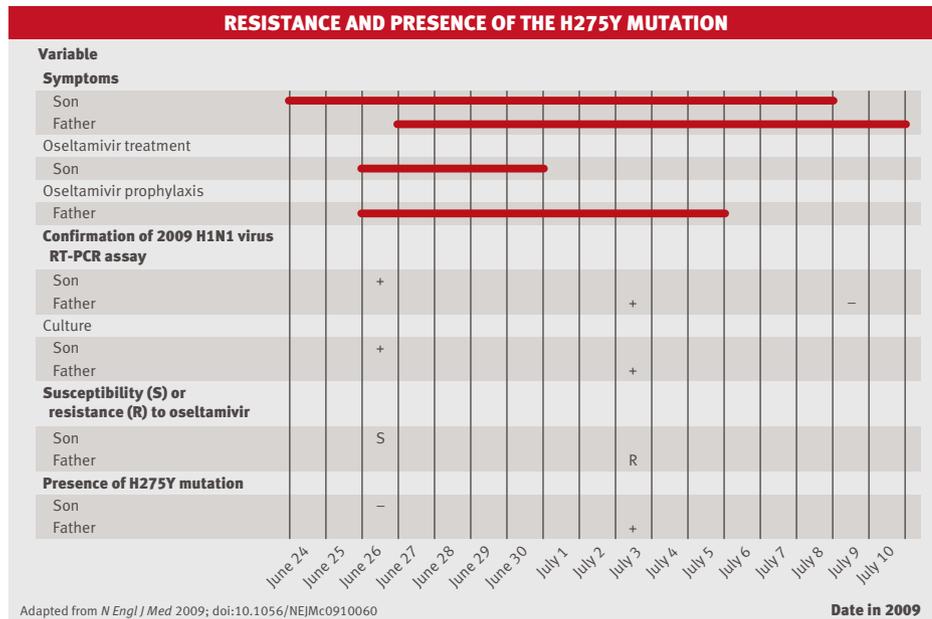


SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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Resistant swine flu emerges in Canada

Doctors in Quebec, Canada, report the emergence of pandemic influenza resistant to oseltamivir in a 59 year old man. He began taking oseltamivir after his son developed laboratory confirmed pandemic H1N1 influenza A (swine flu). Twenty four hours later the man developed symptoms himself. A nasopharyngeal aspirate taken at the end of the week contained the same pandemic strain of H1N1 that infected his son. But whereas the son's virus had been completely susceptible to oseltamivir, the father's virus was completely resistant. Genotyping detected a single substitution in the neuraminidase protein—oseltamivir's target. The mutant protein was 400 times more resistant than the wild-type protein. The man made a full recovery and didn't infect anyone else in the household.

This mutation is already familiar to influenza surveillance authorities in the US, who noticed a spike in its prevalence during the last two flu seasons.

The doctors treating this case suspect that resistance emerged because the man was taking a subtherapeutic dose (75 mg once a day) of oseltamivir during early viral replication. They suggest that people taking prophylaxis should switch to a higher therapeutic dose as soon as they get symptoms. There may also be a case for further restrictions on post-exposure prophylaxis.

N Engl J Med 2009 doi:10.1056/NEJMc0910060

Statins linked to lower risk of gallstones

An analysis of data from more than 130 000 primary care patients in the UK suggests that statins are associated with a reduced risk of symptomatic gallstones. The link emerged in adults taking any statin for more than a year, and it seemed to get stronger with longer use.

The researchers began with 27 035 primary care patients with a record of gallstones and cholecystectomy on a national research database. These cases were compared with 106 531 controls with no record of gallstones. After multiple adjustments, adults currently using statins had a 22% lower odds of gallstones than adults not using statins (odds ratio 0.78, 95% CI 0.73 to 0.83). The odds ratio was 0.85 (0.77 to 0.93) for adults with five to 19 prescriptions for statins and 0.64 (0.59 to 0.7) for adults with at least 20 prescriptions. The link was evident for men and women, and for adults over and under 60 years.

The authors ruled out confounding by age, sex, body mass index, smoking, comorbidities and use of oestrogen, but they were unable to adjust for social factors such as poverty. They emphasise that these observations, however well analysed, can't establish cause and effect. The study was independent of any funding from companies manufacturing or marketing statins.

JAMA 2009;302:2001-7

Litigation uncovers biased reporting of gabapentin trials

Research documents made public during legal proceedings against drug manufacturers provide useful insights into the subtle (and often advantageous) changes that can occur between the protocol stages of a trial and final publication. When researchers recently scrutinised industry sponsored trials evaluating off-label use of gabapentin, they found that in eight of 12 trials the primary outcome in the published paper was different from the primary outcome specified in the protocol. In five trials, primary outcomes specified in the protocol were missing from the published paper. In six trials, the published paper reported a completely new primary outcome. In two trials, the primary outcome specified in the protocol was relegated to a secondary outcome in the published paper. The treatment effect (measured by the P value) and the primary outcome matched in just one of nine trials that were published in full.

Secondary outcomes were even less consistent—122 of the 180 secondary outcomes listed in trial protocols were omitted from published reports.

This kind of selective reporting isn't confined to industry sponsored trials, say the authors, but it generally distorts the published evidence in favour of the treatment under investigation—in this case gabapentin. Systematic reviews should be updated when protocols and unpublished trials are released through litigation. In the meantime, journal publication "should not be used as a marketing tool for off-label drug use."

N Engl J Med 2009;361:1963-71

Chronic pain often follows surgery for breast cancer

In a new survey almost half (47%) of Danish women reported having enduring pain two years after surgery for breast cancer. Among 3253 women, 733 had light pain, 595 had moderate pain, and 201 had severe pain in the breast, axilla, arm, or side. Fifty eight per cent (1882/3253) of respondents reported sensory disturbances or discomfort.

Younger women were more likely to report pain or sensory disturbances than older ones. So were women who had had an axillary

lymph node dissection (adjusted odds ratio for pain relative to sentinel lymph node biopsy 1.77 (95% CI 1.43 to 2.19)). Radiotherapy was associated with pain, but not sensory disturbances. Type of surgery was not associated with either, after adjustments for age and other treatments. The survey had a response rate of 87% (3253/3754).

These figures are the most reliable so far, says an editorial (p 2034), and they confirm other work on chronic pain after breast surgery. Around half of women experience chronic pain or sensory disturbances, such as numbness paraesthesia, phantom breast sensations, or burning. Nerve damage caused by surgery or radiotherapy is one explanation, but doctors treating women with chronic pain should also consider brachial plexus compression from lymphadenopathy or infiltration by tumour tissue, carpal tunnel syndrome, or a second primary tumour. Only a fifth of the women reporting pain in this survey consulted a doctor (306/1543). A quarter took analgesics, and about the same proportion tried other treatments such as physiotherapy or massage. *JAMA* 2009;302:1985-92

Waiting times rise steadily in US emergency departments

A time trends analysis has confirmed that US emergency departments are struggling to cope with increasing numbers of patients. Median waiting times in a

nationally representative sample of departments increased steadily from 22 minutes in 1997 to 33 minutes in 2006, with the biggest increases for the sickest patients. The proportion of patients seen within the recommended time after triage fell over the same period. Again, the decline was steepest among emergency patients, who should have been seen within 15 minutes (from 59.2% in 1997 to 48% in 2006). Overall, the odds of being seen on time was 30% lower in 2006 than in 1997 (adjusted odds ratio 0.7, 95% CI 0.55 to 0.89).

The looming crisis in US emergency departments is already well documented, write two observers (p 1836), and at a local level changes in processes and procedures are already under way to help accelerate throughput. Nationally, the picture is more complicated and harder to fix. Overcrowding in emergency departments is just one symptom of a failing system that shifts responsibility for care away from the community, and pays doctors less for working where they are needed most, they write. It also fails to recognise the challenges of emergency care, such as a fluctuating and unpredictable out of hours workload, and the financial insecurity that goes with an unfunded legal mandate to provide care to all comers, regardless of their ability to pay. The system-wide problems that cause overcrowding in emergency departments require urgent system-wide reform, they conclude. *Arch Intern Med* 2009;169:1857-65

Prone positioning improves oxygenation, not survival

We already know that ventilating critically ill patients on their fronts—a practice known as prone positioning—improves overall oxygenation. We still have no firm evidence that it prolongs survival or saves lives, however. In the latest trial, mortality at 28 days was about the same for patients ventilated when prone (31.0% (52/168)) or supine (32.8% (57/174); relative risk 0.97, 95% CI 0.84 to 1.13). Participants had acute respiratory distress syndrome and those randomised to prone ventilation were in this position 18 hours a day for up to 28 days. Prone positioning had no effect on length of stay in intensive care or duration of ventilation.

As expected, patients ventilated when prone need lower inspired oxygen than controls to maintain good oxygenation. But they also had significantly more complications including airway obstruction, haemodynamic instability, loss of vascular access, and vomiting.

Subgroup analyses hinted at possible survival benefits for patients with severe hypoxaemia, and an editorial (p 2030) says further research in this subgroup is still justified, despite the non-significant result. It also makes sense to try prone positioning for patients at imminent risk of death from hypoxaemia, says the editorialists. This trial does not support prone positioning for anyone else.

JAMA 2009;302:1977-84

Cite this as: *BMJ* 2009;339:b4816

Laser treatment may relieve neck pain, but how?

Non-specific neck pain is common, burdensome, and difficult to treat. Low level laser treatment, or cold laser, is one non-invasive option worth considering, says an editorial (doi:10.1016/S0140-6736(09)61837-7), after a systematic review showed that treatment relieves neck pain for up to 22 weeks. The review analysed 16 randomised trials and a total of 820 patients. The trials were small but reasonably well reported. Most were double blind and placebo controlled. The participants had acute or chronic neck pain, with an overall mean score of 57 mm on a 100 mm visual analogue scale.

In a pooled analysis of 11 trials confined to chronic neck pain, low level laser treatment reduced pain scores by nearly 20 mm more than placebo (weighted mean difference 19.86, 95% CI 10.04 to 29.68). The improvements were discernible soon after treatment and persisted in the seven trials that followed patients for one to 22 weeks after the end of treatment. Results for acute pain were less conclusive—one higher quality trial found laser treatment was beneficial, the other lower quality trial found it wasn't. Both trials were small.

The editorial says the review's methods were sound and the results broadly agree with previous reviews of non-invasive treatments for neck pain. Low level laser treatment looked safe in this review. Doctors will want to know more about how it works, however. The review's authors favour an anti-inflammatory effect.

Lancet 2009; doi:10.1016/S0140-6736(09)61522-1

