Short cuts

What's new in the other general journals

Learning from Lance Armstrong: heat treatments for cancer

After cyclist Lance Armstrong survived advanced metastatic testicular cancer he went on to become one of the world's most successful athletes. Many others have also made dramatic recoveries from testicular cancer when, stage for stage, tumours from any other site would have killed them. What makes testicular cancer so easy to treat? One theory is that testicular cancer cells, like normal testicular germ cells, are very sensitive to heat. Once they spread inside the body away from the cooling protection of the scrotum, the cancer cells become weaker and potentially more sensitive to cancer treatments such as radiation or cytotoxic chemotherapy.

The theory, otherwise known as the Lance Armstrong effect, is certainly biologically plausible, according to three cancer scientists from the United States. Heat is an important regulator in many biological systems, including cancers, although heat treatments have always been impracticable because of the potential for collateral damage. Now technologies are at last emerging that could help bring thermal therapy for cancer within reach, write the scientists. One of them uses nanoparticles filled with magnetic iron that can be heated up with an external magnetic field once they reach their target. The hope is that thermal therapy will make cancer cells more vulnerable to established treatments including immunotherapy, thereby extending the remarkable Lance Armstrong effect to patients with other disseminated tumours.

JAMA 2006;296:445-8

Faulty cardiac devices are often best left alone

About two million people worldwide have an implantable cardiac device such as a pacemaker or cardioverter defibrillator. Defects noticed after marketing have led to recalls or warnings affecting about 200 000 of the devices. Few data exist on what happens to people with defective devices, so researchers are reduced to guesswork and mathematical modelling to help them decide whether to risk replacing the devices.

The latest study concludes that it's often safer to leave well alone. Using Markov modelling, the researchers calculate that for patients who depend on their pacemaker, the defective device should be left in unless the risk of failure exceeds 0.3%. For patients with cardioverter defibrillators, the risk of failure should probably exceed 3% before most patients would benefit from a replacement. If the device was put in for a condition that is not life threatening (such as an oversensitive carotid sinus) then replacement isn't justified for most people, whatever the warning says about the likelihood of device failure.

These are necessarily rough figures for doctors to use as a starting point in what can be difficult discussions with patients, say the authors. The researchers were unable to estimate the psychological impact of living with a potentially faulty device.

JAMA 2006;296:412-20

New test may simplify risk assessment for venous thrombosis

Anticoagulant treatment for unprovoked venous thromboembolism usually lasts a few months. Some patients need more treatment because their risk of further thrombosis is greater than their risk of a serious bleed. But identifying those patients can be difficult. One simple possibility is to measure the generation of thrombin, say researchers from Austria. Their study of 914 patients with a first venous thrombosis (deep vein thrombosis or pulmonary embolism) showed that this one laboratory measurement can divide patients reasonably accurately into those more or less likely to have another thrombosis and can inform the decision about which patients should keep taking their anticoagulants.

The study was confined to patients with no underlying cause for their clot and excluded patients who'd had cancer, had been pregnant, had experienced trauma, or

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had surgery within the previous three months. People with protein S, protein C, or antithrombin deficiencies were also excluded. Among the rest, the risk of another thrombus within four years of the first was only 6.5% (95% CI 4% to 8.9%) in patients whose thrombin generation peaked below 400 nM, compared with 20% (14.9% to 25.1%) in patients whose thrombin generation peaked higher than 400 nM. Two thirds of the patients in this study were in the low risk cohort.

The researchers hope their findings will eventually help to simplify risk assessment in patients with venous thrombosis, a process that is currently complicated, expensive, and often inconclusive.

JAMA 2006;296:397-402

New trial clarifies antiretroviral therapy for HIV

Patients with HIV infection are usually treated initially with a regimen of three drugs. Treatment guidelines recommend that at least two of them should be nucleoside analogue reverse transcriptase inhibitors. But for the third, patients and their doctors can choose either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor. This third drug accounts for most of the variation in treatment for HIV, and researchers are still trying to establish the best option.

The latest trial favoured the non-nucleoside reverse transcriptase inhibitor efavirenz, which seemed to work better over three years than the protease inhibitor nelfinavir and also worked better than the combination of both these drugs. Patients given efavirenz had a significantly better virological response—in 74% of these patients the viral load was undetectable compared with 62% for each of the other groups. Additionally, they were significantly less likely to stop treatment for more than a

month. All patients started the trial taking didanosine and stavudine.

Choice of treatment had no impact on CD4 count, however, and the researchers found similar numbers of new AIDS illnesses and deaths in each group. There was little to choose between the treatments with respect to side effects, although the time between start of regimen and the reporting of any side effects that required treatment modification was shorter among patients taking four drugs than among patients in either of the groups taking three (74 weeks *v* 111 for efavirenz and 131 for nelfinavir; *P* = 0.03).

Lancet 2006;368:287-98

Clinically relevant research deserves higher priority in UK

Recent proposals to unify public funding for medical research in the United Kingdom present a golden opportunity to redress the current imbalance between basic science research, which is overwhelmingly popular, and research that matters in clinical practice, which is badly neglected—writes a leading stroke researcher from Oxford.

Many factors explain why disease prevention, diagnosis, and treatment have taken a back seat for so long. The excitement of new genetic technologies and the unfulfilled promises of molecular medicine are at least partly to blame, but it's also possible that the people setting the research agenda are simply unaware of the pressing need for research with an immediate practical pay-off, he writes. The agenda setters may also have a fundamentally different notion of "clinical research" from practising doctors and other consumers, who are unlikely to include in that definition the sequencing of genomes or the development of DNA technology.

Only a small fraction of research funding outside the drug industry goes to practice oriented research, and any new funding arrangements must give such research the priority it deserves, concludes the author, saying, "While it is imperative

that high quality basic science is not undermined, we have been unwise in the past to put quite so many of our eggs in the laboratory basket."

Lancet 2006;368:262-6

Statins probably reduce proteinuria

Statins have well known effects on serum lipids and cardiovascular risk. They probably also help to protect vulnerable kidneys by reducing proteinuria. In a meta-analysis of 15 placebo controlled trials, treatment with statins reduced proteinuria or albuminuria by almost half in people whose kidneys were leaking more than 30 mg a day. The trials lasted a mean of 24 weeks and included a total of 1384 people. More than half (57%) had diabetes and about a quarter had renal disease. Most of the trials tested simvastatin or pravastatin (five and four respectively).

These findings are consistent with what we already know about the renal effect of statins and, if true, could be due to improvements in endothelial dysfunction, better renal perfusion, and a decrease in vascular permeability to plasma proteins. But the authors and a linked editorial (pp 147-9) agree that conclusions are limited by the weaknesses in individual trials. Generally, the trials were small, heterogeneous, and badly done, with a mean quality score of only 3 out of a possible 8. There's still need for bigger and much better trials, preferably testing whether statins can preserve renal function and delay the onset of end stage renal failure.

Ann Intern Med 2006;145:117-24

Can your patient read?

Doctors should be more aware of adult illiteracy, a common problem that makes it hard for patients to follow the instructions on their pill packaging, understand their diagnosis, or navigate successfully through complex healthcare systems that depend on the written word to function. Well educated

doctors rarely consider whether their patients can read, writes one general physician from the United States, and patients rarely tell them because "nobody wants to look dumb, especially not in front of their doctor." But large surveys estimate that one in seven adult Americans cannot read well enough to get even basic information from written text. The situation is even worse for older adults—about a quarter of Americans aged over 64 cannot decipher food or drug labels, and a third have such poor numeracy that they couldn't compare prices in the shops.

People who can't read have worse health than people who can, although it's still unclear exactly how much of their ill health is directly attributable to being illiterate. Some experts say that health professionals should screen patients for poor reading ability, others say it's better to assume it and adapt consultations accordingly, writes the physician. Videotapes, colour coded medication, simple information, and adult literacy programmes may all help. But as a start, health professionals should simply think twice before jotting down those important instructions on a piece of paper.

N Engl J Med 2006;355:339-41

Inhaled nitric oxide remains unproved for premature babies

Despite a promising start and several years of active research, inhaled nitric oxide remains an experimental treatment for preterm babies that should be reserved for the controlled environment of clinical trials, says an editorial. Commenting on two recent trials published in the same journal, the editorial concludes that inhaled nitric oxide is still of unproved benefit, has the potential to cause harm, and costs \$3000 (£1600; €2360) a day, making it one of the most expensive treatments available for children.

Both placebo controlled trials included babies weighing between 500 g and 1200 g at birth who were mechanically ventilated. In one trial, inhaled nitric oxide for 24 days improved survival to 36 weeks without bronchopulmonary dysplasia (43.9% *v* 36.8%; *P* = 0.042) but only in those babies who began treatment between seven and 14 days after delivery (pp 343-53). In the other trial, three weeks of inhaled nitric oxide did not save lives or prevent bronchopulmonary dysplasia, except possibly in the minority that were born weighing between 1000 g and 1250 g (pp 354-64).

Although these trials suggest that nitric oxide can work for some preterm babies, it's unclear which babies are most likely to benefit, says the editorial. There's also more work to be done on the dose, timing, duration, and long term safety of treatment.

N Engl J Med 2006;355:404-6

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