SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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Power, violence, and HIV in women

Agencies charged with controlling HIV should develop strategies to redistribute power within sexual relationships and prevent violence against women, say researchers. Lack of power in relationships and violence were both independently associated with incidence of HIV in a cohort of young poor South African women (incidence rate ratio for women with "low power equity" 1.51, 95% CI 1.05 to 2.17; IRR for women reporting violence 1.51, 1.04 to 2.21). Lack of power accounted for an estimated 13.9% (2.0 to 22.2) of new infections in this study. Violence by intimate partners accounted for 11.9% (1.4 to 19.3).

All 1099 women were HIV negative at the start of the study, and 128 women acquired HIV during follow-up. Analyses were adjusted for age, sexual behaviour, and infection with herpes simplex virus type 2 (HSV2). The researchers are confident that their findings are real, not statistical artefact. The link between power, violence, and HIV in young women may be causal, and trials should be done to test decisively whether empowering young women and tackling abusive male behaviour prevents HIV. These women had a mean age of 18.

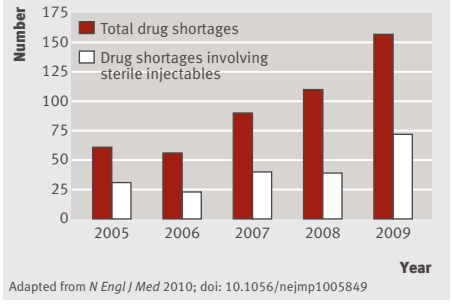
Women in violent relationships are in double jeopardy, says a linked comment (doi:10.1016/S0140-6736(10)60971-3). Their partners are more likely than other men to acquire HIV and more likely to transmit the infection. The US has already pledged $30m (£20m; €24m) to design and test programmes to prevent abuse, says the comment. Hopefully more money will follow. Changing entrenched cultural norms that place men firmly in control of sex may be harder.

Lancet 2010; doi:10.1016/S0140-6736(10)60548-X

FDA urges action on drug shortages

The US drugs regulator has urged doctors and other health professionals to report drug shortages by email, so it can act quickly to find alternative supplies of essential medicines. Figures from the Food and Drug Administration (FDA) suggest that shortages are on the increase in the US, particularly shortages of sterile injectable drugs, including anaesthetics. Supplies of propofol, a widely used induction and maintenance anaesthetic, became critical earlier this year when two of the three US manufacturers had to withdraw from the market—one of them permanently. The FDA is temporarily allowing unlicensed imports to plug the gap. An article by experts at the FDA's drug shortages programme also reports recent shortages of popular neuromuscular blocking drugs, intravenous metoclopramide, prochlorperazine, and ephedrine.

DRUG SHORTAGES IN THE US



Adapted from *N Engl J Med* 2010; doi: 10.1056/nejmp1005849

Drug shortages can have a profound effect on patient care, says the article. Complex manufacturing processes and limited suppliers are at least partly to blame. But the wider economic reality is that drugs become cheaper when their patents expire. Although the savings can be good news for healthcare providers and patients, it is not so good for manufacturers, who can and do look elsewhere for profits.

Regulators cannot force companies to maintain supplies of a particular drug. But they can take other remedial action if potential shortages are picked up and reported quickly by doctors, institutions, or the industry.

N Engl J Med 2010; doi:10.1056/nejmp1005849

Slim pickings from research on the determinants of cognitive decline

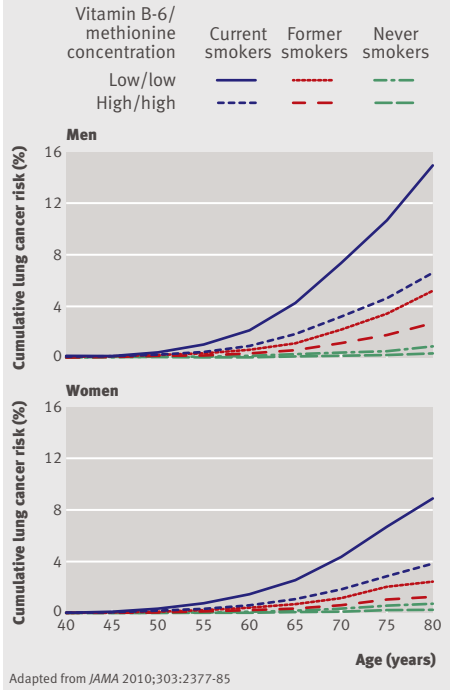
Middle aged adults who want to know how to protect cognitive function as they get older will be disappointed by the available evidence. Researchers have studied dozens of nutritional, pharmaceutical, social, environmental, lifestyle, and genetic factors that might influence cognition in later life. High quality evidence supports just one: a single randomised trial reported a small but sustained benefit of cognitive training. Reviewers found low quality evidence linking apolipoprotein E e4 genotype, diabetes, smoking, metabolic syndrome, and depression with cognitive decline. And more low quality evidence linked a healthy diet, omega 3 fatty acids, and exercise with decreased risk.

Among 22 trials, 16 systematic reviews, and 127 observational studies, reviewers found very little to inform concrete recommendations, partly because studies were so diverse. Researchers used different definitions of cognitive decline, studied multiple exposures (variously defined), and studied populations that sometimes included people with cognitive impairment. Adjustments were often inadequate and power under reported, so many negative studies were unreliable. After a lot of hard work the reviewers concluded that "critical improvements in research methods are needed." Once achieved, they should be applied to the few hopeful leads to come out of this review—brain training, exercise, and nutrition.

Ann Intern Med 2010; online 15 June; www.annals.org/content/early/2010/06/11/0003-4819-153-3-201008030-00258.full?aimhp

Vitamin B-6 and methionine are linked to risk of lung cancer

CUMULATIVE RISK OF LUNG CANCER IN MEN AND WOMEN



Adapted from *JAMA* 2010;303:2377-85

Lung cancer is a leading cause of death worldwide, and most of it is caused by smoking. Low serum concentrations of vitamins B-6 and methionine are also associated with lung cancer, say researchers, who found the link in a large European cohort of mostly middle aged adults.

"If you are the monozygotic twin of a baby with pyloric stenosis, your risk of needing a pylorotomy is increased about 200-fold. Even if you're just a half cousin, your chances of enriching the soil . . . with a projectile offering of curdled milk go up by about 60%."
Richard Lehman's journal blog, doc2doc.bmj.com

In a case-control analysis, adults with the highest serum concentrations of vitamin B-6 at recruitment were half as likely to develop lung cancer as those with the lowest concentrations (adjusted odds ratio comparing top quarter with bottom quarter 0.44, 95% CI 0.33 to 0.60). Results were similar for methionine (0.52, 0.39 to 0.69).

The researchers tried hard to isolate the effects of B-6 and methionine from the dominating presence of smoking, by adjusting their analyses for cotinine concentrations and by doing separate analyses for current smokers, former smokers, and never smokers. The results were consistent.

Serum concentrations of B-6 and methionine should be modifiable in theory, although the researchers caution against trials of supplements. Previous trials of vitamin B supplements haven't prevented cancers, including lung cancers, and may have encouraged growth of pre-existing disease. Dietary intake of B-6 was not associated with cancer risk in this study. Variations in absorption, distribution, and metabolism may have a greater effect on serum concentration of these nutrients than straightforward dietary intake, say the researchers.

JAMA 2010;303:2377-85

Protecting the babies of women with HIV

Breast feeding is an important route for HIV infection in infants born in sub-Saharan Africa. Two new trials tested a total of five different drug regimens—four for mothers and one for infants—in an attempt to prevent transmission. All of them worked.

In the first trial, a triple drug regimen for HIV infected mothers and a single drug regimen (nevirapine) for their HIV negative infants both helped prevent HIV transmission during 28 weeks of breast feeding. The experimental regimens were started after delivery and after all mothers and babies had received the same perinatal prophylaxis. The second trial compared three drug regimens for HIV infected women, all starting in the last trimester of pregnancy. All were associated with effective viral suppression in mothers. More than 90% of women in the three groups had viral RNA counts below 400 copies per millilitre at delivery and throughout breast feeding. Just 1% of live born infants were infected at six months (8/709). Only two were infected during breast feeding. These are the lowest transmission rates ever reported in Africa, says an editorial (p 2316). All infants in the trial were given a dose of nevirapine at birth, followed by four weeks of zidovudine.

The choice of regimen may be less important than the timing, says the editorial. Ideally, antiretroviral treatment should begin in pregnancy and continue during breast feeding. The World Health Organization already recommends this approach, and health professionals should not wait for more precise guidance. Women with HIV need treatment and their babies need protection, sooner rather than later.

N Engl J Med 2010;362:2271-81, 2282-94

Which NSAID strategy best protects the lower gut?

Non-steroidal anti-inflammatory drugs (NSAIDs) are well known for their upper gastrointestinal side effects, but less so for their potential to damage the gut below the duodenum. Lower gastrointestinal side effects are less common but can be just as serious and include bleeding, ulceration, and perforation.

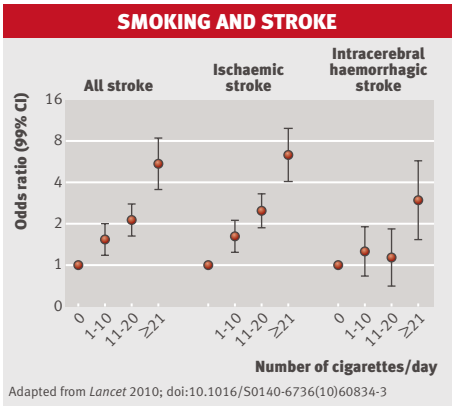
Strategies to minimise risk to the upper gut mucosa include use of NSAIDs that selectively inhibit cyclo-oxygenase-2 (COX 2), or use of a traditional NSAID plus a proton pump inhibitor. The manufacturer of celecoxib, Pfizer, recently compared the two strategies in one of the first trials to look for adverse events throughout the whole gastrointestinal tract.

Celecoxib looked safer than diclofenac plus omeprazole for high risk patients with arthritis. Researchers reported 20 gastrointestinal events over six months in 2238 patients given celecoxib (0.9%) and 81 events in 2246 patients given diclofenac and omeprazole (3.8%; hazard ratio 4.3, 95% CI 2.6 to 7.0). So should high risk patients switch to a COX 2 inhibitor?

Not yet, says a linked comment (doi:10.1016/S0140-6736(10)60839-2). The difference was driven not by haemorrhages or perforations, but by a reduction in the number of patients in the celecoxib group that developed "clinically significant anaemia" (15 *v* 77). Researchers failed to find the source of the bleeding in most of these patients, so changes to practice would be premature. This trial wasn't powerful enough to establish the relative cardiovascular risks of the two treatment options. People taking aspirin were excluded.

Lancet 2010 doi:10.1016/S0140-6736(10)60673-3

Known risk factors explain most strokes worldwide



Adapted from *Lancet* 2010; doi:10.1016/S0140-6736(10)60834-3

High blood pressure, smoking, abdominal obesity, unhealthy eating habits, and lack of exercise accounted for more than four fifths of all strokes in an epidemiological study from 22 countries (population attributable risk 83.4%, 99% CI 77.7 to 87.8). Hypertension was the most important risk factor everywhere, including low and middle income countries of South America, South East Asia, Africa, and India. Smoking was also universally associated with strokes, both ischaemic and haemorrhagic. Controlling smoking and blood pressure should be a priority for policy makers in developing countries where most strokes occur, says a linked comment (doi:10.1016/S0140-6736(10)60975-0).

This analysis of 3000 cases of acute stroke and 3000 matched controls fine tunes the size of the risk associated with well known determinants of stroke, and it lists the top 10 that together explain more than nine out of 10 strokes worldwide. In addition to the five above they are: alcohol intake (more than 30 drinks a month), stress and depression, diabetes, cardiac causes of stroke such as atrial fibrillation, and the balance of apoliproteins in the blood (90.3%, 85.3 to 93.7).

Alcohol intake was more consistently associated with haemorrhagic stroke than with ischaemic stroke. The link between serum lipids and stroke was more complex. The balance of apolipoproteins looked more important than the balance of traditional serum lipids such as high density lipoprotein cholesterol, low density lipoprotein cholesterol, and total cholesterol.

Lancet 2010l; doi:10.1016/S0140-6736(10)60834-3

Cite this as: *BMJ* 2010;340:c3296