Short cuts

What's new in the other general journals

Atomic bombs leave a long legacy of benign as well as malignant thyroid disease

DOSE-RESPONSE FOR THYROID DISEASES

Sixty years after atomic bombs dropped on Hiroshima and Nagasaki, researchers are still studying the effects of radiation exposure on the local population. In the latest cross sectional study of survivors, over half the women (1397/2739, 51%) and nearly a third of the men (436/1352, 32%) had thyroid disease, and 15% of the whole cohort had solid nodules, 2% had cancers (mostly papillary), and 8% had benign cysts.

Using sophisticated techniques to measure radiation exposure and equally sophisticated techniques to look for thyroid disease, the researchers found a clear link between radiation dose and the prevalence of all thyroid nodules. They estimated that

37% of cancers, 31% of benign nodules, and 25% of thyroid cysts in this elderly cohort were caused directly by radiation from the two bombs. Survivors aged under 10 at the time seemed most vulnerable, presumably because their thyroid glands were more radiosensitive than those of young adults.

The researchers found no dose-response relation between radiation dose and autoimmune thyroid disease, however, which tips the weight of evidence against a causal link between the two.

JAMA 2006;295:1011-22

New vaccine protects young children against otitis media

European scientists have developed a new vaccine that seems to protect young children against otitis media. The vaccine contains antigenic material from 11 different serotypes of *Streptococcus pneumoniae*, each one carried by a protein derived from *Haemophilus influenzae*. Between them, these pathogens are the most important causal agents of otitis media in young children.

In a randomised trial, the new vaccine reduced by about a third the overall incidence of otitis media among children under 2 years in the Czech Republic and Slovakia (333/2455, 14% v 499/2452, 20%). The 2455 vaccinated children were 57.6% (95% CI 41.4 to 69.3) less likely to develop otitis media caused by *S pneumoniae* and 35.3% (1.8% to 57.4%) less likely to develop otitis media caused by *H influenzae* than control children, who were vaccinated instead against hepatitis A.

The new vaccine schedule included injections at 3, 4, and 5 months of age, followed by a booster at 12-15 months. Fourteen adverse events were related to the vaccines, seven in each group. Side effects caused by the new vaccine included fever, vomiting, agitation, and purpura; all resolved spontaneously. The trial was designed, sponsored, and analysed by the manufacturers, GlaxoSmithKline.

Lancet 2006;367:740-8

Natalizumab is a potent treatment for multiple sclerosis but may not be safe

Two large trials reported last week on the benefits of the monoclonal antibody natalizumab for patients with relapsing multiple sclerosis. The treatment worked in

both trials, reducing the risk of relapse, reducing disability, and slowing progression of the disease by a substantial and significant margin compared with placebo. The monoclonal antibody seemed to work on its own (reducing the risk of relapse by 68% over one year) and in combination with interferon beta, a current standard treatment.

Worries remain about serious side effects, however, particularly multifocal leucoencephalopathy, a progressive and potentially lethal brain disease caused by the human JC virus. Natalizumab prevents activated T cells from sticking to endothelial surfaces, reducing the inflammatory component of multiple sclerosis plaques. When three patients treated with the drug developed multifocal leucoencephalopathy (two of them in the combined treatment trial), experts assumed that an opportunistic virus had taken advantage of reduced lymphocyte traffic to the brain. The manufacturers voluntarily suspended natalizumab in February last year after only four months on the market, one month before the scheduled end of the combined treatment trial.

In a third study (pp 924-33) researchers found no further cases among 3116 patients treated with natalizumab during other trials. A linked editorial (pp 965-7) says natalizumab looks like a potent and effective treatment for multiple sclerosis but may not be safe in the long term, particularly when combined with interferon beta. The risk of multifocal leucoencephalopathy seems to be about one in 1000 patients treated for 18 months.

N Engl J Med 2006;354:899-910, 911-23

Subclinical hypothyroidism does not cause heart disease in older Americans

We already know that an excess of thyroid hormone causes atrial fibrillation and other disturbances of heart rate and rhythm. Controversy continues about the role of thyroid dysfunction in other kinds of cardiovascular disease, especially coronary heart disease. In an attempt to resolve the issue, US researchers looked for associations between thyroid dysfunction and cardiovascular disease or death in a community based cohort of 3233 Americans aged 65 or over who were tested for thyroid disease at recruitment, then followed up for nearly 13 years.

As expected, the researchers found that men and women with subclinical hyperthyroidism were more likely to develop atrial fibrillation than those who were euthyroid at baseline (hazards ratio 1.98; 95% CI 1.29 to 3.03). People with clinical or subclinical hypothyroidism at baseline were, however, no more likely to develop new or recurrent coronary heart disease or cerebrovascular disease than the euthyroid group. Euthyroid and hypothyroid participants had comparable all cause and cardiovascular mortality rates during follow-up. Researchers defined subclinical hypothyroidism as a serum concentration of thyroid stimulating hormone between 4.5 mU/l and 20 mU/l with a normal concentration of free T₄ (thyroxine).

These essentially negative findings stood firm through various analyses and adjustments, which the authors say makes them more trustworthy than the conflicting findings of many previous studies. In this cohort, however, only 51 participants had clinical hypothyroidism, so the negative findings in this group may be less trustworthy than the rest.

JAMA 2006;295:1033-41

Community acquired MRSA reveals its secret weapons

A team of researchers from the US has sequenced the entire genome of a strain of community acquired methicillin resistant *Staphylococcus aureus* (MRSA). The bacterium, known as USA300, is already widespread in the US and is emerging in Europe and Canada, according to a commentator based in London (pp 705-6). Embedded in its sequence scientists found the cluster of genes that probably give the pathogen its remarkable ability to evade host responses and get deep into tissues. The cluster seems to have originated in the harmless skin commensal *S epidermidis*, then spread to USA300, where it now sits close to the region responsible for drug resistance. This kind of gene sharing is a bad habit of staphylococci. USA300 is particularly dangerous because it can cause epidemics. The scientists also found in USA300 a "pathogenicity island" encoding for two powerful enterotoxins, the mediators responsible for toxic shock.

So now that we know what it's made of, are the days of this "uniquely threatening" pathogen finally numbered? A genomic sequence is a good start, says an editorial (p 704). But it could take a while for researchers to translate it into effective weapons against this and other MRSA. "Until then, keep washing those hands."

Lancet 2006;367:731-9

US soldiers report poor mental health on return from Iraq

Mental health services for the US military are being stretched to the limit by the war in Iraq, warn researchers after their observational study found that nearly one in five returning veterans had mental health problems.

All US soldiers coming home from war zones fill in a health questionnaire that includes screening questions about post-traumatic stress disorder, depression, and suicidal ideation. Completed questionnaires are held on a database that also records healthcare visits and demographic and employment data.

An analysis of database records from 303 905 soldiers and marines returning from Iraq, Afghanistan, and other locations such as Bosnia and Kosovo found that Iraq veterans were significantly more likely to screen positive for mental health problems than other veterans (Iraq 19% (42 506/222 620), Afghanistan 11.3% (1843/16 318), others 8.5% (5534/64 967)). Nearly one in 10 Iraq veterans screened positive for post-traumatic stress disorder, and one in 100 reported suicidal ideation. In the year after they got back, 35% of all Iraq veterans accessed the army mental health services.

In this study, mental health problems among Iraq veterans were associated with active combat and with hospitalisation in the war zone. In the year after their deployment, 17% of Iraq veterans left the army—an attrition rate significantly higher than the rate among veterans from other locations.

JAMA 2006;295:1023-32

Pulmonary vein ablation restores sinus rhythm in some patients with chronic atrial fibrillation

Pulmonary vein ablation is already an established treatment for paroxysmal atrial fibrillation. It can also restore sinus rhythm in some patients with chronic atrial fibrillation, according to a randomised trial. The 146 participants were young (mean age 57) and relatively fit. None had prosthetic heart valves. Very few had coronary heart disease (7 patients) or other structural abnormalities such as diseased valves (1) or congenital heart disease (1). But the 77 who were treated with pulmonary ablation were significantly more likely than controls to be in sinus rhythm one year later (57/77 (74%) v 40/69 (58%); $P = 0.05$).

All the patients in this trial had chronic and refractory atrial fibrillation. Patients in both groups had three months' treatment with amiodarone. Controls had cardioversion, as did 18 of the 77 patients who had pulmonary ablation. In the end, three quarters of controls crossed over to pulmonary vein ablation, because so few responded to medical treatment and cardioversion. Only 4% (3) of controls who did not cross over were in sinus rhythm one year after cardioversion.

These results are encouraging, says a linked editorial (pp 967-9). But they probably won't apply to most patients with chronic atrial fibrillation—who tend to be older, sicker, and more likely to have structural heart disease than the participants in this trial. More needs to be done before this procedure finds its way into standard practice.

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