

# Medical Mythology: What is the Evidence for Common Practices?

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# 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.

An 82 yo woman is evaluated for fatigue. Lab eval reveals a hemoglobin of 8 with an MCV of 114. B12 level is 90 (NL > 200). Folate level is normal. Urine methylmalonic acid level is high. What would you recommend for this patient?

- A) Schilling test
- B) Oral B12 1000 mcg a day
- C) Blood transfusion, then IM B12 monthly
- D) IM B12 load, then monthly B12 injections

## Conventional Wisdom

“Since the defect is one of absorption, replacement should be administered parenterally, specifically in the form of intramuscular cyanocobalamin (if intramuscular administration is contraindicated or refused, cobalamin deficiency can be managed by oral replacement therapy, at doses of 300 to 1000 mcg daily, it is an expensive mode of treatment which requires close medical supervision to avoid relapse).”

Harrison's textbook of Medicine. 13th edition 1994.

# The Source of the Problem

“In the management of a disease for which parenteral therapy with Vitamin B<sub>12</sub> is a completely adequate and wholly reliable form of therapy, it is unwise to employ a type of treatment which is, at best, unpredictably effective.”

9th announcement of U.S.P. anti-anemia preparations advisory board. JAMA 1959; 171: 2092-2094.

# Oral Replacement of Vitamin B<sub>12</sub>

## Problems with early studies

- Used low doses 6 - 150 mcg
- Often with intrinsic factor (animal)
- Antibodies often developed to IF

# Oral Treatment of Pernicious Anemia with Vitamin B<sub>12</sub>

- 27 patients with pernicious anemia treated with 300 mcg of B<sub>12</sub> po daily
- Clinical response excellent in all (normalization of Hb/HCT)
- Follow up at one year, all in clinical remission
- Serum B<sub>12</sub> levels rose from 90 to 321 and were maintained

Ann Intern Med 1963. 58 (5): 810-817

## Oral Treatment of Pernicious Anemia with B<sub>12</sub>

- 33 patients with PA received 1000 mcg B<sub>12</sub> orally each week
- No clinical or hematologic relapse in any patient (follow-up up to 6 1/2 years)
- Serum B<sub>12</sub> levels remained low (mean value < 100 micro mcg/ml)
- Conclusion - 1000 mcg/wk leads to clinical remission, but low serum levels.

Arch Int Med 1960. 106: 280-292

# Oral treatment of Pernicious Anemia with Vitamin B<sub>12</sub>

- 64 patients with established B<sub>12</sub> deficiency from three Swedish Medical Centers
- Received 500 or 1000 mcg of oral B<sub>12</sub> each day
- All 64 had normal serum B<sub>12</sub> levels on therapy
- No patient developed neurological abnormalities or hematologic abnormalities due to B<sub>12</sub> deficiency on therapy

Acta Med Scand 1968. 184:247-258

## Treatment of B<sub>12</sub> deficiency with oral Cobalamin

- 38 newly diagnosed B<sub>12</sub> deficient patients randomly assigned to receive IM Cobalamin (1 mg 9x in 3 mo) or 2 mg orally daily
- B<sub>12</sub> levels and Methylmalonic acid levels were measured before and after treatment

- IM B<sub>12</sub> group

Serum B<sub>12</sub> 95 pg/ml → 325 pg/ml

Methylmalonic acid 3,850 nmol/l → 265 nmol/l

Oral B<sub>12</sub> group

Serum B<sub>12</sub> 93 pg/ml → 1,005\* pg/ml

Methylmalonic acid 3,850 nmol/l → 169 nmol/l

\*p <.0005 comparing oral vs. IM. Blood 1998; 92(4):1191-1198

# Oral Replacement of Pernicious Anemia with Vitamin B<sub>12</sub>

## Conclusions

- Both IF dependant and independent absorption occurs
- 1.2 - 1.5% of the dose is absorbed in patients with PA (IF independent)
- Doses of 500 - 1000 mcg allow for safety zone
- Long term outcome is excellent
- Cost is low

# Vitamin B<sub>12</sub> Replacement Cost (US \$)

- 1000 mcg tablets \$ 5.02/100 tablets
- Hydroxycobalamin injection \$ 7.37  
1000 mcg/ml (30 doses)
- Visiting nurse visit \$75.00
- Clinic charge \$15.00

# Conventional Wisdom is Improving!

- “Because the defect is nearly always malabsorption, patients are generally given parenteral treatment, specifically in the form of IM cyanocobalamin. Parenteral treatment begins with 1000mcg cobalamin a week for 8 weeks, then 1000 mcg a month for life. However, cobalamin deficiency can also be managed very effectively by oral replacement therapy with 2 mg of B12 a day”
- Harrison’s 15<sup>th</sup> edition 2001

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  
5<sup>th</sup> 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 for Digital Blocks?

- No reported cases of finger gangrene due to epinephrine use
- Most textbooks discourage use for digits, nose, earlobe

- 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 HIS 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 2<sup>nd</sup> division of the trigeminal nerve and 62% experienced bilateral forehead and maxillary pain with their HA's.
- Headache 2007;47:213-224

# Tip Offs That a Headache is Not of Sinus Origin

- Absence of fever
- Absence of purulent drainage
- Chronicity

A 34 yo woman burns her left arm when hot grease spills on it. She presents for treatment. She has a 4cm X 6cm partial thickness burn involving the left forearm. What treatment would you recommend?

- A) Hydrocolloid dressing (Duoderm)
- B) Silver sulfadiazine (Silvadene)
- C) Honey
- D) Biobrane

# Honey vs Silvadene for Treatment of Burns

- 50 patients with superficial burns randomized to honey (25 patients) or Silvadene (25 pts)
- In the honey treated patients epithelialization occurred in 84% by 7 days and 100% by 21 days. In Silvadene treated patients epithelialization occurred in 72% by 7 days and 84% by 21 days ( $p < .05$ )
- Evidence of wound infection in 0 patients treated with honey at 21 days and 5 patients treated with Silvadene at 21 days.

Burns 1998; 24:157-161

# Honey vs Silvadene in Treatment of Burns

- 104 patients with partial thickness burns randomly assigned to honey or silver sulfadiazine (52 in each group)
- In the honey treated group 45 patients were healed by 15 days, where it took 40 days to have a similar number (47) healed in the SSD group  $p < .001$ .

Br J Surg 1991;78:497-498

# Efficacy of Honey in Inhibiting *Pseudomonas Aeruginosa* From Infected Burns

- 17 strains of *Pseudomonas Aeruginosa* isolated from infected burns were tested for sensitivity to 2 kinds of honey (pasture honey and manuka honey)
- All strains showed sensitivity to the honeys with MIC below 10%, and MBC of 9% (compared to 19% for artificial honey)
- J Burn Care Rehabil 2002;23:366-370.

## Hydrocolloid Dressing (Duoderm) vs Silver Sulfadiazine (Silvadene)

- 42 patients with second-degree burns randomized to treatment with hydrocolloid dressing (22) or silver sulfadiazine (20)
- Pain and itch less in hydrocolloid treated patients
- Less time for dressing changes, less interference with daily activities and quicker healing with hydrocolloid ( $p < .01$ )

J Trauma 1990;30: 857-865.

- A 49 yo with type 1 DM is evaluated for increasing dyspnea. He has a history of CAD, CHF and renal insufficiency. His current meds are furosemide, carvedilol, simvastatin and aspirin. Chest x-ray shows pleural effusions.

BP 140/80 p-60. Urea 38 Cr 3.4 K 4.3

What would you recommend?

- A) Amlodipine
- B) Enalapril
- C) Nitrates
- D) Nitrates + Hydralazine

# Use of ACEI in Patients With Renal Insufficiency

- Retrospective study of 20,902 medicare patients with LVEF < 40%
- Outcome measures :1 year survival for patients who did or did not receive an ACEI at hospital discharge
- Receipt of ACEI associated with 37% lower mortality for patients with Cr> 3.0, 16% lower mortality for patients with Cr<3.0.

Arch Int Med 2000; 160(17): 2645-50.

# ACEI and Renal Insufficiency

- Randomized control trial of Benazepril vs placebo in patients with CRI
- Dose escalation to 20 mg Benazepril, followup to 3 ½ years. Endpoints doubling of Cr, ESRD or death
- 94/422 patients excluded in the initial phase of study, mostly due to cough (72)
- 41% of patients on Benazepril vs 60% on placebo reached a primary endpoint during the 3.4 years of the study
- Risk reduction 19%, NNT for 3.4 years was 5.3
- NEJM 2006; 354:131-140

- A 57 yo woman comes to clinic to discuss worsening hot flashes. She has tried natural products without benefit. She is healthy with no major medical problems. No past surgical Hx. FH of breast cancer in her mother (diagnosed last year). What would you recommend?

- A) Estrogen + Progesterone
- B) Estrogen
- C) Vanlafaxine
- D) Tamoxifen
- E) Raloxifene

# What Did The WHI Tell Us?

- A) The risk of coronary disease, breast cancer and endometrial cancer is higher in women taking estrogen + progestin
- B) The risk of coronary disease, breast cancer and premature mortality is higher in woman taking estrogen + progestin
- C) The risk of coronary disease, breast cancer and premature death is not elevated in women who receive estrogen only

# WHI: The Facts

	RR HRT	Excess risk/10,000
CHD	1.29	7 more events
Breast CA	1.26	8 more events
CVA	1.41	8 more events
PE	2.13	8 more events
Colon cancer	.63	6 fewer events
Hip fx	.66	6 fewer events
Death	.92	

# WHI: Estrogen Only

	RR HRT	Excess risk/ 10,000
CHD	.91	5 less
Breast Ca	.77	7 less
CVA	1.39	12 more
PE	1.34	7 more
Hip Fx	.61	6 less
Death	1.04	

# Estrogen Therapy and Coronary Artery Calcifications in Post Menopausal Women

- Women who had received a hysterectomy randomized to conjugated estrogen vs placebo
- 1079 received a CT to evaluate for coronary artery calcification
- Agatson calcium score 83 for those receiving estrogen vs 123 for those receiving placebo (p=.02)
- The risk of extensive calcification (score > 300) was 40% less in those receiving estrogen
- NEJM 2007;356:2591-2602.

# Questions or Comments

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