

Disinfecting some Infectious Disease Myths



Lack of Disulfiram-Like Reaction with Metronidazole and Ethanol

Jukka-Pekka Visapää, Jyrki S Tiihonen, Pertti S Kaihovaara, and Mikko P Salaspuro

12 male volunteers - double-blind - 5 days of metronidazole or placebo

Then given 0.4 g/kg of alcohol (approx 3 drinks)

Blood acetaldehyde and ethanol concentrations

Vital signs

“This study shows that metronidazole does not have an effect on blood acetaldehyde concentrations when ingested with ethanol and does not have any objective or subjective disulfiram-like properties. However, it is possible that disulfiram-like reaction can occur in some subgroups and by other mechanisms than the inhibition of hepatic ALDH”

Ann Pharmacother 2002;36:971-4

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

Caroline S Williams and Kevin R Woodcock

“Previously published reviews of the medical literature before 1982 found no convincing evidence to support the existence of a disulfiram-like reaction between metronidazole and ethanol, and our review of case reports since that time has found nothing to contradict their findings.”

“Since the clinical consequences of drug-related adverse events can be serious, patients should continue to be advised to avoid ethanol during metronidazole therapy until more conclusive evidence is available.”

Ann Pharmacother 2000;34:255-7

Oral contraceptive efficacy and antibiotic interaction: A myth debunked

Johanna S. M. Archer, MD,* and David F. Archer, MD[†] Charleston, South Carolina, and Norfolk, Virginia

“There are no pharmacokinetic data...to support the contention that oral antibiotic use decreases the efficacy of OCs, except for antituberculosis drugs such as rifampin.

“There are also no prospective, randomized clinical trials of OC efficacy and antibiotic use”

“case reports used to support an effect of antibiotics on OC efficacy are anecdotal and subject to recall bias and lack adequate controls and medication documentation”

J Am Acad Dermatol 2002;46:917-23

β-lactam versus antibiotics with activity against atypical organisms (Mycoplasma, Chlamydia, Legionella)

18 studies - 6,749 subjects

4 unpublished

meta-analysis to compare the efficacy of beta lactam antibiotics with antibiotics active against atypical pathogens in adults with community acquired pneumonia

BMJ (published 31 January 2005)

β-lactam versus antibiotics with activity against atypical organisms (2% overall mortality)

	% failing to achieve clinical cure or improvement
Macrolide	17
β-lactam	20
Quinolone	18
β-lactam	18
Total	18
β-lactam	18

All results NSS

BMJ (published 31 January 2005)

β-lactam versus antibiotics with activity against atypical organisms (found in 7-8% of patients)

	# failing to achieve clinical cure or improvement		
	Mycoplasma	Chlamydia	Legionella
Macrolide/Quinolone	11/152	8/63	4/38
β-lactam	20/159	2/52	15/38
	NSS	NSS	SS

BMJ (published 31 January 2005)

Non-severe community-acquired pneumonia - duration

“there was no difference in the risk of clinical failure between the short-course (7 days or less) and extended-course regimens (>7 days)” - RR 0.89, 95% CI (0.78-1.02)

Am J Med 2007;120:783-90

“The evidence of this review suggests that a short course (three days) of antibiotic therapy is as effective as a longer treatment (five days) for non-severe CAP in children under five years of age. However, there is a need for more well-designed RCTs to support our review findings”

Cochrane CD 005976

Three versus eight days of antibiotics for pneumonia

Patients

119 adults with pneumonia (mild to moderate-severe) who had substantially improved after 3 days of IV therapy - median age 57, approx 60% male,

Treatment

3 days IV amoxicillin followed by placebo or oral amoxicillin for 5 days

Duration

8 days

Results

Cure rates - 3 day (90%), 8 days (88%)

Mild adverse events 3 day (11%), 8 days (21%)

BMJ 2006;332:1355-61

Ciprofloxacin for 7 days vs 14 days

Women with acute pyelonephritis - fever and at least one other symptom - 44 years old - 90% E. coli

7 days or 14 days of cipro 500 mg BID

Clinical and bacteriological outcome 10-14 days after completion of active treatment

248 patients - only 156 assessed - because randomly assigned before a definitive diagnosis was established

Short term/cumulative efficacy - roughly 95% success rate both groups

Side effects - 0 patients in 7 day had mucosal candida infection - 5 in the 14 day group

Lancet August 4, 2012

Cipro 100mg BID x three days

“A number of large, double-blind studies have evaluated the effectiveness of ciprofloxacin 100 mg bid for 3 days for the treatment of acute uncomplicated lower UTI in women”

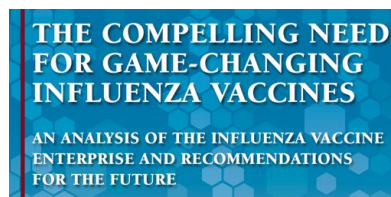
1/4 of a 500 mg tablet twice daily for three days
TWO TABLETS

J Antimicrob Chemother 1999;43 (Suppl. A):85-93

The flu vaccine How well does it work?

New report questions science behind flu vaccine efficacy and use policy

BY HELEN BRANSWELL, THE CANADIAN PRESS OCTOBER 15, 2012



It's all about the numbers

Previous evaluations - 70-90% effective

Every year 1-10% adults get the flu – roughly 5% - therefore chance reduced to 1% - less if unmatched

5-20% per year in children – roughly 10% - therefore reduced to 2%

New report - no new studies - but looked at different diagnostic endpoints – earlier evaluations used studies that used antibodies as the diagnosis – this one used culture

Instead of the effect being 70-90% - they found a 60% effect for the flu shot – nasal spray was 85% effective in children 6 months to 6 years old

5% down to 2% (1%) in adults

10% down to 4% (2%) in children



BMJ

EDITORIALS

A prescription for improving antibiotic prescribing in primary care
Comprehensive education programmes can reduce antibiotic prescriptions, but the impact on clinical outcomes is unclear.
BMJ 2012;344:d7955. doi:10.1136/bmj.d7955 (Published 22 February 2012)
James Macdonald professor, University of Aberdeen; Professor

**If you say it enough
it becomes the truth”**

“a reasonable approach for most primary care infections would be to tell the patient to continue the antibiotic until they have been asymptomatic or afebrile for 72 hours and then to stop”

Other flu evidence

In patients with asthma

No effect seen in reducing exacerbations caused by influenza

In patients with COPD

Does reduce the number of exacerbations

In the elderly – some effect but

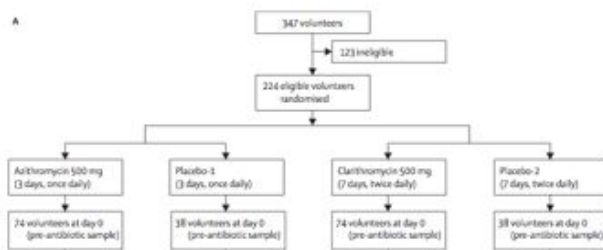
The available evidence is of poor quality BUT SUGGESTS BENEFIT and provides no guidance regarding the safety, efficacy or effectiveness of influenza vaccines for people aged 65 years or older.

How long do we treat?

There is lots of evidence that treatment for longer than 5 days for AECB, otitis media, and GABHS tonsillopharyngitis is unnecessary and increases the chance of adverse effects.

Drugs 2003;63:2169-84

Resistance to macrolides



Lancet 2007;369:482-90

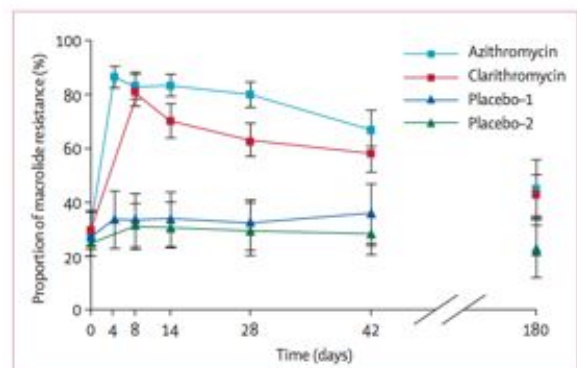


Figure 2: Temporal changes in the proportion of macrolide-resistant streptococci after azithromycin and clarithromycin use
Data shown are for all 204 volunteers followed through to day 42, and for 99 volunteers followed through to day 180. Error bars are 95% CI.

	No history of allergy to sulfonamide antibiotic	History of allergy to sulfonamide antibiotic	History of allergy to penicillin
Reaction within 30 days of a sulfonamide non-antibiotic	1.6%	9.1%	14.6%

N Engl J Med 2003;349:1628-35

A prescription for improving antibiotic prescribing in primary care

Comprehensive education programmes can reduce antibiotic prescriptions, but the impact on clinical outcomes is unclear

James McCormack professor¹, G Michael Allan associate professor²

¹Faculty of Pharmaceutical Sciences, University of British Columbia, BC, Vancouver, Canada V8T1Z2; ²Department of Family Medicine, University of Alberta, AB, Edmonton, Canada

Stemming the Tide of Antibiotic Resistance (STAR) incorporated many of the approaches other reviews have identified as helpful, such as education, feedback, and patient involvement
STAR - reduction of 4.2% (CI 0.6-7.7) fewer oral antibiotics
Cost - \$4713 per practice

- 1) Finland - 50% reduction in use of erythromycin reduced Strep resistance from 17% to 9%
- 2) 5% decrease in amoxicillin - 1% reduction in resistance
- 3) 20% reduction in amp/amox - 1% reduction in resistance

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¹Faculty of Pharmaceutical Sciences, University of British Columbia, BC, Vancouver, Canada V8T1Z2; ²Department of Family Medicine, University of Alberta, AB, Edmonton, Canada

Delayed prescriptions

Delayed prescriptions reduce the proportion of people who receive antibiotics

Upper respiratory tract infections
93% down to 32% - 14% still get them if you don't initially prescribe an antibiotic

Urinary tract infections
97% down to 77%

"Most community acquired infections still respond to the same antibiotics that have been used for decades and many guidelines still support their use"

Sputum colour for diagnosis of a bacterial infection in patients with acute cough

Table 1. Sputum colour and microbiological proof of bacterial infection

	Bacterial infection	No bacterial infection	Totals
Yellowish or greenish sputum sample	22 (16.2%)	114 (83.8%)	136 (100%)
Colourless sputum sample	6 (5.7%)	99 (94.3%)	105 (100%)
Totals	28 (11.6%)	213 (88.4%)	241

"Our study confirms that the colour of sputum or discharge cannot be used in the consultation with otherwise healthy adult patients suffering from acute cough to differentiate between viral and bacterial infections. Thus it should not be used to make a decision on the choice of therapy and especially not on whether to prescribe an antibiotic"

Scandinavian Journal of Primary Health Care 2009;27:70-3

Sputum colour and bacteria in chronic bronchitis exacerbations: a pooled analysis

Marc Miravittles^a, Frank Kruesmann^a, Daniel Haverstock^a, Renee Perroncel^a, Shurjeel H. Choudhri^a and Pierre Arvis^b

4,003 sputum samples
Pathogen identified
green - 59%
yellow - 46%
rust - 39%
white - 18%

"patterns of colours were similar for all species isolated; therefore no specific colour can be associated with a given microorganism"

"it should be noted that the presence of a microorganism in the sputum does not confirm its role as a cause of an exacerbation"

Eur Respir J 2012;39:1354-60

Pneumonia

Mechanism - reduce acid - organisms survive in the stomach - reflux - micro-aspiration - pneumonia

data not really strong

2004 - 4.5 times higher - 1 per 226 patients

2009 - 1.3 times higher - 2.5% absolute increase

Cleveland Clinic J Med 2011;78:39-49



C. difficile infections

C difficile - 23 studies - case control and cohort studies
Overall RR is 1.69 (1.40–1.97)

Am J Gastroenterol advance online publication, 19 June 2012; doi:10.1038/ajg.2012.179

42 studies - case control and cohort studies
1.74 (1.47-2.05)
Am J Gastroenterol 2012;107:1011-9

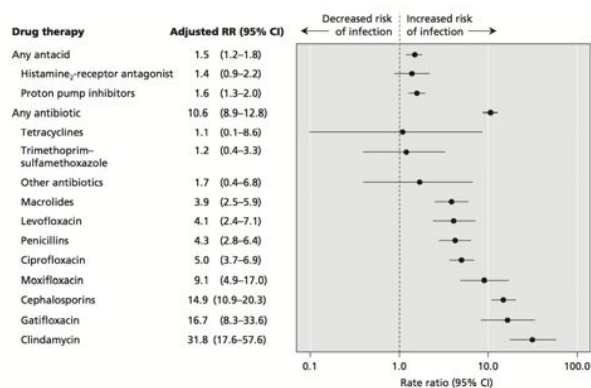
Hospitalized - chance of C.difficile infection

Non-PPI users ~1.5%

PPI users ~ 3% - likely less (2-2.5%) on H₂RA

Community patients - risk about 1/1000

Am J Gastroenterol 2012; 107:1011–1019; doi:10.1038/ajg.2012.108; published online 24 April 2012



CMAJ 2008;179:767-72

Adding aminoglycosides to β -lactams

“no clinical benefit was found for the use of a β -lactam with an aminoglycoside compared with a β -lactam alone”

Populations Studied

1. Immunocompetent patients with sepsis
2. Cancer patients with neutropenia
3. Patients with infections caused by *Pseudomonas*

Cochrane reviews, Int J Antimicrob Agents 2011;37:491-503

A Critical Reevaluation of the “Therapeutic Range” of Aminoglycosides

James P. McCormack and Peter J. Jewesson

From the Faculty of Pharmaceutical Sciences, University of British Columbia; the Department of Pharmacy, St. Paul's Hospital; and the Department of Pharmacy and Division of Infectious Diseases, Department of Medicine, Vancouver General Hospital, Vancouver, British Columbia, Canada

Clin Inf Dis 1992;14:320-39

“After a critical review of the literature, it was concluded that the evidence was insufficient to support the presently accepted normal therapeutic range.”

ALTERNATIVE VIEWPOINTS

Pharmacotherapy 2000;20:1524-7

An Emotional-Based Medicine Approach to Monitoring Once-Daily Aminoglycosides

James P. McCormack, Pharm.D.
(Pharmacotherapy 2000;20(12):1524-1527)

“no clinical trials show or suggest that monitoring of serum aminoglycoside concentrations for ODA is of benefit.”