



CHOOSING WISELY XXIV

Recommendations from the American College of Occupational and Environmental Medicine, American College of Medical Toxicology, American Academy of Clinical Toxicology, American College of Medical Genetics and Genomics

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This is my 24th article on Choosing Wisely from the Board of Internal Medicine Foundation. As previously noted, each specialty group is developing “Five, Ten, or Fifteen Things that Physicians and Patients Should Know.”

I. RECOMMENDATIONS FROM THE AMERICAN COLLEGE OF OCCUPATIONAL AND ENVIRONMENTAL MEDICINE

1. Opioids should not be used for the treatment of acute or chronic pain for workers who perform safety-sensitive jobs such as operating motor vehicles, forklifts, cranes or other heavy equipment. Even weak opioids have been consistently associated with increased risk of motor vehicle crashes caused by sedation and/or impaired cognitive function.

2. Injured workers with acute non-specific low back pain should not have X-rays ordered initially. For work-related injuries, they are unnecessary initially unless red flags are present, and there is no medical or legal reason to obtain them as a “baseline.”

3. Low back X-rays should not be part of a routine preplacement medical examination. These examinations are conducted to determine the individual’s ability to perform a job’s essential functions. These X-rays are costly, result in unnecessary radiation exposure, and neither address the worker’s abilities nor predict future injuries.¹

4. X-rays for the diagnosis of plantar fasciitis/heel pain in employees who stand or walk at work should not be routinely ordered. In most cases, the diagnosis of plantar fasciitis is evident from the worker’s history and physical examination. Unless underlying medical conditions such as fracture or infection are suspected, routine evaluations with X-ray are not recommended.

5. Workers suffering from chronic fatigue/insomnia should not routinely have sleep studies (polysomnogram) to screen for sleep disorders. Those who suffer from fatigue, but do not have other sleep apnea symptoms (e.g., waking with a very sore or dry

throat, loud snoring) or risk factors (obesity, increased neck diameter, fullness of soft tissues in the oropharynx, etc.), may not need a sleep study. A sleep study is not usually necessary for assessing insomnia, although it may be an essential tool in diagnosing many sleep disorders. If lack of sufficient sleep or the job schedule is affecting the patient’s sleep patterns, behavioral modification and attempts to modify the sleep schedule and improve sleep hygiene should be attempted first.

II. RECOMMENDATIONS FROM THE AMERICAN COLLEGE OF MEDICAL TOXICOLOGY AND THE AMERICAN ACADEMY OF CLINICAL TOXICOLOGY

1. Homeopathic medications, non-vitamin dietary supplements, or herbal supplements should not be used as treatments for disease or preventive health measures. Alternative therapies are often assumed to be safe and effective, just because they are “natural,” but many herbal and dietary supplements lack stringent quality control of their ingredients. There is little science-based evidence that these products are effective, and substantial evidence that they may produce harm, especially when they delay or replace more effective forms of treatment. They also can compromise the efficacy of conventional medicines, and cause significant drug interactions.

2. A chelating agent should not be administered prior to testing urine for metals. This maneuver is called “provoked” urine testing. Evidence-based studies show that chelating agents lead to increased excretion of various metals into the urine, even in healthy individuals without metal-related disease.

3. Heavy metal screening tests to assess non-specific symptoms should not be ordered in the absence of exposure to metals. Diagnosis of any metal poisoning requires an appropriate exposure history, and clinical findings consistent with poisoning by that specific metal. Specific metal testing should be ordered only if there is concern for a specific poisoning, based on the history and physical examination.

4. Chelation should not be recommended except for documented medical intoxication, which has been diagnosed, using validated tests and appropriate biological samples. Chelation does not improve objective outcomes in autism, cardiovascular disease, or neurodegenerative conditions like Alzheimer's disease. Edetate disodium is not FDA approved for any condition. Chelating drugs may have significant side effects, including dehydration, hypocalcemia, kidney injury, liver enzyme elevations, hypotension, allergic reactions, essential mineral deficiencies, and neurodevelopmental toxicity, teratogenicity and death. Inappropriate chelation may also cost hundreds to thousands of dollars.

5. Mercury-containing dental amalgams should not be removed. These release small amounts of mercury but randomized clinical trials demonstrate that the mercury present in amalgams does not produce illness. Removal of amalgams is expensive and subjects the individual to absorption of greater doses of mercury than if left in place.

6. Phenytoin or fosphenytoin should not be used to treat seizures caused by drug toxicity or drug withdrawal. Except for rare exceptions, phenytoin is ineffective for convulsions caused by drug or medication toxicity. It is ineffective for the treatment of isoniazid-induced seizures and withdrawal seizures, and may potentially be harmful when used to treat seizures induced by theophylline or cyclic antidepressants. First-line treatment of toxin-induced seizures and withdrawal seizures is benzodiazepines, followed by GABA-A receptor agonists, such as barbiturates.

7. "Detoxification" through colon cleansing, or promoting sweating for disease treatment or prevention, is not recommended. There is no evidence-based scientific research that supports a role for colonic irrigation, and there are no U.S. FDA-approved colonic hydrotherapy systems for nonmedical purposes like colon cleansing. These systems can cause cramping, pain, dehydration, electrolyte imbalances, infections, and bowel perforation.

Promoting sweating does not produce clinically relevant elimination of toxins. Side effects of promoting sweating include heat stroke, dehydration, burns, myocardial injury, carbon monoxide poisoning, and liver and/or kidney damage. These might also compromise toxin elimination.²

8. Tests should not be ordered to evaluate or to diagnose "idiopathic environmental tolerances," "electromagnetic hypersensitivity," or "mold

toxicosis." These labels indicate that patients have adverse non-allergic reactions to normal environmental stimuli. They are based on self-reported symptoms or non-validated testing procedures, and evidence-based assessments fail to support these diagnoses as disease entities. Labeling a patient with these diagnoses can affect their lifestyle, obscure the real etiology of their symptoms, and promote unnecessary testing.

9. Hair or nail testing to screen for "metal poisoning" should not be performed in patients with nonspecific symptoms. Clinical assessment for exposure to metals should consider the precise exposure, symptoms, signs, root of exposure and dose. Hair and nail testing is often unreliable, has limited utility, and is rarely required. Testing should be tailored to look for specific metal exposures, based on an appropriate evaluation. Once again, patients can be labeled with potentially harmful diagnoses, followed by detrimental therapy.³

10. Fasciotomy should not be performed in patients with snake envenomation without direct measurement of elevated intra-compartmental pressures. Crotalinae snakebites produce findings that mimic compartment syndrome, and rarely indicate actual compartmental syndrome. Myonecrosis results from venom toxicity, rather than from elevated compartment pressures. Fasciotomy does not prevent, and may worsen, necrosis.

Even in some cases with elevated compartment pressures, treatment with antivenom without fasciotomy has been successful. There is no available evidence to indicate when fasciotomy should be performed in the management of snakebites. To repeat, fasciotomy, if considered, should not be performed without first documenting elevated compartment pressure.⁴

III. RECOMMENDATIONS FROM THE AMERICAN COLLEGE OF MEDICAL GENETICS AND GENOMICS (ACMG)

1. A duplicate genetic test for an inherited condition should not be ordered unless there is uncertainty about the validity of the existing test result. The health care provider should ask a patient about prior genetic testing and review the medical record for previously performed genetic tests. Repeating the tests should be considered if the existing result is inconsistent with the individual's clinical presentation or if the test methodology has changed and may yield a different result from the original report that could impact the patient's management.

2. APOE genetic testing should not be ordered

as a predictive test for Alzheimer disease (AD). APOE is a susceptibility gene for later-onset AD. The presence of an ε4 allele is neither necessary nor sufficient to cause AD. The relative risk conferred by this allele is confounded by the presence of other risk alleles, gender, environment and possibly ethnicity. APOE genotyping for AD risk prediction has limited clinical utility and poor predictive value.⁵

3. Risk assessment of hereditary thrombophilia should not be accomplished with MTHFR genetic testing. The common MTHFR gene variants, 677C/T and 1298A/G, are prevalent in the general population. Recent meta-analyses have disproven an association between the presence of these variants and venous thromboembolism.⁶

4. HFE genetic testing should not be done in a patient without iron overload or a family history of HFE-associated hereditary hemochromatosis. The majority of hereditary hemochromatosis is due to inheritance of the HFE gene mutations. These are common among individuals of European ancestry. Only a small proportion of individuals with these mutations develop clinical disease. HFE genotyping should only be performed among individuals with iron overload (e.g. elevated fasting transferrin saturation > 45%) or known family history of HFE-associated hereditary hemochromatosis.

5. Obtain an informed consent that includes the possibility of secondary findings before ordering exome or genome sequencing. This informed consent should include the possibility of secondary findings unrelated to the indication for testing. Before the order, review with the patient the potential benefits (e.g., confirming a suspected genetic diagnosis), potential harms (e.g., psychosocial concerns), limitations of testing (e.g., a mutation may be missed), implications of the test results for family members, and alternatives to exome or genome sequencing.

Top Tips

OMEGA-3 FATTY ACIDS HAVE SHOWN NO CARDIOVASCULAR DISEASE BENEFIT

From 2005 to 2012, at least 24 rigorous studies of fish oil pills were published, of which 22 showed no benefit in preventing heart attacks or strokes in high risk populations: those who were obese, did not exercise, ate meat daily, smoked, had a history of heart disease, or had high cholesterol, high blood pressure, or Type 2 diabetes.⁷

Another meta-analysis has suggested that daily supplementation with marine-derived omega-3 fatty acids (FAs) does not significantly reduce the rate of fatal or nonfatal coronary heart disease or any major vascular events in high-risk individuals.⁸

After examining data from ten randomized trials that followed nearly 78,000 participants who had coronary heart disease (CHD) or a prior stroke, or were at high risk for cardiovascular disease (CVD), researchers found that at least 12 months of supplementation had no significant effect on rates of any CHD events, including nonfatal MI or CHD deaths. These trials lasted a mean of 4.4 years.

A senior author, Dr. Robert Clarke, stated that the present meta-analysis is different from previous meta-analyses in that it assessed the effects of omega-3 FAs on prespecified CVD subtypes and CVD in a range of patient populations. Nevertheless, the authors wrote that the 95% confidence intervals in the analysis “cannot exclude a 7% lower risk of major vascular events and a 10% lower risk of CHD associated with omega-3 FA supplements.”

Two large ongoing trials – VITAL in the United States and ASCEND in the United Kingdom – will provide additional evidence later this year on the effects of 1 g of omega-3 FA daily in another 40,000 patients.

Many experts would await the results of these trials before revising the guidelines. Patients are still advised to eat fish at least two times per week. Several studies have shown that eating fish is associated with reduced risk for heart attacks, but this does not mean that eating fish prevents heart attacks. It could be that people who eat lots of fish eat less red meat, a known heart attack risk factor.

A key unanswered question is whether omega-3 FAs can reduce the risk of MI, stroke, CV, mortality, and other CVD events, when used for primary prevention in those with a “usual” risk of CVD.

North Americans now spend more than \$1.1 billion on fish oil pills per year. If you take fish oil pills, for which there is no proven benefit, test each bottle to see if the oil is rancid. Oxidized fish oil smells like stale fish. If you cut open a fish oil capsule and it smells or tastes fishy, it is rancid and you should throw the bottle away or return it to the store. You should do this with each batch that you buy. Prescription pills might be preferable to over-the-counter ones, but they too can sometimes be rancid.

EVIDENCE REVIEWED ON E-CIGARETTES AND HEALTH

The Committee on the Health Effects of Electronic Nicotine Delivery Systems, which was established under the National Academies of Sciences, Engineering, and Medicine, has issued its comprehensive report based on a systematic review of more than 800 peer-reviewed studies.⁹

Applying its strength-of-evidence framework, the committee found conclusive evidence to answer eight questions, substantial evidence to answer 10 questions, moderate evidence to answer eight questions, limited evidence to answer 12 questions, insufficient evidence to answer four questions and no available evidence to answer five questions.

The report that resulted from this exhaustive analysis concluded that e-cigarettes cannot be simply categorized as either beneficial or harmful to health. The net public health outcome depends on the balance between adverse and beneficial outcomes.

In some circumstances their adverse effects warrant concern. These include their use by previously non-smoking adolescents and young adults, use of devices prone to explosion, and the presence of constituents in e-cigarette liquids that are of major health concern (e.g., diacetyl and some other flavorings). In other circumstances, when smokers of regular cigarettes use e-cigarettes to successfully quit smoking, e-cigarettes may reduce smoking-related illness.

Because of these conflicting outcomes, blanket regulations that restrict or permit the manufacture, marketing, and sale of all e-cigarettes for all populations are unlikely to maximize their benefits and minimize their risks.

NEW GUIDELINES ON EARLY TREATMENT IN ACUTE PANCREATITIS

The American Gastroenterological Association (AGA) has a new clinical guideline for the management of acute pancreatitis in the first 48-72 hours after hospital admission. These were published in *Gastroenterology* based on new scientific evidence.¹⁰

The strong recommendations all have “moderate quality” of evidence and include:

- Cholecystectomy for acute biliary pancreatitis should be performed during the initial admission rather than following discharge.
- Patients with acute alcoholic pancreatitis should have brief alcohol intervention during admission.
- Oral feedings as tolerated should be given

to patients with acute pancreatitis within the first 24 hours, and they should not be kept NPO.

- Patients with acute pancreatitis who cannot feed orally should receive enteral rather than parenteral nutrition (see below for route).

Conditional recommendations include the following:

- Prophylactic antibiotics should not be used in patients with predicted severe acute pancreatitis and necrotizing pancreatitis (low quality evidence).
- Patients with acute biliary pancreatitis and no cholangitis should not routinely undergo urgent endoscopic retrograde cholangiopancreatography (ERCP) (low quality evidence).
- Enteral nutrition for predicted severe or necrotizing pancreatitis should be given by either the naso-gastric or naso-enteral route (low quality evidence to prefer one over the other).
- Hydroxyethyl starch (HES) fluids are not recommended in acute pancreatitis (very low quality evidence).
- Patients with acute pancreatitis should receive goal-directed therapy for fluid management (very low quality evidence).

PEDIATRIC DENTAL HEALTH

The American Academy of Pediatrics Academy of General Dentistry encourages families to have access to a dental home by the time a child is 1 year old to deter the development of tooth decay. They also recommend that after the first dental visit, the child should be seen by the dentist every six months, or according to a schedule recommended by the dentist based on the child’s individual needs.

It’s important to practice good oral health habits both during pregnancy and once the child is born. For many years, it has been recommended that if an infant is put to bed with a bottle or sippy cup, it should only contain water. Formula, breast or other milk, and juices have natural sugars that can cause bacterial growth and cavities.

As soon as infants have a tooth/teeth, brushing should begin twice a day with a water-dampened baby toothbrush or a finger brush. The American Academy of Pediatric Dentistry recommends no more than a rice-size amount of fluoridated toothpaste for children less than 3 years of age. Above that age the size should be that of a pea.

If a child does not have a dental home, risk assessments should be performed and a referral made

(https://www.aap.org/en-us/Documents/oralhealth_RiskAssessmentTool.pdf). Risk should be assessed at six and nine months of age.

In addition, recommendations for fluoride supplementation have been added; it should be considered at 6-12 months of age, and then at 18 months through 16 years of age if the water source is deficient in fluoride.

Because there have been some rare historical on-look wells in southern Lancaster County with some fluoride in them, I've always urged that - at least once in the life of a well - parents should check the fluoride in their well water. The risk of fluorosis (too much fluoride) is the development of small white striations or opaque areas on some of the teeth, which can be permanent. If fluoride is detected in the water sample, the parent should notify the person prescribing the child's oral fluoride supplements to make an adjustment in the dosage based on what is found in the water sample. Obviously if there is fluoride in their municipal or community water supply, no added fluoride in the form of supplements should be given.

Take note that there are a number of home water treatment systems that are effective in removal of fluoride from water, including reverse osmosis and distillation. If these are in use, make sure that your child is being supplemented with fluoride. Common home carbon filters (e.g. Brita, PUR) do not remove fluoride from water. These can be recommended for families who are concerned about heavy metals or other impurities in their home water supply, but who wish to retain the benefits of fluoridated water.

Fluoride varnish is recommended in the primary care setting every 3-6 months, starting at tooth emergence. Over-the-counter fluoride rinse is not recommended for children younger than 6 years of age because of the risk of swallowing higher than recommended amounts of fluoride.

UPDATE ON ADHD DIAGNOSIS AND TREATMENT

The Agency for Healthcare Research and Quality (AHRQ) has published a systematic review of 103 articles (covering 90 distinct studies) on the diagnosis and treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents.

For diagnosis of patients aged 7-17 years, the Attention and Executive Function Rating Inventory and Childhood Executive Functioning Inventory proved better than the Cambridge Neuropsychological Test Automated Battery (evidence strength: low). Electroencephalography or neuroimaging were deemed insufficient to determine an ADHD diagnosis in patients aged 7-17 years.

Since 2011 there has been limited new evidence showing that methylphenidate is effective for children under 6 years of age with ADHD, and that psychostimulants can be effective for children aged 6-12 years. The most common side effects associated with two ADHD treatments, atomoxetine (Strattera®; Eli Lilly) and methylphenidate (Ritalin®; Novartis) were somnolence and mild gastrointestinal problems. Atomoxetine had higher rates of gastrointestinal effects than methylphenidate (evidence strength: low).

This review showed cognitive behavioral therapy may improve ADHD symptoms (evidence strength: low). Where child and parent training helped improve ADHD symptoms, it did not have an impact on academic performance (evidence strength: low). Omega-3 supplementation had no effect on ADHD symptoms (evidence strength: moderate). For all of the treatments, there was little evidence about the risk of serious adverse events, including cardiovascular risk.

Overall, this review showed insufficient evidence regarding new diagnostic approaches or the harms associated with being labeled as having ADHD. There were no data regarding optimal monitoring. Obviously, many more studies are needed.

REFERENCES

1. Talmage J et al. Low back disorders. In: Hegmann, K, ed. Occupational Medicine Practice Guidelines. 3rd ed. Elk Grove Village, Ill: American College of Occupational and Environmental Medicine; 2011. p. 377.
2. Mishori R et al. The dangers of colon cleansing. *J Fam Pract* 2011 Aug;60(8):454-7.
3. Calabrese EJ. Hormesis is central to toxicology, pharmacology and risk assessment. *Hum Exp Toxicol*. 2010 Apr;29(4):249-61.
4. Mazer-Amirshahi M, et al. Elevated compartment pressures from copperhead envenomation successfully treated with antivenin. *J Emerg Med*. 2014 Jan;46(1):34-7.
5. Statement on the use of apolipoprotein E testing for Alzheimer disease. American College of Medical Genetics/American Society of Human Genetics Working Group on ApoE and Alzheimer disease. *JAMA*. 1995 (Nov 22-29); 274(20):1627-9.
6. Hickey SE et al. ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. *Genet Med*. 2013 Feb;15(2):153-6.
7. Grey A, Bolland M. Clinical trial evidence and use of fish oil supplements. *JAMA Int Med*. 2014;174(3):460-462.
8. Aung T, Halsey J, et al. Associations of omega-3 fatty acid suppl. use with cardiovascular disease risks: meta-analysis of 10 trials. *JAMA Cardiol*. 2018; 3(3):225-234
9. Public Health Consequences of E-cigarettes. National Academies Press, Washington, DC. 2018.
10. Crockett SD, Wani S, et al. Am. Gastroenterol. Assoc. Institute guideline on initial management of acute pancreatitis. *Gastroenterol*. 2018; 154 (4): 1096-1101.