

Herbal and Dietary Supplements

Popular Uses/Potential Dangers

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Objectives:

1. Explain the prevalence of herbal and dietary supplements in the United States.
2. Define CAM (complementary and alternative therapies) and understand what is included in this category.
3. List several reasons why patients use alternative and complementary therapies.
4. Explain how herbal preparations and dietary supplements are regulated in the United States.
5. Describe which medicinal herbs have good evidence for their efficacy.
6. List potential drug interactions between herbal and dietary supplements and commonly prescribed medications.
7. List the top selling herbal remedies in the U.S.
8. List specific concerns generated by the use of complementary and alternative therapies in children.
9. Develop an interview style, which includes asking about alternative and complementary therapies for all patients.

Complementary and Alternative Therapies (CAM)

The use of complementary and alternative therapies (CAM) in the U.S. has increased astronomically and subsequently has come under intense discussion. Alternative therapies have been defined as those therapies not traditionally taught in U.S. medical schools. This definition, however, is outdated as more and more medical schools include some aspect of these therapies in their curriculum.

References

1. Nelson, L. & Perrone, J., (November 2000). Pharmacologic Advances in Emergency Medicine. Herbal and Alternative Medicine. Emergency Medicine Clinics of North America. 18 (4).

The scope of CAM therapies is large. It is helpful to organize it by category.

Type of therapy	Examples
Herbal medicines	Ginseng, Green Tea, Echinacea, Kava
Dietary Supplements	DHEA, Megavitamins, Amino acids
Chiropractic	
Acupuncture	
Manual healing	Acupressure, Reiki
Magnetic therapies	
Chelation therapy	
Homeopathy	“Like can cure like” is the concept

This lecture will focus on a variety of herbal remedies and dietary supplements and the implications for patient care.

Prevalence of Herbal and Dietary Supplement Use in the United States

Why should we care about complementary and alternative therapies?

1. Americans spend **billions** of dollars a year on these therapies. Most of this is out-of-pocket expense. In 1997, it was estimated that Americans spent approximately \$5.1 billion dollars on these remedies.
2. A national telephone survey in 1997 reported that 42.1% of American used at least one form of CAM therapy in the preceding year. This is up from 34% in 1990.
3. **All medication**, whether herbal or conventional, have potential side effects and interactions with other medication.

References

1. Eisenberg DM, David RB, Ettner SL, et al: (1998). Trend in alternative medicine use in the United States, 1990-1997. JAMA 280:1569-1575
2. Eisenberg DM, Kessler RC et al: (1993). Unconventional Medicine in the United States. Prevalence, Cost, and Patterns of Use. New England Journal of Medicine 328:246-52.

Who Uses Herbal Medicines and Dietary Supplements?

- The use of these therapies is not confined to any one segment of the population. In general, studies have shown that educated, middle class white persons ages 25-49 are more likely to use alternative therapies. However, it is important to note that the use of these therapies is not limited to any one group.
- There are also many groups that are targeted by alternative practitioners and advertising for herbal and dietary supplements. Groups commonly targeted include:
 1. Cancer patients
 2. HIV infection
 3. Chronic disease
 4. Allergies
 5. Back problems
 6. Menopause
 7. Headache
 8. Obesity
- Some of these patients are at risk of being taken advantage of because they have life threatening conditions or chronic problems that are difficult to cure. For example, millions of people suffer from low back pain. For some, various treatments based on conventional medicine have given these individuals relief from their condition. The other segment of this population continues to

live with pain and frustration! It is this part of the population who are willing to try anything in search of relief and often look to alternative treatment for the answers

References

1. Astin J., (May 1998). Why Patients Use Alternative Medicine. Results of a National Study. JAMA, 275 (19). 1548-1553.

Why Do People Use Herbal and Dietary Supplements?

Is it out of dissatisfaction with conventional medicine?

- Not really. The results of a national study looked at users of alternative medicine. Generally, it was found that the use of these therapies was more consistent with a person's own philosophical worldview. They were more compatible with people's beliefs regarding what is natural and holistic.

References

1. Astin J. (May 1998). Why Patients Use Alternative Medicine. Results of a National Study. JAMA, 275 (19). 1548-1553.

How are dietary supplements and herbal remedies regulated in the U.S.?

- The Dietary Supplement and Health Education Act of 1994 (DSHEA) created a new category including vitamins, minerals, herbs, and amino acids that is nearly free of FDA regulation.
- Companies can manufacture and sell these remedies without demonstrating safety and efficacy as required by prescription medications. Claims written on bottles like "boosts immune system", "supports cardiovascular health" or "eases symptoms of menopause" are commonly made. The FDA relies on reports of adverse reactions to take action. Under DSHEA, companies are able make these types of claims provided that they do not claim effectiveness to treat a specific disease. There must also be a disclaimer that the FDA has not evaluated the product.

References

1. De Smet, P.A.G. M., (December 2002). Herbal Remedies. New England Journal of Medicine 347 (25).

Efficacy of Herbal Preparation

- The traditional use of herbal preparations is the basis of modern pharmacology. However, it is important to remember that even though a herb has been used for hundreds of years it does not mean that it is either effective or without side effects.
- The best way for us to know whether or not a preparation is effective or safe is to turn to evidence from the medical literature.

- The Office of Alternative Medicine within the National Institute of Health (NIH) is funding further investigation of herbs and supplements to examine efficacy and safety.
- The best evidence continues to be gathered from placebo controlled randomized trials.

References

1. Nelson, L. and Perrone, J., (November 2000). Pharmacologic Advances in Emergency Medicine. Herbal and Alternative Medicine. Emergency Medicine Clinics of North America. 18 (4)

Herbal Remedies with Proven Effectiveness

Herb	Indication studied	Overall Conclusion
Ginkgo	dementia	evidence that ginkgo delays deterioration of cognition
Ginkgo	intermittent claudication	longer walking distance than placebo
St. John's wort	depression-mild/moderate	better than placebo
Kava	anxiety	better than placebo
Horse chestnut	chronic venous insufficiency	decreased signs & symptoms

References

1. Ernst E., Pittler M.H. Herbal Medicine. Medical Clinics of North America. Vol86.no1. Jan 2002.
2. Linde K, Ramirez G et al. St. John's wort for depression-an overview and meta-analysis of randomized clinical trials. British Medical Journal 1996;313:253-8.
3. LeBars P, Katz M.M., et al. A placebo-controlled, Double-blind, randomized trial of an extract of Ginkgo Biloba for dementia. JAMA, october22/29, 1997. vol278. no16, pp1327-1332.
4. Pittler MH, Ernst e. Horse-chestnut seed extract for chronic venous insufficiency. Arch Dermatology. Vol134, Nov.1998:1356-1360

The caveat to this is to review safety data on these preparations.

Ginkgo

Should not be used with anticoagulants such as coumadin until we have further data. Serious bleeding has been reported with Ginkgo including 2 subdural hematomas and one case of bleeding in the anterior chamber of the eye.

References

1. The Medical Letter. Vol 40 (issue 1029) June 19, 1998.
2. Rowin J, Lewis S.L. Spontaneous bilateral subdural hematomas associated with chronic Ginkgo biloba ingestion. Neurology 1996;46:1775-1776.
3. Matthews M.K. Association of Ginkgo biloba with intracerebral hemorrhage. To the editor. Neurology 50 June 1998pp1933-1934.

St. John's wort

Multiple drug interactions have been reported. Decreased serum concentration of cyclosporine has been linked to transplant rejection. The case report cited reports heart transplant rejection linked to St. John's wort.

Drug interactions have also been reported with warfarin, HIV drugs, oral contraceptives, theophylline and amitriptyline.

The serotonin syndrome has developed in patients taking both St. John's wort and SSRI (selective serotonin reuptake inhibitor) antidepressants. Symptoms of the serotonin syndrome include mental status change, tremor, headache, restlessness, and autonomic instability.

References

1. Ruschitzka F, Meier PJ et al. Acute heart transplant rejection due to Saint John's wort. *The Lancet*. Vol 355. Feb12, 2000.pp548-549.
2. *The Medical Letter*. Vol 42(issue 1081) June 26,2000.

Kava

There have been recent case reports of severe hepatotoxicity (liver injury). The use of Kava has necessitated liver transplant. Current recommendation is that the risk of Kava outweighs the benefit.

References

1. De Smet, P.A.G.M... Herbal Remedies. *New England Journal of Medicine*, vol. 347, No. 25. December 19, 2002.

Herbal Medicines with Inconclusive Results

Herb	Indication	Overall result of pooled studies
Ginseng	Studied for several indications	Efficacy not shown beyond doubt
Ginkgo	Tinnitus (ringing in ears)	Efficacy not shown beyond doubt
Feverfew	Migraines	Efficacy not shown beyond doubt

References

1. Ernst E., Pittler M.H. Herbal Medicine. *Medical Clinics of North America*. Vol86.no1. Jan 2002.

The following herbs were shown not to be efficacious after review of multiple randomized control trials:

Evening primrose

Has been used for premenstrual syndrome (PMS). There were 11 clinical trials that examined evening primrose showing there is little value for its use in the treatment of PMS.

Garlic

Has been used to treat high cholesterol. Overall results indicate that Garlic **did** have an effect on total cholesterol but the effect was **too small** to be clinically relevant.

Guar gum

Has been marketed on the Internet for weight loss. This remedy has been shown to be ineffective in weight reduction.

References

1. Ernst E., Pittler M.H. Herbal Medicine. Medical Clinics of North America. Vol86.no1. Jan 2002.

Top Sellers

Despite lack of data for each of these herbal preparations, they continue to sell. Sales of these products initially soared. Over the past three years there has been a slow decrease in sales. It is presumed that this is because consumers are becoming more educated regarding efficacy and safety of these preparations.

Top Sellers- 2001

2001 U.S. Herbal food store, drug store, mass-market retail sales.
(Herbal Gram 2002;55:60)

Ginkgo	46 million US dollars
Echinacea	40
Garlic	35
Ginseng	31
Soy	28
Saw Palmetto	25
St. John's Wort	24
Valerian	12
Cranberry	10
Other	86
Total	\$337 MILLION US DOLLARS

References

1. Watkins RW. Herbal Therapeutics: The Top 12 Remedies. Emergency Medicine March 2002. pp12-19.

Herbs and Children

With the ever-growing popularity of CAM therapies, children are also being given herbal and dietary supplements.

Why do parents treat their children with CAM therapies?

Parents use CAM therapies with their children for a variety of possible reasons including:

1. Advice from friends and family
 2. Personal control over their child's care.
 3. The belief that herbal/dietary supplements and alternative therapies are "natural" and without side effects.
 4. Frustration with chronic childhood illnesses such as juvenile diabetes, cancer, juvenile rheumatoid arthritis, cystic fibrosis, asthma.
 5. Fear of conventional tests and procedures
- However, these remedies are not without their side effects, contaminants, and drug interactions.
 - Some herbal products given to children contain licorice. Licorice can cause high blood pressure and hypokalemia (low potassium). Severe hypokalemia can lead to cardiac dysrhythmia and death.
 - Ma Huang, which is the herb ephedra, has the active ingredient ephedrine. This stimulant is linked to myocardial infarction, dysrhythmias, stroke and even death. This drug is popular with adolescents and used by young athletes to enhance performance.

References

1. Pediatric Medicine Reports. Complementary and Alternative Medicine Use in Children. April 2001.

Case 1 - Liver Failure

You are called to the dorm room of a college freshman. The patient is a 19-year-old male who is obtunded. His roommates came home from class and found their friend confused and called 911. The roommates report that the patient has not been well and was seen at the student health center 2 days prior for vomiting, diarrhea, and abdominal pain.

He was diagnosed as an outpatient with possible food poisoning and was treated with Tylenol (acetaminophen) and Imodium AD (loperamide hydrochloride). Upon arrival to the dorm, you look around his room and find the above-mentioned medications. You also find a half-empty box of what is labeled "tea" in the patient's handwriting. You bring them all into the Emergency Department.

Past Medical History:

- No known medical problems

Medication:

- None

Family History:

- Family healthy

Social History:

- Occasional use of alcohol and marijuana

Physical Exam:

Young man unresponsive. Withdraws from painful stimuli.

T: 37C
P: 159 beats/min
RR: 30 breaths/min
BP: 130/85 mmHg

Pertinent positive finding on physical exam:

Eyes: conjunctivae icteric (yellow)

Abdomen: soft, hypoactive bowel sounds, liver palpable 1cm below right costal margin

Laboratory values:

Glucose 19

Normal value 70-115

The remainder of the laboratory data from the ER shows fulminant hepatic failure.

Initial Treatment:

What would you do if called to the home of this patient?

Treatment:

- The patient is unresponsive. As always, remember your ABC's.
- Airway control first. Ventilate the patient with your BVM.
- Place endotracheal tube or call for ALS back up if available
- The patient is hypoglycemic. Even though he has no history of diabetes, glucose is still the treatment of choice. Administer 1 AMP of D50 IV.
- Start dextrose- containing IV fluids (D5 or D10) (Re-check fingerstick glucose en route to the hospital)
- Activated charcoal down a Naso-Gastric tube after the airway is controlled with an endotracheal tube. (NEVER administer charcoal by mouth to a patient who has a depressed level of consciousness!!!)
- Monitor the patient en-route to the hospital. Watch closely for changes in vital signs and respond accordingly.

Discussion: Fulminant Hepatic Failure

The differential diagnosis is large.

Infection

- Viral hepatitis

Drugs

- Seizure medication, antibiotics, NSAIDS

Toxins/Chemicals

- Rat poison (yellow phosphorus), Methylenedioxymethamphetamine (Ecstasy), Mushroom poisoning (Amanita phalloides), herbal medicines and teas

Cardiovascular

- Portal vein thrombosis, Budd-Chiari syndrome, tumor, shock

Metabolic

- Hereditary diseases of metabolism, Reye's syndrome

Hospital Course

So what happened?

- After admission further history was obtained. The "tea" you found in his room was mushroom tea. The patient and some friends drank an unknown quantity of the tea four days prior to admission. The patient drank the dregs (sediment) and ingested the most toxins.
- Presumptive diagnosis is **mushroom toxicity** cause by the Amanita species of mushroom.
- Amanita phalloides is found in many regions of the United States: Pacific Northwest, Northeast and California. The lethal dose of the amatoxins in humans is 0.1 mg/kg of body weight. Even one mushroom can be fatal. The toxin has no taste or smell and is not destroyed by cooking. The mortality of those **treated** for this type of poisoning is **20-30%**.

Patient course:

- This patient underwent a liver transplant.

References

1. Pomerance H.H. et al. Grand Rounds. A 15 year old boy with fulminant hepatic failure. Journal of Pediatrics. vol. 137. no 1. July 2000.

Take home point:

A good history taken early in the course of a toxic ingestion can lead to early use of charcoal and gastroduodenal lavage to limit the absorption of the toxin.

Herb-Drug Interactions

EMT's must always be vigilant in looking for drug interactions. Whether the reaction is drug-drug or drug-herb interaction. Often pre-hospital personnel are often the only ones to get a complete list of medications a patient is taking. By collecting all the bottles a patient has at home and bringing them to the ER you are doing a great service to the patient. No other provider has this opportunity!

Remember to also report on any herb and/or dietary supplements a patient is taking. Patients routinely do not tell their physicians about these medications. Their reluctance may be that they are

concerned what the doctor will say or that they simply do not consider the herb/supplement a drug and therefore forget to mention it.

Either way your vigilance can help diagnose a potential drug-herb or drug-drug interaction.

Which patients are at greatest risk of a drug-herb interaction?

1. Patients with cardiac disease on anticoagulants or digoxin. As mentioned above, Ginkgo plus warfarin may increase a patient's risk of serious bleeding.
2. HIV patients on protease inhibitors. St. John's wort decreases serum levels of indinavir.
3. Those patients on cyclosporine. Patients may be on this immunosuppressant after organ transplant or may be on it with autoimmune diseases. St. John's wort can alter serum levels of the drug. This can lead to potential transplant rejection or worsening symptoms of the disease treated.

Case 2

You arrive on scene of a 65 year-old businessman complaining of weakness and black, tarry stools.

Upon arrival you find a pale, diaphoretic gentleman who states he feels generally unwell. He states he has been having black tarry stools for the past 48 hours and is now too weak to walk. He denies any pain. He states he has been short of breath with exertion but denies any other symptoms. You immediately suspect a GI-bleed as the etiology of his problem.

Past Medical History:

- Atrial fibrillation
- Transient Ischemic Attacks

Medications:

- Metoprolol
- Coumadin

Allergies:

- None known

Social History:

- Drinks occasional alcohol

Physical Exam:

Vital Signs: Heart Rate 110 and irregular
Skin: Pale: Diaphoretic
Lungs: Clear
Heart: Irregular
Abdomen: Non-tender

Extremities: No edema

Knowing coumadin reacts with many medications and dietary supplements, you ask if he has been taking any other medications including over-the-counter preparations, herbal remedies, or dietary supplements and vitamins.

He states he has always taken vitamins, but has recently started taking Gingko to help his memory. His last blood test for coumadin was 3 weeks ago. He started the Gingko two and a half weeks ago.

You bring his meds, including the Gingko with you to the hospital.

In this case, a thorough history and an accurate medication list lead to rapid diagnosis and treatment.

Quality and Safety of Herbal Remedies

As discussed, the DSHEA has largely led to a deregulated industry. Standardization is difficult and contaminants in herbal preparations have been documented. Heavy metals, pesticides and bacteria have all been found in herbal preparations.

References

1. De Smet, P.A.G.M., Herbal Remedies. New England Journal of Medicine, vol. 347, No. 25. December 19, 2002.

Take Home Points:

Remember to ask patients in a nonjudgmental way about herbal remedies and dietary supplements they may be taking. After you collect a prescription medication list is a good time to ask, "is there anything else you are taking, for example, vitamins, herbs, or dietary supplements?"

Pregnant or nursing women should not use herbal remedies. There may be unpredictable effects from adulterants or contaminants in the preparation or adverse effects from the herb itself.

The use of herbal and dietary supplements should be discouraged in children. Exploring the reasons for use may reveal needs for care of the child or family that have not been previously met by the medical community.

A straightforward nonjudgmental approach in discussing herbal remedies with patients is the best way to uncover unmet medical needs, potential toxicities, side effects, and drug interactions.

The sicker the patient, the higher the risk of drug-drug or drug-herb interaction.

If it has a therapeutic effect, it has the potential for side effect, no matter how gentle or mild it may be.