Complementary and Alternative Treatments for Hypertension

Donald Miller, Pharm.D.
Professor of Pharmacy Practice
North Dakota State University

Disclosure

- I have no financial or other conflicts of interest for this presentation.
- I will be discussing (many!) unlabeled and non-FDA approved uses of products during this presentation.

Learning Objectives

- Describe and classify Complementary and Alternative Methods (CAM) based on common features.
- Evaluate the efficacy of several forms of CAM in reducing blood pressure.
- Describe how to best incorporate CAM into a busy practice.

Case Study

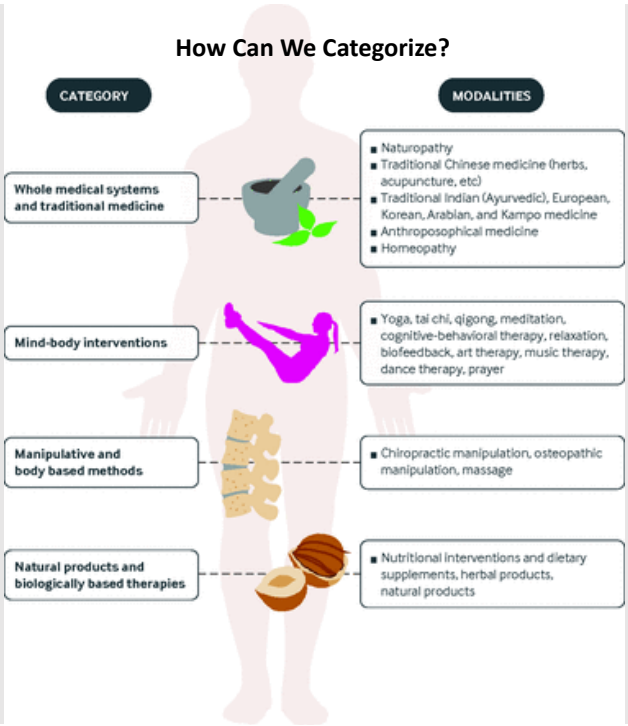
- You see a 47 yo female with a one-year history of hypertension, and a blood pressure today of 142/88. She also has hyperlipidemia (total cholesterol 209, LDL 134, HDL 140 and TG 137). Her medication list consists of hydrochlorothiazide 25 mg daily and rosuvastatin 10 mg daily.
- However, when you ask about compliance the patient admits she has not taken her meds recently, as she prefers a more natural approach to health. She says she does take a multivitamin, an aged garlic supplement and turmeric daily. She also eats “healthy” with a vegetable heavy diet and has begun practicing tai chi and seeing a homeopath.
- How would you approach this patient? Are you OK with non-drug treatments and if so, are her current supplements and lifestyle likely to help her blood pressure?

What is Complementary and Alternative Medicine?

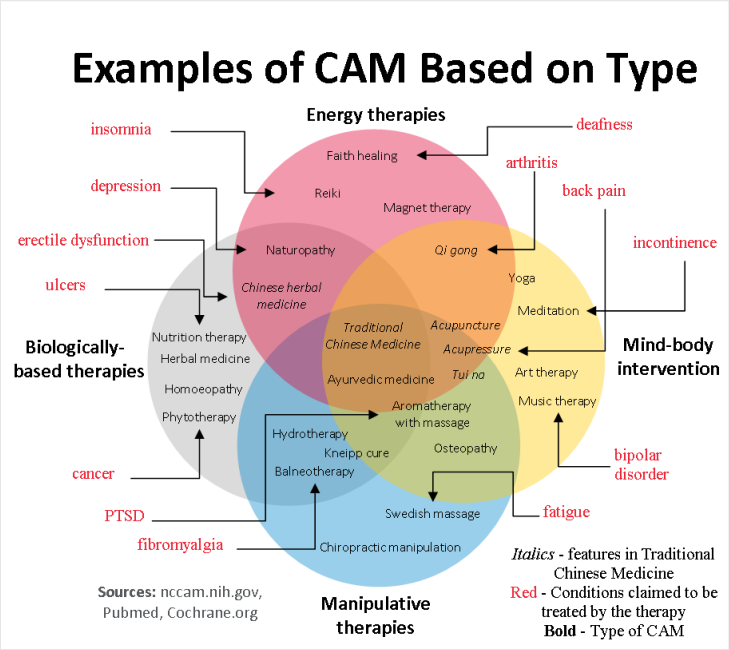
- Any of various systems of healing or treating disease (such as homeopathy, chiropractic, naturopathy, traditional Chinese medicine, Ayurveda, or faith healing) that are *not included in the traditional curricula* taught in medical schools of the United States, Canada and Britain.
- Generally includes specific treatments with poor scientific basis or proof of efficacy (e.g. many dietary supplements).

Definitions (somewhat arbitrary since boundaries are fluid)

- **Complementary** – an option not in competition or conflict with mainstream medicine, but which adds to it and is generally meant to be used with it.
- **Alternative** – an option typically meant to be instead of, not used with, mainstream medicine. True adherents see a dualistic contrast between organized medicine and their alternative approach to care.
- **Integrative Medicine** – attempts at integrating different forms of treatment. Many, but not all, see it as *selectively* integrating evidence-based CAM options with traditional approaches. May integrate individual treatments or different *dimensions* of care (biological, psychological, sociological, and spiritual).
- **Holistic Medicine** – an approach that incorporates comprehensive management of a person (not one disease at a time), including body, mind, and spirit – in the quest for optimal health and wellness. Many persons crave such an approach and it is a big reason for CAM popularity.



BMJ 2017; 357 :j1284



https://themedschoolproject.wordpress.com/2012/08/24/epq-project-introduction-to-complementary-and-alternative-medicine/

History of CAM

- CAM has always existed. Many forms of health practitioners have co-existed throughout history. And all forms are fluid as they continue to evolve and exchange ideas.
- While its popularity was already increasing, major turning points in modern acceptance of CAM occurred with passage of the Dietary Supplement Health and Education Act of 1994 and legislation establishing the National Institute for Complementary and Integrative Health (originally NCCAM) in 1998.

Who Uses CAM?

- Well educated persons are the heaviest users.[1,2] Well-educated persons have the income to pay out-of-pocket for the many therapies not covered by health insurance.
- CAM users overall are more likely to be in poor health,[1] and people with multiple chronic conditions are more likely to be users.[3]
- However, compared to nonusers, *dietary supplement users* are more likely to report very good to excellent health, have health insurance, be nonsmokers, exercise frequently, and use alcohol moderately.[2]
- The majority of users add CAM to conventional medicine rather than use as complete alternatives.[1,4] They regard CAM as more congruent with their own values and orientation toward health, and allowing greater control over one's health care.[1]
- CAM often is bad science but good medicine!

1. Why patients use alternative medicine. JAMA 1998;279:1548-53
2. Why US adults use dietary supplements. JAMA Intern Med 2013;173:355-61
3. Multiple chronic conditions and use of CAM among adults. Preventing Chronic Disease 2016;13:150501
4. Association between use of unconventional therapies and conventional medical services. JAMA 1999;282:651-6

Mind-Body Therapies for Hypertension

- Lifestyle modification is a cornerstone of hypertension treatment, yet most recommendations currently focus on diet and exercise and do not consider stress reduction strategies.
- Mind-body therapies may reduce blood pressure through reducing stress, increasing parasympathetic activation, and altering baroreceptor sensitivity.
- Include meditation, yoga, tai chi, qigong, and spiritual approaches.

Meditation

- Many types but with the same end in mind – focused attention aimed at relaxing and clearing the mind.
- Mindfulness is a currently popular type of meditation.
- A meta-analysis of nine randomized controlled, clinical trials was conducted regarding transcendental meditation and blood pressure, and it found an average reduction of systolic and diastolic pressure of 4.7 and 3.2 mm Hg respectively.
- Benefit was fairly consistent across patient subgroups and low versus high quality studies.

Anderson JW, Liu C, Kryscio RJ. Blood Pressure Response to Transcendental Meditation: A Meta-analysis. *American Journal of Hypertension 2008;*21: 310–316)

Yoga

- Tyagi and Cohen performed a 2014 systematic review of yoga, finding 39 cohort studies, 30 nonrandomized, controlled trials, 48 randomized, controlled trials, and 3 case reports with durations ranging from 1 week to 4 years and involving a total of 6693 subjects. Most studies reported that yoga effectively reduced BP in both normotensive and hypertensive populations. These studies suggest that yoga is an effective adjunct therapy for hypertension, yet the great heterogeneity of yoga practices and the variable quality of the research makes it difficult to recommend any specific yoga practice for HPT.

Tyagi A, Cohen M. Yoga and hypertension: a systematic review. *Altern Ther Health Med*. 2014;20(2):32–59.

Yoga

- A more recent meta-analysis has shown that yoga, incorporating breathing techniques and meditation/mental relaxation at least 3 times/week, is effective in reducing blood pressure in the order of 11/6 mmHg (Mayo Clin Proc 2019;94(3):432-46).
- However up to 20% of regular yoga practitioners reported at least one injury at some point (usually minor). Strains, repetitive use injuries, and spinal problems may occur. The riskiest poses include headstand and lotus positions (Mayo Clin Proc 2019;94(3):385-7).

Qigong

- **Qigong** (pronounced CHEE-gung and literally: "Life Energy Cultivation") is a holistic system of coordinated body posture and movement, breathing, and meditation used for health, spirituality, and martial arts training. Based on Chinese medicine, philosophy, and martial arts, qigong is viewed as a practice to cultivate and balance qi (chi).
- Qigong is a lifestyle and harnesses energy from special movements, breath methods and uses specific foods to reverse specific diseases. It is likened to a Chinese version of Yoga.
- According to Taoist, Buddhist, and Confucian philosophy, qigong allows access to higher realms of awareness, awakens one's "true nature", and helps develop human potential.
- Qigong practice typically involves moving meditation, coordinating slow flowing movement, deep rhythmic breathing, and calm meditative state of mind, thus very appropriate for older persons. https://en.wikipedia.org/wiki/Qigong
- Similarities to Tai Chi

Qigong

- Two systematic reviews have been published. Poor quality studies, at high risk for bias, in general.
  - Guo et al. 2008 9 RCTs, n = 908
    - Significant lowering of SBP and DBP (17/10 mm Hg) compared with no intervention controls but no difference versus persons receiving pharmacologic treatment or exercise as controls.
  - Xiong et al. 2015 20 RCTs, n = 2,349
    - Significant lowering of SBP and DBP (17.4/10.2 mm Hg) versus no intervention
    - In 2 trials exercise was superior to qigong for SBP lowering but not DBP
    - Qigong Less effective than antihypertensive drugs
    - Added to drug therapy, qigong lowered pressure by an additional 12/5.3 mm Hg
    - Almost no reporting of adverse events

Guo X, Zhou B, Nishimura T, Teramukai S, Fukushima M. Clinical effect of qigong practice on essential hypertension: a meta-analysis of randomized controlled trials. *J Altern Complement Med*. 2008;14(1):27–37. doi:10.1089/acm.2007.7213

Xiong X, Wang P, Li X, Zhang Y. Qigong for hypertension: a systematic review. *Medicine (Baltimore)*. 2015;94(1):e352. doi:10.1097/MD.0000000000000352

Spiritual Approaches - Religious Membership and Attendance

- A longitudinal study of 144 nuns matched to 138 lay women followed them for all 30 years. Lay women had a substantial increase in systolic and diastolic BP, versus no change among the nuns (Blood Press 1997;6:81-7).
- Numerous studies have found a correlation between religious service attendance and lower mortality. Most of this can be explained by attendees following better health habits and having greater social capital. Social capital also creates more happiness and better health. Prayer may calm in the same way as meditation, etc.
- Overall these findings support a holistic approach to health.

Chiropractic

- One published RCT with sham control. Fifty patients with stage 1 hypertension *and evidence of Atlas misalignment* randomized to control or chiropractic intervention to correct cervical spine alignment at the Atlas (C1) vertebra that allegedly may cause brainstem ischemia and compromise brainstem neural pathways. (Bakris G et al. J Hum Hypertens 2007;21:347-52 https://chiro.org/research/ABSTRACTS/Atlas_Vertebra_Realignment.shtml)
- At 8 weeks after baseline, systolic BP was reduced by a mean of 17 mmHg and diastolic by 10 mmHg in the intervention group versus 3 and 2 in the sham control group.
- In 2016, however, a duplication of the study, done at the Palmer College of Chiropractic, concluded that upper cervical manipulation did not lower systolic or diastolic blood pressure. The study was largely ignored by subluxation-based chiropractors who continue to quote the findings of the 2007 study to support use of upper cervical manipulation as a treatment for high blood pressure and a variety of other health problems. (https://sciencebasedmedicine.org/upper-cervical-chiropractic-nucca–the-legacy-of-hio/)
- Problems with the original study may have included a single chiropractor doing all interventions and possibly all the BP measurements as well!

Osteopathic Manipulation

- Osteopathy is a type of medicine that emphasizes physical manipulation of muscle tissue and bones.
- "Osteopathic manipulative treatment (OMT) is the process through which osteopaths treat somatic dysfunctions. OMT is characterized by different techniques, i.e. myofascial release, craniosacral therapy, High Velocity Low Amplitude (HVLA) manipulation, Balanced Ligamentous Tension (BLT), Muscle Energy Technique, biodynamic, strain-counterstrain, etc. This wide range of techniques permits the operator to choose the more appropriate to apply on a patient in a given moment. During scientific studies, OMT can be used as an approach, as was done in this study, or as an isolated technique".

Osteopathy

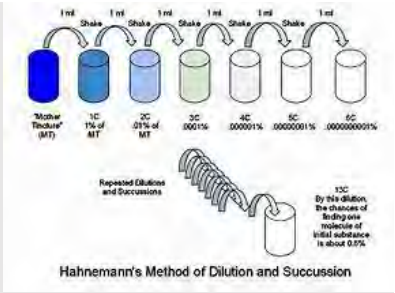
- A non-blinded, non-randomized trial conducted in Italy included consecutive subjects affected by hypertension and vascular alterations, using pre-post differences in intima-media thickness, systolic and diastolic blood pressure as the primary endpoints. A total of 31 out of 63 eligible subjects followed by a single cardiologist were assigned non-randomly to receive osteopathic treatment in addition to routine care (which included drug therapy); the other 32 received routine care only. Clinical measurements were recorded at baseline and after 12 months.
- Osteopathic treatment was significantly associated to an improvement in all primary endpoints. Multivariate linear regression showed that, after adjusting for all potential confounders, osteopathic treatment performed significantly better for intima-media thickness (pre-post differences in treated and control groups: 0.52; 95% CI: 0.68, 0.35) and systolic blood pressure (4.5 mm Hg; CI 6.3, 2.7), but not for diastolic blood pressure after one year of biweekly treatments.
- Authors claim that the manipulation techniques have anti-inflammatory effects.

Cerritelli F, et al. Osteopathic manipulation as a complementary treatment for the prevention of cardiac complications: 12-Months follow-up of intima media and blood pressure on a cohort affected by hypertension. Journal of Bodywork and Movement Therapies 2011;15:68-74

Homeopathy Case

- The patient in our initial case scenario was seeing a homeopath.
- How would you define homeopathy?
- What toxicities would you be concerned about?
- How likely is it that homeopathic medicines would work to reduce blood pressure?

Homeopathy



Hahnemann's Method of Dilution and Succussion

- Homeopathy is based on the principle that substances that are poisonous in large doses can be very beneficial in small doses.
- Homeopathy uses animal, vegetable and mineral preparations to cure a person's illness. For hypertension, belladonna and nux vomica are often listed.
- Dilutions of substance are done in distilled water or alcohol and vigorously shaken. Products with suspended solids are filtered in specific ways. Insoluble substances are pulverized and diluted with lactose. One part of the dilution is again diluted and **shaken** and the process repeated until the desired final dilution is achieved.
- Serial dilutions of 1:10 are designated by the Roman numeral X, so 1X=1/10, 2X=1/100 and 6X=1/1,000,000 etc.
- Serial dilutions of 100-fold are designated with C, so 1C=1/100, 2C=1/10,000 etc.

Homeopathy

Controlled Randomized Double-Blind Study for the Comparison of the Treatment of Patients With Essential Hypertension With Homeopathic and With Pharmacologically Effective Drugs

- In a randomized double-blind cross-over study the effects of antihypertensive pharmacotherapy were compared with those of homeopathic treatment in 10 patients with essential hypertension. The conclusions are: 1. The blood pressure lowering effect under pharmacotherapy is clearly superior to that under homeotherapy, where it was negligible and statistically not significant. 2. As far as improvement of subjective complaints of the patients is concerned there was no superiority of pharmacotherapy over homeopathic treatment. 3. The cross-over design appears less suitable than, perhaps, a design with parallel treatment groups because of the long duration of such a study and the observed carry-over effect.

Hitzenberger G, et al. Kontrollierte randomisierte doppelblinde Studie zum Vergleich einer Behandlung von Patienten mit essentieller Hypertonie mit homöopathischen und pharmakologisch wirksamen Medikamenten [Controlled randomized double-blind study for the comparison of the treatment of patients with essential hypertension with homeopathic and with pharmacologically effective drugs]. *Wien Klin Wochenschr*. 1982;94(24):665–670

Acupuncture

- **Cochrane Review: Yang J et al. Cochrane Database Syst Rev 2018;11(11):CD008821**
- **Main results:** Twenty-two RCTs (1744 people) met our inclusion criteria. The RCTs were of variable methodological quality (most at high risk of bias because of lack of blinding). There was no evidence for a sustained BP lowering effect of acupuncture; only one trial investigated a sustained effect and found no BP lowering effect at three and six months after acupuncture. Four sham acupuncture controlled trials provided very low quality evidence that acupuncture had a short-term (one to 24 hours) effect on SBP (change) -3.4 mmHg (-6.0 to -0.9) and DBP -1.9 mmHg (95% CI -3.6 to -0.3). Pooled analysis of eight trials comparing acupuncture with angiotensin-converting enzyme inhibitors and seven trials comparing acupuncture to calcium antagonists suggested that acupuncture lowered short-term BP better than the antihypertensive drugs. However, because of the very high risk of bias in these trials, we think that this is most likely a reflection of bias and not a true effect. Safety of acupuncture could not be assessed as only eight trials reported adverse events.
- **Authors' conclusions:** At present, there is no evidence for the sustained BP lowering effect of acupuncture that is required for the management of chronically elevated BP. The short-term effects of acupuncture are uncertain due to the very low quality of evidence. The larger effect shown in non-sham acupuncture controlled trials most likely reflects bias and is not a true effect. Future RCTs must use sham acupuncture controls and assess whether there is a BP lowering effect of acupuncture that lasts at least seven days.

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008821.pub2/full

Foods and Dietary Supplements

- **What dietary supplements do your patients use for hypertension or other diseases?**
- Dietary supplements are regulated as food products (the Dietary Supplement Health and Education Act of 1994) – so the FDA Center for Food Safety and Applied Nutrition has oversight. Thus, supplements are NOT approved for sale and marketing by FDA and impurities or contamination are more likely than with drugs. Manufacturers have the responsibility for product composition and FDA has oversight only when:
  - A claim is made that is false and misleading (i.e. a drug claim)
  - The product is unsafe (FDA has burden of proof)
  - The product fails to comply with regular FDA food regulations, such as being contaminated or misbranded
- Claims about maintenance of structure and function (helps create strong bones, helps support a strong immune system) are allowed but not disease claims.

Health Claims for Foods

- A health claim as defined by the FDA must contain a substance and a disease or health related condition.
- Authorized vs Qualified
- Qualified health claims (QHCs) are supported by scientific evidence, but do not meet the more rigorous “significant scientific agreement” standard required for an authorized health claim (AHCs).
- QHCs must be accompanied by a disclaimer regarding the level of scientific evidence supporting the claim as given by the FDA in a Letter of Enforcement Discretion.
- Manufacturers can petition the FDA in order to make a health claim. The FDA looks at the submitted evidence and posts the petition for a comment period. The FDA then looks at any additional information and passes judgement.

Omega-3-fatty acids (fish oil)

FDA Announcement June 2019 https://www.fda.gov/food/cfsan-constituent-updates/fda-announces-new-qualified-health-claims-epa-and-dha-omega-3-consumption-and-risk-hypertension-and

- Response to a health claim petition submitted by The Global Organization for EPA and DHA Omega-3s in a letter of enforcement discretion.
- "The FDA determined that the overall evidence did not meet the "significant scientific agreement" standard required for an authorized health claim but did meet the "credible evidence" standard for a qualified health claim in the labeling of conventional foods and dietary supplements".
- "There is some credible evidence suggesting that combined intake of EPA and DHA from conventional foods and dietary supplements may reduce the risk of hypertension by lowering blood pressure; this evidence is inconclusive and highly inconsistent."

Omega-3-Fatty acids (fish oil)

Qualified supplements/foods must contain at least 0.8g per serving but supply no more than 5g per day (average American intake is 77mg/day). Acceptable labeling claims for foods or supplements are:

1. Consuming EPA and DHA combined may help lower blood pressure in the general population and reduce the risk of hypertension. However, FDA has concluded that the evidence is inconsistent and inconclusive. One serving of [name of the food or dietary supplement] provides [ ] gram(s) of EPA and DHA.
2. Consuming EPA and DHA combined may reduce blood pressure and reduce the risk of hypertension, a risk factor for CHD (coronary heart disease). However, FDA has concluded that the evidence is inconsistent and inconclusive. One serving of [name of the food or dietary supplement] provides [ ] gram(s) of EPA and DHA.
3. Consuming EPA and DHA combined may reduce the risk of CHD (coronary heart disease) by lowering blood pressure. However, FDA has concluded that the evidence is inconsistent and inconclusive. One serving of [name of the food or dietary supplement] provides [ ] gram(s) of EPA and DHA.
4. Consuming EPA and DHA combined may reduce the risk of CHD (coronary heart disease) by reducing the risk of hypertension. However, FDA has concluded that the evidence is inconsistent and inconclusive. One serving of [name of the food or dietary supplement] provides [ ] gram(s) of EPA and DHA.
5. Research shows that consuming EPA and DHA combined may be beneficial for moderating blood pressure, a risk factor for CHD (coronary heart disease). However, FDA has concluded that the evidence is inconsistent and inconclusive. One serving of [name of the food or dietary supplement] provides [ ] gram(s) of EPA and DHA.

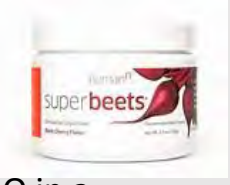
Aged Garlic

- Garlic (*allium sativum*) is referenced for medicinal uses as early as 2600-2100 BC in Samaria and was used in ancient China, Egypt, and Greece.
- Many studies have documented mild properties in lowering cholesterol and blood pressure.
- Allicin, an organosulfur compound, is the chemical component that provides aroma but it is unstable. *S*-allylcysteine (SAC) is the major breakdown chemical that appears to have vasodilating properties. Still, potency of garlic is likely related to allicin content. The allicin content of any garlic product can vary at least 3-fold depending the garlic used.
- Blood pressure lowering effect is thought to be caused by stimulation of intracellular NO and hydrogen sulfide production, and blockage of angiotensin II production, promoting vasodilation
- ConsumerLab has found quality (purity, non-contamination, disintegration) issues with 40% of tested products, as well a huge variation in total allicin content

Aged Garlic

- The dosage form and amount taken in a day has an impact.
- Supplements are required to list amounts of key ingredients. Garlic supplements should contain at least 2400 mcg of total allicin (actual plus potential allicin) per day, or 700 mcg of SAC for aged garlic powder.
- Well tolerated – potential body odor and bad breath, gastrointestinal upset. Increased bleeding time is possible, but has been used safely with warfarin.
- A review article:
  - Though many studies are of poor quality, garlic supplementation reduced blood pressure by 7–16 mm Hg (systolic) and 5–9 mm Hg (diastolic) compared with placebo (4 meta-analyses and 2 original studies). It reduced total cholesterol by 7.4–29.8 mg/dl (8 meta-analyses).
  - The most consistent benefits were shown in studies using aged garlic extract.
  - Varshney R, Budoff MJ. Garlic and Heart Disease. *The Journal of Nutrition*, 2016;146(2):416S–421S. https://doi.org/10.3945/jn.114.202333

Beets/Beetroot Juice and Bread



- Inorganic nitrate supplementation is hypothesized to generate NO in a meaningful amount. (However some studies found better effect in lower content juice!)
  - Bioavailability data from studies is conflicting
  - Small sample sizes, short duration, and heterogeneity of studies don't lend well to pooling
  - No serious side effects. Can cause red urine and red stools
- Three systematic reviews have been done
  - Siervo et al. 2013 16 RCTs, n= 254
    - Inorganic nitrate and beetroot juice consumption were associated with greater changes in systolic BP [-4.4 mm Hg (95% CI: -5.9, -2.8); P < 0.001] than diastolic BP [-1.1 mm Hg (95% CI: -2.2, 0.1); P = 0.06]. A meta-regression showed an association between daily dose of inorganic nitrate and changes in systolic BP (P < 0.05).

Siervo M, Lara J, Ogbonmwan I, Mathers JC. Inorganic nitrate and beetroot juice supplementation reduces blood pressure in adults: a systematic review and meta-analysis. *J Nutr*. 2013;143(6):818–826. doi:10.3945/jn.112.170233

Beets/Beetroot Juice and Bread

- Bahadoran et al. 2017 22 RCTs, interventions n= 650, controls n= 598
  - Overall, mean SBP (−3.55 mm Hg) and DBP (−1.32 mm Hg) were significantly lower in the beetroot juice–supplemented groups than in the control groups. The mean difference of SBP was larger between beetroot juice–supplemented and control groups in the longer than in the shorter (≥14 compared with <14 d) study durations and the highest compared with the lowest doses of beetroot juice.
- Ashor et al. 2017 13 RCTs, n= 325
  - BP lowering seen in resting clinical settings (4.1/2.0 mmHg) over 1 to 6 weeks not corroborated by 24-h ambulatory or daily home monitoring in 3 of the studies

Bahadoran Z, Mirmiran P, Kabir A, Azizi F, Ghasemi A. The Nitrate-Independent Blood Pressure-Lowering Effect of Beetroot Juice: A Systematic Review and Meta-Analysis [published correction appears in Adv Nutr. 2018 May 1;9(3):274]. *Adv Nutr*. 2017;8(6):830–838.

Ashor AW, Lara J, Siervo M. Medium-term effects of dietary nitrate supplementation on systolic and diastolic blood pressure in adults: a systematic review and meta-analysis. *J Hypertens*. 2017;35(7):1353–1359.

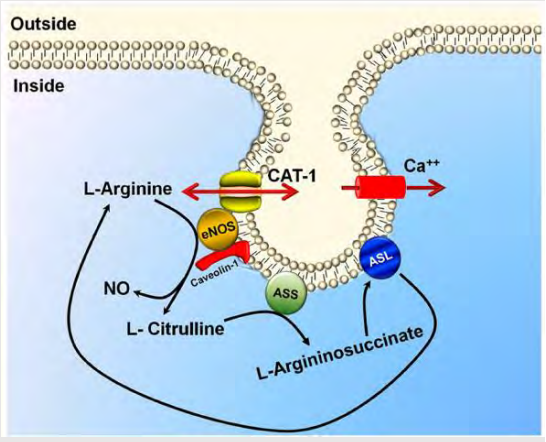
L-arginine

- A substrate utilized by endothelial nitric oxide synthase (eNOS) to produce NO
  - Supplementation hypothesized to increase NO production
- Dong et al. 2011 11 RCTs n=387, all blinded RCTs
  - Meta-analysis found significant lowering of SBP (5.4 mmHg) and DBP (2.7 mmHg) in mostly normotensive subjects
  - No statistically significant association between dose (4-24g/day), duration of supplementation (2-24 weeks), or baseline BP and change in SBP or DBP was found
  - ADRs: occasional abdominal cramps, bloating, headache
  - Authors call for more robust long term trials and caution when interpreting their results due to sample size, quality of studies, and mostly short duration

Dong J.Y., Qin L.Q., Zhang Z., Zhao Y., Wang J., Arigoni F., Zhang W. Effect of oral L-arginine supplementation on blood pressure: A meta-analysis of randomized, double-blind, placebo-controlled trials. Am. Heart J. 2011;162:959–965. doi: 10.1016/j.ahj.2011.09.012

L-Citrulline (watermelon)

- A similar amino acid (but better oral absorption) and possible supplement to increase NO production
- Khalaf et al 2019 meta-analysis reviewed L–arginine and L-citrulline
  - Variability in study results but BP lowering seems similar to L-arginine
- More studies need to be done to determine if there is benefit



- Khalaf D, Krüger M, Wehland M, Infanger M, Grimm D. The Effects of Oral l-Arginine and l-Citrulline Supplementation on Blood Pressure. *Nutrients*. 2019;11(7):1679. doi:10.3390/nu11071679

Vitamin C

- Vitamin C works as an antioxidant and enzyme modulator to possibly increase NO production, may also affect prostacyclin production.
- Systematic reviews
  - McRae 2006 14 RCTs, n= 284
    - 2 of 14 reported statistically significant difference in DBP
    - 7 of 14 reported statistically difference in SBP
    - Overall mean change 3.9/2.1 mmHg
  - Juracheck et al. 2012 29 RCTs, n= 1407
    - Mean dose 500 mg/day over 8 weeks, change in BP 3.8/1.5 mmHg
  - Small sample sizes and heterogeneity of studies don't lend well to pooling.

McRae MP. Is vitamin C an effective antihypertensive supplement? A review and analysis of the literature. *J Chiropr Med*. 2006;5(2):60–64. doi:10.1016/S0899-3467(07)60134-7

Juraschek SP, Guallar E, Appel LJ, Miller ER 3rd. Effects of vitamin C supplementation on blood pressure: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*. 2012;95(5):1079–1088. doi:10.3945/ajcn.111.027995

Coenzyme Q10 (CoQ10)

- May work is an antioxidant acting directly on vascular endothelium for vasodilation, or by reducing super oxide synthesis. Often claimed that supplements improve CV health due to age-related CoQ10 deficiency.
- Rosenfeldt et al. 2007 12 studies n=362, mostly open-label
  - Doses of 34 mg to 225 mg/day
  - Significantly lowers both SBP (up to 17 mmHg) and DBP (up to 10 mmHg), with one crossover study showing an 11/8 change versus placebo.
- Studies had poor methodological qualities (nonblinded, prior meds stopped, etc.) making them very susceptible to bias
- ADRs: nausea, vomiting, heartburn

Rosenfeldt FL et al. Coenzyme Q10 in the treatment of hypertension: A meta-analysis of the clinical trials. J Hum Hypertens 2007;21:297-306

Chinese Herbal – Corn Silk

- Corn silk is a waste material from corn cultivation and a traditional Chinese medicinal plant. It apparently induces diuresis. In Chinese theory, it excretes dampness and alleviates internal stagnation of fluid.
- A review article/meta-analysis found 5 RCTs in the Chinese literature, involving 567 patients, all of low quality, lasting from 1 to 12 weeks.
- No adverse events were reported.
- In all studies corn silk was added to standard therapies. The meta-analysis only reported results as a relative risk ratio for successful BP lowering (RR=1.27, $p<0.0001$)

Shi S, et al. Corn silk tea for hypertension: A systematic review and meta-analysis of randomized Controlled trials. Evidence based Complementary Alternative Medicine 2019;article ID 2915498 https://doi.org/10.1155/2019/2915498

Chinese Herbal Medicine Use

- Chinese patients base personal decisions about using herbal medicines on family traditions, professional and quasi-professional recommendations, and self-medication.
- Quasi-professional recommendations emerge from the traditional herb store, which has been a fixture in China for millennia and is part of any community with a substantial Chinese population. These recommendations are typically based on a blend of oral tradition, family practice, and quasi-professional endeavor. The level of expertise from the stores ranges widely.

West J Med 2002;176:275-9

Safety of Chinese Herbs

- There have been many reports of products being mislabeled, or contaminated with drugs, toxins, or heavy metals, especially those that are imported from outside North America. Drug contamination can include inclusion of corticosteroids or NSAIDs in Chinese arthritis remedies, codeine in cough syrup, etc. (West J Med 2002;176:275-9 and https://www.cbc.ca/news/canada/calgary/drugs-seized-sunrise-lee-chinese-herbs-calgary-1.5128576)
- Herbal extracts can be toxic if containing sufficient levels of active ingredients. They may interact with other drugs. (BMJ 1999;319:1050-3).
- Some of the herbs used in Chinese medicine can interact with drugs, can have serious side effects, or may be unsafe for people with certain medical conditions. For example, the Chinese herb ephedra (ma huang) was linked to serious health complications, including heart attack and stroke. In 2004, the FDA banned the sale of ephedra-containing dietary supplements, but the ban does not apply to TCM remedies.

Approaching Asian Patients About Herbals

- Determining whether or not your patient is using Chinese herbal medicines requires sensitivity. Patients may be disinclined to provide this information even when asked directly. Making an open-ended inquiry couched in supportive terms is helpful. You may preface your inquiry with an encouraging generalization, such as: “I understand that in China there are many herbs that can be used to treat diseases. Some of them can be very helpful. Are there any herbs that you like to use? Are you taking any herbs or other medicines now?”
- Information on contents may be obtained from the prescribing herbalist, as patients may not know what the contents are.

Case Study

- You see a 47 yo female with a one-year history of hypertension, and a blood pressure today of 142/88. She also has hyperlipidemia (total cholesterol 209, LDL 134, HDL 140 and TG 137). Her medication list consists of hydrochlorothiazide 25 mg daily and rosuvastatin 10 mg daily.
- However, when you ask about compliance the patient admits she has not taken her meds recently, as she prefers a more natural approach to health. She says she does take a multivitamin, an aged garlic supplement and turmeric daily. She also eats "healthy" with a vegetable heavy diet and has begun practicing tai chi and seeing a homeopath.
- How would you approach this patient? Are you more comfortable with her current supplements and lifestyle? How will you now engage her and monitor?

Conclusions and Recommendations for Practice

- While a number of different complementary and alternative therapies have been investigated for hypertension, quality of evidence is poor. Positive studies may be poorly reproducible and also subject to publication bias.
- Based on available evidence, mind-body therapies such as meditation and yoga are reasonable adjuncts to medical therapy for hypertension.
  - When discussing lifestyle issues with patients you may want to encourage any mind-body approach, helping to individualize lifestyle options.

Conclusions and Recommendations for Practice

- A few supplements – fish oil, aged garlic, beetroot juice, and L-arginine, may also be helpful, but patients may need to use good quality products in appropriate doses. It is impossible to know which supplements are good quality without access to a good resource (most expensive not necessarily the best!). Effects mostly moderate in size, comparable with diet changes and exercise implementation.
- Poor evidence for acupuncture and chiropractic, osteopathic and homeopathic interventions.
- Herbals from China (or India) can be contaminated with impurities and very difficult to obtain good information on.
- Overall, for patients who inquire about CAM for hypertension, encourage discussion. You may point patients toward mind-body treatments and certain supplements as safe and modestly effective *adjuncts* to medical therapy.

Good Information Sources

- ConsumerLab.com
  - https://www.consumerlab.com/index.asp
  - Strong database of reviews on vitamins, herbs and other supplements, includes an Alternative Therapies index with reviews on CAM, and also tests products for quality - need a subscription to access information.
- National Center for Complementary and Integrative Health
  - https://nccih.nih.gov/
  - Database with evidence based recommendations
  - Produces a new app for mobile devices called **HerbList** with science-based summaries on over 50 popular herbs. https://nccih.nih.gov/Health/HerbListApp?nav=govd
- Examine.com
  - https://examine.com/
  - Database of evidence based recommendations on nutrition and supplements. Gives grades of the evidence available. Need subscription to access most information, but a lot of good stuff for free.
- Science-based Medicine
  - https://sciencebasedmedicine.org/about-science-based-medicine/
  - Evidence based, skeptical approach

Additional Reviews

- Wong AP, et al. Beyond conventional therapies: Complementary and alternative medicine in the management of hypertension: An evidence-based review. Pak. J. Pharm. Sci. 2018;31(1):237-244
- Chrysant SG, Chrysant GS. Herbs Used for the Treatment of Hypertension and their Mechanism of Action. Current Hypertension Reports 2017;19:77 https://doi.org/10.1007/s11906-017-0775-5
- Levenberg K et al. Nutraceuticals with Blood Pressure Lowering Potential: A Summary of Clinically Relevant Information. Journal of Hypertension and Management 2019;5:038 https://doi.org/10.23937/2474-3690/1510038