MIXED BAG

Long-term proton pump inhibitor therapy and the risk of hip fracture

It is known that proton pump inhibitors (PPIs) may interfere with calcium absorption by inducing hypochlorhydria. They also appear to reduce bone resorption by inhibiting osteoclastic vacuolar proton pumps.

The authors of this paper in the *Journal of the American Medical Association* looked at any association between PPI therapy and the risk of hip fracture. They used a case-control study using the General Practice Research Database (1987 - 2003), which contains information on patients in the UK. The cohort studied were people aged 50 and older who did and did not use PPI therapy. All patients who suffered a hip fracture were recorded. There were 13 556 hip fracture cases and 135 386 controls. The risk of hip fracture was significantly increased among patients who were prescribed long-term high-dose PPIs. The longer PPIs were taken, the greater the risk of hip fracture.

My mother recently suggested peppermint for indigestion. Perhaps she is right.

Yu-Xiao Y *et al*. *JAMA* 2006; 296: 2947-2953.

Pandemic flu mortality: how many will die?

There is currently a high level of interest in avian flu, both the epidemic in birds and in the relatively small number of human cases around the world. Media coverage is high, the public are concerned and governments are debating policy. Governments and donor agencies have pledged very large amounts of money to fight the spread of avian flu – $3.8 billion by the USA and AUD$555 million by Australia alone. These amounts may seem unreasonably large given all the current acute medical problems in the world, but people are spurred on by estimates of mortality ranging from 2 million to even up to 1 billion if avian flu were to become pandemic.

But what is a reasonable estimate? Christopher Murray, from the Harvard Initiative for Global Health, and colleagues are attempting to provide a rational analysis. As they point out, various models of the effect of flu pandemics on mortality have been developed. The models make strong assumptions about attack rates and case fatality rates in flu cases. But, regardless of what assumptions underly the models, it is the 3 pandemics of the 20th century that are the main source of evidence for the potential number of people affected in the next pandemic – in 1918 - 1920, 1957 - 1958 and 1968 - 1970. Of course it is the 1918 - 1920 Spanish flu pandemic that caused the greatest mortality and which is the one that is most often used to set the upper limits on the potential number of deaths in the next pandemic. Estimates of deaths in this pandemic range from 20 million to 100 million.

In this paper, the authors aim to assess the vital registration data from the 1918 - 1920 pandemic because this was the largest of the 3 and also provides a clearly identifiable effect on mortality. The effects are calculated for a pandemic in 2004, which is the most recent year for which per-head gross domestic product in international dollars is available.

Their estimates are that, if a strain of flu were to emerge in 2004 that was similar to the one that caused the 1918 - 1920 pandemic, between 51 and 81 million individuals would die. Their results also suggest that deaths would be concentrated in the age groups 0 - 14, 15 - 19 and 30 - 44. They also estimate that 96% of these deaths would occur in the developing world. If this mortality were concentrated in a single year, it would increase global mortality by 114%.

However, the authors question the assumption that is usually made that it is the 1918 - 1920 pandemic data that would set the upper limit on mortality from any future flu pandemic. They point out that there is no logical or biological reason why this pandemic should represent the maximum possible mortality in a future pandemic. They point out that random genetic mutation could produce a more lethal virus. There is also the uncertainty about whether the low older adult mortality in the 1918 - 1920 pandemic was produced by acquired immunity from the pandemics of the mid-19th century. They also question the assumption that increased travel and mixing could lead to larger epidemics, because historical records show that nearly all human populations were eventually exposed to the 1918 - 1920 flu virus.

Fears of massive mortality are very real but, as the authors point out, today there are many reasons to think that a similar pandemic flu strain may not cause similar mortality to that of the 1918 - 1920 strain. First, symptomatic medical management is much better today, although this would probably only benefit individuals who have access to high-end medical care – either in high- to middle-income countries or in high-income sections of poorer countries. In the developing world, public health systems would be overwhelmed. Second, access to anti-flu drugs may have a positive effect, but this cannot be quantified, because these drugs have not yet been used in this situation. Thirdly, vaccination with a lag of 4 - 6 months from the onset of a pandemic could reach a large fraction of high-income populations. The speed of the pandemic will determine the potential benefit of vaccination. However, restricted vaccine production capacity and reality of health system coverage suggest that vaccination would have little or not effect on the poorest populations.

Quarantine measures may also be successful, if strictly implemented and combined with prophylaxis. Strict quarantine in American Samoa seems to have avoided the 1918 - 1920 pandemic and quarantine efforts in Australia appear to have delayed, but not avoided, the pandemic.

Fourth, in 1918 - 1920, a large number of deaths were caused by secondary bacterial pneumonia after primary viral pneumonitis. Now, antibiotics for pneumonia would make a very real difference to case-fatality rates. This would be particularly true in middle- and low-income settings, where access to affordable antibiotics would be the most cost-effective strategy to prevent excess mortality. But, the conclusion is still that it is the countries and regions that can least afford to prepare for a pandemic that will be affected the most. This presents these countries with a policy dilemma – when they can scarcely afford to deal with their current health problems what justification is there for spending scarce resources on preparing for such an uncertain threat? The suggestion is that focusing on practical and affordable strategies for low-income countries would be prudent, given that this is where the biggest threat lies. The developed world's record of putting resources into developing world health problems doesn't suggest that this focus will be forthcoming.

Murray CJL *et al*. *Lancet* 2006; 368: 2211-2218.

Bridget Farham

IN MEMORIAM

Mark Elliott (1959 – 2006)

I knew Mark for the last 4 years of his life – a life as rich in experience as in its refined complexity. On 6 February 2006, six months to the day of being diagnosed with pancreatic cancer, Mark died. In his inimitable style, Mark broke the news of the cancer to me in a perfunctory, yet exquisitely composed SMS. I met with him a few days later. Mark was in good spirits as he spoke, eloquently as ever, of his fate: a fate he had clearly accepted with equanimity. I will remember the warmth of that August afternoon forever.

Mark Elliot was born on 4 March 1959 in Johannesburg. He grew up in Natal, where he completed his schooling at Thomas More College. He studied medicine at the University of the Free State and took up general practice in Bulwer, Melmoth and Pretoria.

I came to know Mark in 2002, when he joined the Forensic Unit at Sterkfontein Hospital, Krugersdorp, as a medical officer. I immediately realised Mark was no ordinary doctor: here was a post-modern doctor of the old school. His caring and empathy were no mere clinical aids; they represented his very nature, his *kind* – in the true sense. State patients revered him. His bedside manner was faultless; his clinical presentations succinct, delightful, sometimes funny, always respectful.

Mark's gift for language allowed him to weave words like 'ruse' and 'ribald' into his descriptions of mental state. It was therefore not surprising to discover that Mark was an accomplished poet. Two extracts from his poem *Antigravity* illustrate how his art buttressed him during those last days:

'They had become less common now:

Minutes to moments

Antigravity of the soul…

Mercurial minutes

Slipping away, gently

Through the fingers of my mind.'

Mark readily assimilated psychiatry's apparently arcane subtleties. Expanding on the literary theme, he researched the topic of deceit and illness-endorsing behaviour, presenting his integrated view in a talk entitled 'Was Hamlet a malingerer?'. Mark read widely and could speak with unaffected authority about God, the pineal, mouse, man, machine and Mozart.

In colleagues, friends and patients, I could see his love; in his parents, its origins; in his siblings, its likeness and in his children, its sempiternity. Mark, you were a fine man. I will miss you.

Conrad Visser