Busting Medical Myths When Dogma is for the Dogs

Disclosure of Financial Relationships

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Has no relationships with any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

Why Do Medical Myths Occur?

- Physiology that makes sense
- Case reports
- Tradition- Really never been studied before

Myths Patients Believe

I don’t want a flu shot because it gives me the flu

How Common are Side Effects from Influenza Vaccine?

- 1806 patients age > 60 randomized to flu vaccine vs placebo
- Patients completed questionnaire four weeks later
- 23% of vaccine recipients vs 14% of placebo had adverse reactions
- Local side effects made up the difference, 17.5% of vaccine group vs 7.3% placebo
- No differences in systemic side effects (11% vs 9.4%)
- BMJ 1993 307:988-990

Frequency of Adverse Reactions to Influenza Vaccine in the Elderly

- Randomized, placebo controlled, double blind crossover trial
- Patients (336) received either saline or trivalent influenza vaccine, interviewed for side effects and after a 1 week washout period received the other then interviewed again for side effects
- Only significant symptom difference was sore arm after vaccine
- JAMA. 1990;264:1139-1141

I Can’t Have a Flu Shot Because I am Allergic to Eggs

What Is The worry About Egg Allergic Patients Receiving Influenza Vaccine?

- Based on the fear that administering a vaccine that was grown in eggs and could contain egg protein might cause anaphylaxis in patients with immunoglobulin E antibodies against egg proteins.

What Happens to Children With Egg Allergy Who Get Influenza Vaccine?

- Study of children with egg allergy confirmed with skin testing (average age of the study group was 3 years) receiving influenza vaccine
- Included in the study were 27 patients with a history of anaphylaxis or severe reactions after egg ingestion
- No patients suffered severe reactions with the vaccine, with only four patients having mild, self-limited symptoms.
- J Pediatr. 1998 Nov;133[5]:624-8

What is All The Data?

- 28 studies with a total of 4,315 patients with egg allergy who received Egg based Influenza vaccine
- 656 with history of anaphylaxis with egg ingestion
- None of these patients developed a serious reaction when they received influenza vaccine.
- Expert Rev Vaccines. 2014 Aug;13[8]:1049-57

What Should We Tell Our Patients

- All patients with egg allergy of any severity should receive inactivated influenza vaccine annually, using any age-approved brand
- There are no special waiting periods after vaccination of egg allergic patients beyond what is standard practice for any vaccine.

- Ann Allergy Asthma Immunol. 2013 Oct;111[4]:301-2

Vitamin C Prevents Colds

- In 1971, Linus Pauling, did a summary of four relatively small published studies of vitamin C and concluded that vitamin C supplementation helped prevent and lessen colds.He had published a book several years earlier “Vitamin C and the common cold”

- Proc Natl Acad Sci USA. 1971;68:2678-2671.

Direct Inoculation Study

- 91 subjects, 47 received 3 g of ascorbic acid per day for 3 days before inoculation with viruses (a mixture of rhinoviruses, influenza B virus, or B814virus) and for 6 days after inoculation, and 44 subjects received a placebo.
- The incidence of colds was only 6% less for the ascorbic-acid group (18/47) than for the placebo group(18/44); this difference is not statistically significant.

- Brit. Med.J., 1, 603 (1967)

Cochrane Review

- Twenty-nine trial comparisons involving 11,306 participants contributed to the meta-analysis on the risk ratio (RR) of developing a cold while taking vitamin C regularly over the study period. In the general community trials involving 10,708 participants, the pooled RR was 0.97 (95% confidence interval (CI) 0.94 to 1.00).

- Cochrane Database of Systematic Reviews. 2013;1(1).

Really Old Myths

- A 32-year-old man is diagnosed with giardia and prescribed metronidazole. He has no other medical problems. He will be the best man t his brother's wedding tomorrow. What advice should you give him about alcohol use at the reception?
- A. Do not take metronidazole the day of the wedding if you will be drinking alcohol.
- B. Take metronidazole , do not drink alcohol.
- C. It's okay to drink alcohol.

Dogma

- For years, we have advised patients to not use alcohol if they are taking metronidazole because of concern for a disulfiram-like reaction between alcohol and metronidazole. This has been a standard warning given by physicians and appears as a contraindication in the prescribing information. It has been well accepted as a true, proven reaction.

Where Did The Dogma Come From?

- Case reports (1,2)
- The case reports referenced textbooks to substantiate the interaction, but they did not present clear evidence of an interaction as the cause of elevated acetaldehyde levels.

- Br J Clin Pract. 1985 Jul;39(7):292-3.
- Psychiatr Neurol. 1966;152:395-401.

Do Ethanol and Metronidazole Interact to Produce a Disulfiram-Like Reaction?

- Review of reports published between 1969 and 1982 produced no convincing evidence that this reaction exists. Six case reports involving eight patients were evaluated.
- Four of the eight cases were serious, including one death, but the authors of all the reports presumed the metronidazole–ethanol reaction to be an established pharmacologic fact. None provided evidence that could justify their conclusions.
- Ann Pharmacother. 2000 Feb;34(2):255-7.

Does Metronidazole Increase Acetaldehyde Levels?

In the rat model metronidazole can increase intracolonic, but not blood, acetaldehyde levels in rats that have received a combination of ethanol and metronidazole.

- Metronidazole did not have any inhibitory effect on hepatic or colonic alcohol dehydrogenase or aldehyde dehydrogenase
- Rats treated with metronidazole had increased growth of Enterobacteriaceae, an alcohol dehydrogenase–containing aerobe, which could be the cause of the higher intracolonic acetaldehyde levels.

- Alcohol Clin Exp Res. 2000 Apr;24(4):570-5.

Metronidazole + Alcohol

- Small placebo-controlled, randomized trial
- 12 healthy participants
- 1/2 of the study participants received metronidazole three times a day for 5 days; the other half received placebo.
- All participants then received ethanol 0.4g/kg, with blood testing being done every 20 minutes for the next 4 hours. Blood was tested for ethanol concentrations and for acetaldehyde levels. The study participants also had blood pressure, pulse, skin temperature, and symptoms monitored during the study.
- No difference in blood acetaldehyde levels, vital signs, or symptoms
- Ann Pharmacother. 2002 Jun;36(6):971-4

Can Metronidazole Cause a Disulfiram-Like Reaction?

- Case-Control Study Propensity Matched by Age, Sex, and Ethanol Concentration
- A retrospective chart review was performed over 10 years on emergency department patients with ethanol use confirmed via detectable ethanol concentration who received metronidazole while ethanol was predicted to still be present in the serum. A matched comparator group with the same ethanol concentrations, as well as sex and age, was generated for comparison
- Thirty-six patients were included in the study: 18 in the metronidazole group and 18 in the ethanol concentration matched control group.
- There were no significant difference in disulfiram-like effects between the two groups. No patients who received metronidazole and had a detectable ethanol concentration had a suspected disulfiram-like reaction documented in the medical record.
- WMJ. 2023 Jul;122(3):171-177.

CDC 2021 STI Guidelines

- The previous warning against simultaneous use of alcohol and metronidazole was based on laboratory experiments and individual case histories in which the reported reactions were equally likely to have been caused by alcohol alone or by adverse effects of metronidazole.
- Metronidazole does not inhibit acetaldehyde dehydrogenase, as occurs with disulfiram. Ethanol alone or ethanol-independent side effects of metronidazole might explain the suspicion of disulfiram-like effects. Thus, refraining from alcohol use while taking metronidazole (or tinidazole) is unnecessary.
- MMWR.2021;Jul 23:70(4):1-187

A 30 yo woman cuts her finger on a glass jar. She goes to the ER and needs to have sutures on her right ring finger. What would you recommend for anesthesia to prepare the patient for repair?

A) Bupivacaine

B) Lidocaine (Xylocaine) 1%

C) Lidocaine (Xylocaine)1% with Epinephrine

D) Lidocaine (Xylocaine) 2%

E) Saline

Conventional Wisdom

Epinephrine should never be used in an end-arterial field, e.g., digits, pinna, nose, penis.

Emergency Medicine: A Comprehensive Study Guide 5th Edition;McGraw Hill, 2000

Can Epinephrine be Used in Digital Blocks?

- 60 digital block procedures, 31 randomized to Lidocaine with epi and 29 to Lidocaine
- Lidocaine with epi- one patient needed additional anesthesia, Lidocaine 5 needed additional
- Digital tourniquet needed in 9/31 patients with Lidocaine with epi, 20/29 Lidocaine alone $p<.002$
- Two patients with complications after Lidocaine, none with Lidocaine and epi

Plast Reconstr Surg 2001;107:393

Epinephrine Use in the Fingers and Hand

- To examine prospectively the incidence of digital infarction and phentolamine rescue in a large series of patients who received epinephrine in their fingers and hands.
- From 2002-2004 9 hand surgeons prospectively recorded each consecutive case of hand and finger epinephrine injection.
- Journal of Hand Surgery 2005;30 (5): 1061-67

Epinephrine Use in the Finger and Hand

- 3,110 consecutive cases of elective injection of low dose epinephrine in the hands and fingers. There were no cases of digital tissue loss. Phentolamine was never required to reverse vasoconstriction

Journal of Hand Surgery 2005;30(5):1061-67

Epinephrine Use in Toes

- 18,000 patient records over 14 years reviewed, plus an additional 5000 records from the authors practice spanning 27 years reviewed for foot surgery patients. All patients deemed healthy
- 65,000 digital surgical procedures reviewed that used lidocaine with epi. No complications due to epinephrine
- J Am Pod As 1971;61(9); 335-40.

Literature Review

- 39 studies of epinephrine digital blocks in fingers and toes
- No digital necrosis or gangrene in any patients

- J Emer Med 2015;49(5):799-809

Newer Myths

- A 80 yo man with AD is admitted to the hospital after a fall. He is noted to have coughing spells after drinking liquids .He has a swallowing study done which shows severe motility slowing in the esophagus.
- What do you recommend?

A) Feeding tube
B) Thickened liquids
C) Continue current diet

Why is This Important?

- Thickened liquids may have negative effects such as : dehydration, poor oral intake, and worsening quality of life.

- JAMA Internal Medicine July 2024 Volume 184, Number 7 : 786-7

Systematic Review and Evidence-Based Recommendations on Texture Modified Foods and Thickened Liquids for Adults With Oropharyngeal Dysphagia

- There is no convincing evidence that thickened liquid or texture modified diet prevents death or pneumonia nor improves the quality of life, nutritional status, or oral intake in individuals with OD. There is a need for future studies to examine the effect and discuss outcome measures in OD management with thickening agents.

- Clinical Nutrition ESPEN 49 (2022):551-555

Thick Liquids and Clinical Outcomes in Hospitalized Patients With Alzheimer Disease and Related Dementias and Dysphagia

- Cohort study included adults aged 65 years and older with AD, with clinical suspicion of dysphagia during hospitalization and survival for at least 24 hours after hospital arrival. Patients were grouped according to whether at least 75% of their hospital diet consisted of a thick liquid diet or a thin liquid diet.
- 8916 patients with AD and dysphagia included in the propensity score matched analysis. A total of 4458 patients receiving a thick liquid diet were matched with 4458 patients receiving a thin liquid diet. There was no significant difference in hospital mortality between the thick liquids and thin liquids groups (hazard ratio, 0.92; P = .46). Compared with patients receiving thin liquids, patients receiving thick liquids were less likely to be intubated (odds ratio [OR], 0.66), but they were more likely to have respiratory complications (OR, 1.73; 95% CI, 1.56-1.91).
- JAMA Intern Med. 2024;184(7):778-785.

A 59-year-old man presents with abdominal pain. He has a history of small bowel obstruction and diverticulitis. His medical history includes chronic kidney disease (CKD; baseline creatinine, 1.8 mg/dL), hypertension, type 2 diabetes, and depression. He had a colectomy 6 years ago for colon cancer.

He takes the following medications: Semaglutide (1 mg weekly), amlodipine (5 mg once daily), and escitalopram (10 mg once daily). On physical exam blood pressure is 130/80 mm Hg, pulse is 90, and temperature is 37.2 degrees C. normal bowel sounds but guarding in the right lower quadrant.

Labs: HB 13 HCT 39 WBC 13,500 BUN 27 Cr 2.0. KUB is unremarkable

What imaging to you recommend?

A) CT without contrast

B) CT with contrast

C) MRI

D) Abdominal ultrasound

Contrast in Patients with CKD

- Meta-analysis of 13 studies, 25,950 patients
- No increased risk of acute kidney injury (AKI) in patients who received contrast medium compared with those who did not receive contrast
- No difference in AKI in patients with diabetes or CKD.
- McDonald JS et al. Radiology. 2013:267:119-128.

Contrast CT in ED

- 17,934 patients arriving in ED who had CT with contrast, CT with no contrast, or no CT.
- Contrast administration was not associated with increased incidence of AKI (odds ratio, 0.96, CI: 0.85-1.08).

- Hinson JS et al. Ann Emerg Med. 2017;69(5):577-586.

Guidelines From ACR and National Kidney Foundation

- “The risk of acute kidney injury developing in patients with reduced kidney function following exposure to intravenous iodinated contrast media has been overstated.”
- Can give contrast if needed in patients with glomerular filtration rates (GFRs) greater than 30.
- Davenport MS et al. Radiology. 2020;294(3):660-668.

Everyday Myths

- A 55 patient of yours requests new prescriptions from you at a routine appointment. She will be travelling internationally next month and wants to replace her emergency medication kit, as the medications in it (Azithromycin/ Loperamide/Oxycodone) have all expired. What do you do?
- A) Replace the prescription for Azithromycin
- B) Replace all three medications
- C) Tell the patient that all the meds should still be fine

Expiration Date on Medications

- The date that is required of the manufacturer to guarantee 90% potency

Shelf Life Extension Program

- 122 drugs studied representing 3005 lots
- 88% with > 90% potency 1 year past expiration date, with average extension of 5 years
- Ciprofloxacin (55 months)
- Doxycycline (50 months)

- JOURNAL OF PHARMACEUTICAL SCIENCES, 2006. 95 (7): 1549-1560.

Stability of Active Ingredients in Long-Expired Prescription Medications.

- Sealed drugs from a retail pharmacy that were 28-40 years past their expiration date were evaluated
- 12 of the 14 compounds tested were in concentrations at least 90% of the labeled amount
- Codeine, hydrocodone, acetaminophen among the medications studied that retained potency
- Aspirin did break down to less than 1%

- ARCH INTERN MED 2012. 172 (21); 1686-1687.

What About Epinephrine?

- Original parenteral epinephrine remains sterile and detectably pure more than 2.5 years after expiration (1)
- Epi pens less than 25 months past expiration contained at least 90% of the labeled amount (2)
- Of 40 epi pens studied, (1-50 months past expiration), all had > 80% of labeled concentrations (3)

1) Prehosp Emerg Care. 2018 Jan 26:1-5.
2) Ann Allergy Asthma Immunol. 2015;114:354-6.
3) Ann Intern Med. 2017 Jun 20;166(12):918-919.

Expired Albuterol

- Samples from expired lots of albuterol products were analyzed for their levels of their respective active ingredients.
- Manufacturer expiration dates ranged from March 2001 to April 2019
- Nearly all lots of albuterol retained >90% of listed strength >15 years post expiration
- Heliyon 2022;8 (August 5)

Toxic Expired Drugs?

- Only expired medication ever reported to cause toxicity (Fanconi's syndrome) was a tetracycline formulation now off the market (4 patients reported)

- J Am Med Assoc 1963;184:111-3.

- A 46 yo man who lives in Tacoma ,Washington is seen for fatigue. He has a no significant past medical history. He is not taking any medications Labs: Hb 12 HCT 37 MCV 103 , TSH 1.2
- What workup do you recommend?

A) B12, folate testing
B) Alcohol history, B12,folate testing
C) Alcohol history, B12 testing

Why Were We Taught to Test for Folate ?

- In The United States, before 1998 when routine fortification of grain products with folate was started, anemia due to folate deficiency was sometimes seen clinically in the US

Should We Check Folate Levels in Anemia Patients?

- Two Teaching hospitals in Canada
- 11 out of 2154(0.5%) serum folate were low(<7.0 nmol/L) and 4 out of 560 (0.7%) RBC folate were low (<417 nmol/L).
- No subject with low folate could the anemia be attributed to folate deficiency

- BMC Research Notes 2010, 3:22

Low Yield For Folate testing in the US

- Retrospective review of all outpatient serum folate tests performed at an academic medical center in Boston, from January 1, 2003, through December 31, 2013
- 84 187 serum folate levels were measured in 77 627 individuals. There were 47 deficient (0.056%), 166 low-normal (0.197%), 83,974 normal or high .

- JAMA Intern Med. 2014;174(10):1696-1697.

Choosing Wisely Campaign American Society For Clinical Pathology

Do not order red blood cell folate levels at all.

Macrocytosis in the Primary Care Setting

- Evaluation of 300 consecutive primary care patients with MCV > 100
- 4.7 % were anemic
- In 80% of the men, and 35% of the women the cause was alcohol
- No cause found in 6.8% of men and 35% of women
- Alcohol Clin Exp Res. 1991 Oct;15(5):871-6.

- A 29 yo woman presents for evaluation. She reports that she has frequent headaches over the past 12 months that include pressure pain on her forehead, under her eyes and over her cheeks. She usually has nasal congestion as well. She has not had any fevers or purulent nasal discharge. What is the most likely problem?

A) Cluster headaches

B) Migraine headaches

C) Sinus headaches

D) Tension headaches

“Sinus” Headaches Are Usually Migraine Headaches

- 2991 patients screened who reported at least 6 headaches during the previous 6 months self diagnosed or physician diagnosed as sinus headaches
- 88% of these patients met IHS criteria for migraine HA (80%) or migrainous criteria (8%).Most common sx patients reported were sinus pressure (84%), sinus pain (82%) and nasal congestion (63%)
- Arch Intern Med 2004;164 (16): 1769-1772

Sinus, Allergy and Migraine Study

- 100 patients recruited who believed they had sinus headaches. All received a detail history and PE and given headache diagnosis based on IHS criteria
- Final diagnosis were as follows: Migraine with or without aura 52%, probable migraine 23%, chronic migraine with medication overuse HA 11%, nonclassifiable HA 9%. 76% of migraine patients reported pain in the distribution of the 2nd division of the trigeminal nerve and 62% experienced bilateral forehead and maxillary pain with their HA's.
- Headache 2007;47:213-224

Migraine Headaches Misdiagnosed as Sinus

- The study included migraine patients with a past history of sinusitis.
- A total of 130 migraine patients were recruited. Of these patients 106 (81.5%) were misdiagnosed as sinusitis. The mean time delay of migraine diagnosis was 7.75 y± 6.29, range 1 to 38 years.

- The Journal of Headache and Pain 2013, 14:97

Treatment of Sinus Headache as Migraine: The Diagnostic Utility of Triptans

- To determine the response rate to triptans in alleviating “sinus headache” in patients with endoscopy and CT negative sinus exams
- Prospective study of patients with physician or patient self diagnosed sinus headaches with negative workup all treated with triptans
- 54 patients enrolled, 38 completed follow up. 31 patients (82%) had significant reduction in headache pain with triptan use, 35 (92%) had a response to migraine directed therapy.
- Laryngoscope 2008;Dec; 2235-2239.

- A 59 yo woman is admitted with abdominal pain. She has a history of pancreatitis. A contrast CT scan is ordered. She reports a history of severe shellfish allergy and an allergy to betadine when the radiology tech asks as she is checked in for the procedure. You are paged regarding what to do.
- A) Continue with scan as ordered
- B) Switch to MRI scan
- C) Switch to MRI scan with gadolinium
- D) Continue with CT with contrast, give dose of solumedrol
- E) Continue with CT with contrast give IV diphenhydramine

Where This Myth Came From

- Fish and shellfish contain iodine, and allergic reactions to seafood are quite common, with a prevalence ranging anywhere between 2% and 6% of the population.

Why Shellfish Allergy = Iodine Allergy Doesn't Make Sense

- Iodine is present in many other foods (milk, bread, yogurt, iodized salt)
- Allergy to shellfish is due to the proteins parvalbumin and tropomyosins

- J Microbiol Immunol Infect. 1999;32(3):143–154.

How Widespread is This Belief?

- Study to see how pervasive the myth remained among Emergency Medicine (EM) and Radiology providers.
- 20% of EM/Radiology physicians surveyed would not administer contrast to a patient with a shellfish allergy
- A majority of respondents indicated that an iodine allergy limited ability to receive IV contrast or required pre-treatment
- American Journal of Emergency Medicine 37 (2019) 1362–1393

Prevalence of Contrast Reactions in Patients with Seafood Allergies

- Seafood 6-15%
- Milk/Eggs/Chocolate 14%
- General Allergies 13%
- Fruit allergies 13%
- Asthma 11%
- Am J Roentgenol Radium Ther Nucl Med. 1975;124: 145–152.
- Journal of Hospital Medicine 2016; Vol 11 | No 6 |

Current Guidelines

- American Academy of Allergy, Asthma and Immunology does not recommend low- or iso-osmolar radiocontrast media or pretreatment with corticosteroids and antihistamines for patients with a history of seafood allergy, who require radiocontrast media.
- The American College of Radiology recommends pretreatment with corticosteroids only for those patients who have previously experienced moderate to severe reactions to IV contrast

ACR Manual on Contrast Media. Version 9. Reston, VA: American College of Radiology, ACR Committee on Drugs and Contrast Media; 2013.

Journal of Hospital Medicine 2016; Vol 11 | No 6

Guidelines for Betadine?

- “Patients with shellfish or povidone-iodine (e.g., Betadine®) allergies are at no greater risk from iodinated contrast medium than are patients with other allergies (i.e., neither is a significant risk factor). There is no cross-reactivity between different classes of contrast medium. For example, a prior reaction to gadoliniumbased contrast medium does not predict a future reaction to iodinated contrast medium, or vice versa, more than any other unrelated allergy.”

- ACR Manual on Contrast Media 2023, ACR Committee on Drugs and Contrast Media

Colonoscopy Dogma

- Clear liquid diet for 1-2 days before colonoscopy
- 1 gallon of GOLYTELY (PEG 3550/electrolyte)
- Be absolutely miserable

Low Residual Diet vs Clear Liquid Diet

- 200 patients randomized to LRD vs CLD
- LRD allowed meat/eggs/dairy/bread/rice, through day before colonoscopy
- The patients in the low residual diet group had better bowel prep than those in the clear liquid diet group (81% vs 52%, $p < 0.001$)
- Less Nausea $p < .05$, vomiting $p < .01$, headache $p < .01$, weakness $p < .01$, hunger $p < .01$
- Endoscopy 2010;42: 633-8.

LRD vs CLD- Meta-Analysis

- LRD and CLD comparable in regards to adequacy of bowel prep and detection of polyps
- Less nausea ($p<.02$), vomiting($p<.04$), hunger ($P<.001$), headache ($p<.02$) with LRD
- Patients who followed low residue diets showed an increased willingness to repeat it, compared to those who followed clear liquid diet ($P > .005$; OR, 2.23; 95% CI, 1.28-3.89).
- Gastrointest Endosc. 2020 Sep;92(3):508-518.

Real World Effectiveness of Different Bowel Preps

- Lower volume bowel preps SuPrep (P<.001), MoviPrep (p<.004), and Miralax+ Gatorade (P<.001) were all superior to GOLYTELY for bowel cleansing
- Patients taking SuPrep (p<.001), MoviPrep (p<.001), Miralax with Gatorade (p<.001) were more likely to complete the prep than those taking GOLYTELY
- Am J Gastroenterol. 2019; 114(2): 305–314.

Colonoscopy Prep- Bottom Line

- Let them eat! Low residual diets are tolerable and with less symptoms, and work as well as clear liquid diets
- GOLYTELY is a relic of the past- all it has going for it is low cost (with less tolerability)

Questions or Comments

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