomotor slowing, sedation, and somnolence.

What would you recommend?

- **Discussion...**

Case Study

- Heather is a 17 year old senior on the crew team. Her performance in crew has deteriorated recently and she is thinking about quitting. Her college applications are due and she is exhausted. She has been taking all sorts of herbs and supplements to get through the year both to stay awake and to get asleep as well as to keep her healthy.

Caffeine

- **Mechanism of Action**: Xanthine alkaloid which acts on external cell membrane and intracellularly through Calcium and cAMP pathways. Readily crosses blood brain barrier.
- **Uses**: Reduces drowsiness and restores alertness.
- **Clinical Studies**: Smith AP. 2005. Caffeine consumption may have benefits for performance and safety at work
- **Adverse Effects**: Anxiety, nervousness, withdrawal, insomnia, headaches, palpitations, GERD, peptic ulcers, irritability, tremulousness.
**Echinacea**

- **Uses:** Approved in Germany as supportive therapy for upper respiratory infections, urogenital infections and wound healing
- **Mechanism of action:** May stimulate the alternate complement pathway and activate nonspecific T-cell. Echinacea may have immune-modulating effects and can inhibit viral replication, improve the motility of polymorphonuclear cells, enhance phagocytosis and natural killer cell activity.

**Clinical Studies:**
- Taylor JA. 2003. No difference in duration or estimation of severity between URIs treated with echinacea or placebo.
- Turner RB. 2005. Echinacea had no significant effect on either the occurrence of infection or the severity of illness.
- Cochrane Database Syst Rev. 2014 Feb. Echinacea for preventing and treating the common cold. Echinacea products have not here been shown to provide benefits for treating colds, although, it is possible there is a weak benefit from some Echinacea products: the results of individual prophylaxis trials consistently show positive (if non-significant) trends, although potential effects are of questionable clinical relevance.

**Dose:**
- *Echinacea purpurea* leaf is 6 to 9 ml expressed juice tid. *Echinacea purpurea* root tincture; daily dose is 30 to 60 drops tid during a URI
- **Adverse effects:** Should not be used in those who are immunocompromised, in those with autoimmune diseases or in those allergic.

**Zinc**

- **Uses:** Common Cold
- **Clinical Studies: Cochrane Review 2013**
  - Randomised, double-blind, placebo-controlled trials using zinc for at least five consecutive days to treat, or for at least five months to prevent the common cold.
  - Zinc administered within 24 hours of onset of symptoms reduces the duration of common cold symptoms in healthy people but some caution is needed due to the heterogeneity of the data.
- **Dose:** 75 mg per day
- **Adverse Effects:** bad taste and nausea, anosmia

**Melatonin**

- **Uses:** jet lag, insomnia, shift-work disorder, circadian rhythm disorders in the blind, and benzodiazepine and nicotine withdrawal.
- **Mechanism of action:** In the brain, melatonin appears to increase the binding of gamma-aminobenzoic acid (GABA) to its receptors by affecting membrane characteristics, not by increasing the number of receptors.
- **Clinical studies:** Petrie K 1989. Effect of melatonin on jet lag after long haul flights.
- **Dose:** 0.5-5mg po HS
- **Adverse effects:** might inhibit ovulation, impair glucose utilization, decrease prolactin activity, concomitant use of melatonin with alcohol, benzodiazepines, or other sedative drugs might cause additive sedation.

**Case Study**

- Michael is a 11 year old with poor sleep, headaches, OCD and Tourette’s Syndrome.
- The grandmother wants to try natural remedies for Michael because they seem to work for her. She has brought in butterbur, N- Acetyl cysteine (NAC), melatonin, Omega 3 capsules and St. Johns wort.
- Is this ok?
### Butterbur (Petasites hybridus root)

- **Uses:** Migraines
- **Mechanism of action:** Anti-inflammatory effects by inhibiting leukotriene synthesis
- **Clinical Studies:** Pothmann R, Danesch U. Migraine Prevention in Children and Adolescents: Results of an Open Study With a Special Butterbur Root Extract. Headache 2005;45:196-203

### N Acetylcysteine (NAC)

- **N-acetyl cysteine** is used as an antidote for acetaminophen and carbon monoxide poisoning.
- It is used for bipolar disorder, schizophrenia, post-traumatic stress disorder (PTSD), substance use disorders, and **Tourette syndrome.**
- It is also used for reducing lipoprotein (a) levels in patients with hyperlipidemia, reducing risk of cardiovascular events in patients with end-stage renal disease (ESRD), bronchitis, chronic obstructive pulmonary disease (COPD), cystic fibrosis, autism, adrenoleukodystrophy (ALD), hepatitis, kidney disease, ...
- for myoclonus epilepsy, ... and detoxifying heavy metals such as mercury, lead, and cadmium


### St. John’s Wort

- **Uses:** Named after St. John the Baptist because it blooms around his feast day; used for depression.
- **Mechanism of action:** Inhibition of serotonin reuptake, MAO, 5 HT, dopamine, noradrenaline, GABA and glutamate.
- **Clinical Studies:** Cochrane Review 2005. Extracts of St. John’s wort may be more effective than placebo; similar efficacy as standard antidepressants for mild to moderate depression. Major depression treatment effects may be minimal.

**Dose:** 300mg (0.3% hypericin) tid
- **Adverse effects:** Induces cytochrome P450 3A and may increase metabolism of warfarin, cyclosporin, HIV protease inhibitors, theophylline, digoxin and oral contraceptives Can cause decreased platelet aggregation, serotonin syndrome, or photosensitivity.

**Rahimi R1, Abdollahi M. 2012. An update on the ability of St. John’s wort to affect the metabolism of other drugs. Expert Opin Drug Metab Toxicol.**
Butterbur

- **Dose:** 50-75 mg daily in two or three divided doses for ages 8-9 years and 100-150 mg daily in two or three divided doses for ages 10-17 years
- **Adverse Effects:** gastrointestinal (belching, diarrhea, and stomach upset), dermal/allergic (itchy eyes, asthma, and pruritus)

Magnesium

- **Uses:** Magnesium is a cofactor in more than 300 enzyme systems that regulate diverse biochemical reactions in the body, including protein synthesis, muscle and nerve function, blood glucose control, and blood pressure regulation
- **Dose:** 300 – 500 mg citrate versus daily po (soy beans, black beans, tofu, seeds, mits, whole grains, shellfish)
- **Side effect:** Diarrhea, interactions with bisphosphonates, antibiotics and diuretics, *PPI may reduce Mg Levels

Omega 3 fatty acids-Docosahexanoic acid (DHA); Eicosapentanoic Acid (EHA)

- **Uses:** ADHD, depression, heart disease, prevention of macular degeneration
- **Mechanism of Action:** reduce serum triglycerides, promote normal neural and synaptic function
- **Clinical Studies:** Gabbay V. A double-blind, placebo-controlled trial of ω-3 fatty acids in Tourette's disorder. Pediatrics. 2012.
- **Dose:** Typical dose is 5 grams of oil containing 169-263 mg of EPA and 72-312 mg of DHA twice daily.
- **Adverse Effects:** Fishy taste, belching, nosebleeds, nausea, and loose stools. High doses of fish oils might also decrease blood coagulation

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What would you recommend?

- **Discussion...**
WEBSITES

- www.consumerlab.com
- www.naturalmedicines.therapeuticresearch.com
- www.nccih.nih.gov
  - Books: Herbs at a glance
- www.herbmed.org
- www.herbs.org

AAP Section Complementary, Holistic and Integrative Medicine (SOIM)

- Mission: to support the mission of the AAP "to attain optimal physical, mental, and social health and well being for all infants, children, adolescents, and young adults" by:
  - promote policies to enhance patient-centered care;
  - integrate evidence-based, safe and effective complementary therapies into high quality pediatric practice;
  - educate clinicians and families; advocating for appropriated payment for safe and effective services; and
  - respectfully collaborate with diverse health professionals dedicated to enhancing the health of infants, children, and adolescents.

Questions?

- cora.breuner@seattlechildrens.org
  206 999 1208

Case Study

- 7 y/o male was diagnosed with leukemia last month and his family wants to use herbal remedies to support him through his chemotherapy.
- What suggestions can you offer?

Peppermint

- Uses: Irritable bowel syndrome, colic, nausea, decongestant, cough suppressant, anxiolytic, topical analgesic for headache and myalgia.
- Mechanism of action: Calcium channel blocker in GI smooth muscle, vapors stimulate sensory nerve endings in nasal mucosa, triggers cold receptors on the skin causing a sensation of coolness and analgesia.
- Clinical Studies: Kline 2001. In a study comparing enteric peppermint capsules with placebos in children with IBS, 75% experienced improvement in their symptoms.
- Dose: One to 2 enteric-coated capsules containing 0.2 ml of peppermint oil taken 2 to 3 times a day
- Adverse effects: Infantile apnea when applied under/in nose, heartburn, mild rectal burning.
### Arnica

**Uses:** inflammation and immune system stimulation associated with bruises, aches, and sprains.

**Mechanism of Action:** Sesquiterpene lactones, which are esters of helenalin and 11,13-dihydrohelenalin. These constituents seem to have anti-inflammatory, analgesic, and platelet-inhibitory effects

**Clinical Studies:** Adkison JD. The effect of topical arnica on muscle pain. Ann Pharm 2010;44:1579-84.

**Dose:** 2 grams flowerheads in 100 mL water; as a poultice, the tincture of arnica is diluted three to ten times with water

**Adverse Effects:** irritation of mucous membranes, drowsiness, stomach pain, vomiting, diarrhea, allergic reaction in individuals sensitive to the Asteraceae/Compositae family.

### Chamomile

**Uses:** Cultivated worldwide as a sedative, anti-spasmodic, anti-inflammatory and wound healing agent

**Mechanism of Action:** Chamazulene: antispasmodic; Apigenin-anxiolytic; Bisapolo- anti-inflammatory


### Zingiber officinale (Ginger)

**Uses:** Antiemetic, antinausea, circulatory stimulant, anti-inflammatory

**Mechanism of Action:** Ginger contains antiemetic, anti-inflammatory, and analgesic properties. Promotes the flow of bile into the intestine through contraction of the gallbladder. Pharmacologically active components of the oleoresin include gingerols.

**Clinical Studies:** Borrelli F. 2005 Four of the 6 RCTs showed superiority of ginger over placebo in pregnancy induced nausea and vomiting.

**Dose:** 2 to 4 grams of fresh root daily (0.25 to 1.0 g of powdered root) or 1.5 to 3.0 mL (30 to 90 drops) tincture daily.

**Adverse Effects:** May cause heartburn, decreased platelet aggregation. Topical application may cause contact dermatitis in sensitive patients.

### What would you recommend?

**Discussion...**