

Individuals aged 14–20 years in schools and military service were initially affected, with rapid spread to preschool children.² The population older than 30 years had strikingly lower attack rates and overall mortality was low. Gregg and colleagues² noted that “Besides the reappearance of a virus strain not identified anywhere in the world for 20 years, other unusual features of the USSR epidemic were the relative synchronous appearance of the epidemics throughout much of the country, their rapid peaking, and their short countrywide duration”.

The first outbreak caused by this strain in the USA was in a high school in Cheyenne, WY, where the attack rate was more than 70%, but involved solely students; no illness was reported among faculty.³ High attack rates were seen in schools and military bases throughout the USA. There were few reports of this H1N1 strain in people older than 26 years and the death rate in affected individuals was low.²

In his classic text, Kilbourne⁴ wrote: “When the H1N1 (“Russian”) virus in the early 1950s returned in 1977 bearing recycled HA and NA antigens, its distribution was global, and it produced high morbidity. In that sense it was pandemic—but only pandemic in the young. The failure of the virus to penetrate the firm immunity of those more than 25 years of age precluded the usual emergence of excess mortality that follows influenza in older people.”

It might be that the H1N1 circulating now (swine-origin influenza virus) has enough antigenic similarity to related H1N1 influenza strains of the past to protect older individuals exposed to them previously. Mortality could be relatively low by predominantly affecting younger people in the absence of the cytokine storm associated with infection due to other influenza viruses such as the 1918 H1N1.⁵ The months ahead should help us to determine whether this will be the case.

I declare that I have no conflicts of interest.

Leonard A Mermel

lmermel@lifespan.org

Division of Infectious Diseases, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903, USA

- 1 Young JF, Palese P. Evolution of human influenza A viruses in nature: recombination contributes to genetic variation of H1N1 strains. *Proc Natl Acad Sci USA* 1979; **76**: 6547–51.
- 2 Gregg MB, Hinman AR, Craven RB. The Russian flu. Its history and implications for this year's influenza season. *JAMA* 1978; **240**: 2260–63.
- 3 Anon. Influenza—worldwide. *Morbidity and Mortality Weekly Report* 1978; **27**: 40.
- 4 Kilbourne ED. *Influenza*. New York: Plenum Medical Book Co, 1987: 270.
- 5 Kobasa, D, Takada A, Shinya K, et al. Enhanced virulence of influenza A viruses with the haemagglutinin of the 1918 pandemic virus. *Nature* 2004; **431**: 703–07.

Renal sympathetic denervation for resistant hypertension

Henry Krum and colleagues (April 11, p 1275)¹ in a proof-of-principle trial of renal sympathetic denervation in patients with resistant hypertension, conclude that, because office blood pressure was reduced by 27/17 mm Hg at 12 months, the procedure was successful.

Specific details as to how blood pressure measurement was standardised are not given, other than that the latest recommendations of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure were followed. Whatever the detail, the method used could only favour the outcome in that office blood pressure is subject to the placebo and Hawthorne effects, regression to the mean, and most importantly to the white coat effect, all of which would favour a reduction in blood pressure over time.²

In 12 patients, 24-h ambulatory blood pressure was measured before and after the procedure. In nine office responders, the mean change in systolic blood pressure measured over 24 h was –11 mm Hg, compared with –27 mm Hg for office measurement, indicating a substantial white coat

effect equivalent to 16 mm Hg. Ambulatory blood pressure measurement would, therefore, have been a much more sensitive discriminator of the effectiveness of the intervention.

No details are given for nocturnal blood pressure—the most sensitive discriminator of all in these patients³—but the prevalence of non-dipping before (67%) and after (33%) the intervention indicates that nocturnal hypertension was a major characteristic in these patients.

How was an otherwise well designed interventional study approved by five ethics committees when the measurement technique on which the proof-of-principle would depend was clearly flawed but could so easily have been corrected had ambulatory blood pressure been measured on all patients at regular intervals?

I declare that I have no conflicts of interest.

Eoin O'Brien
eobrien@iol.ie

Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Dublin 4, Ireland

- 1 Krum H, Schlaich M, Whitbourn R, et al. Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study. *Lancet* 2009; **373**: 1275–81.
- 2 O'Brien E, Asmar R, Beilin L, et al, on behalf of the European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens* 2003; **21**: 821–48.
- 3 Dolan E, Stanton A, Thijs L, et al. Superiority of ambulatory over clinic blood pressure measurement in predicting mortality: the Dublin Outcome Study. *Hypertension* 2005; **46**: 156–61.

Authors' reply

Ambulatory blood pressure monitoring (ABPM) provides important complementary data to that of office blood pressure recordings. Indeed, the ABPM approach helps overcome several of the drawbacks of office blood pressure measurements, including the white coat effect. It is therefore entirely expected that the size of the reductions in blood pressure on ABPM after



Science Photo Library

renal denervation in our study were less than we saw with office blood pressure measurements. Neither approach will completely overcome the problem of placebo and Hawthorne effects since this requires a control group, which was not formally included in this first-in-man study.

It was always the intention that, if the first-in-man study provided positive safety and efficacy signals, a randomised controlled trial would then be done, with all patients undergoing ABPM as well as office measurements to provide more definitive data on the size of the blood pressure response to this technique. This is indeed the design of the ongoing Ardian Symplicity HTN-2 randomised controlled trial of catheter-based denervation in patients with resistant hypertension.

PS is an employee of Ardian, the developer of the technique. The other authors have no conflicts of interest to declare.

*Henry Krum, Markus Schlaich,
Paul Sobotka, Murray Esler
henry.krum@med.monash.edu.au

Centre of Cardiovascular Research and Education in Therapeutics, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC, Australia (HK); Baker IDI Heart and Diabetes Institute, Melbourne, VIC, Australia (MS, ME); and Ardian Inc, Palo Alto, CA, USA (PS)

Towards a global fund for the health MDGs?

Giorgio Cometto and colleagues (May 2, p 1500)¹ propose an expanded remit for the Global Fund in order to achieve all the health Millennium Development Goals (MDGs). The International HIV/AIDS Alliance welcomes this new and innovative thinking, particularly given the poor progress on maternal health and the fact that the current financial crisis is expected to cause an additional 200 000–400 000 children to die before their fifth birthday. But this proposal also raises serious concerns.

The efficiency of health systems is positively related to health expenditure per head. Performance increases greatly with expenditure up to about US\$80 per head per year. There is a minimum level of health expenditure below which the system simply cannot work well,² and much of sub-Saharan Africa is well below these levels.

Without the necessary additional funding, this proposition will just water down the Global Fund's current ability to deliver effectively and make an impact. It will reverse the gains made in HIV, tuberculosis, and malaria before they can be consolidated.

The Global Fund has produced some spectacular results delivering funding for the three diseases. More than 2 million people are on antiretroviral treatment, 4.6 million people are under treatment for tuberculosis, and 70 million bednets have been distributed. However, the Global Fund currently faces a funding shortfall of \$4–5 billion. Expanding its remit even further would require a very significant upfront funding commitment if it is to deliver tangible results.

The Global Fund is a model of successful health financing that is delivering for those most vulnerable to HIV, tuberculosis, and malaria. Jeopardising its ability to do this well would be a tragedy for the millions who rely on its support.

I declare that I have no conflicts of interest.

Alvaro Bermejo
mail@aidalliance.org

Executive Director, International HIV/AIDS Alliance, Hove BN3 1RE, UK

- Cometto G, Ooms G, Starrs A, Zeitz P. A global fund for the health MDGs? *Lancet* 2009; **373**: 1500–02.
- Evans DB, Tandon A, Murray CJ, Lauer JA. Comparative efficiency of national health systems: cross national econometric analysis. *BMJ* 2001; **323**: 307–10.

Giorgio Cometto and colleagues¹ suggest expanding the mandate of the Global Fund to fight AIDS, Tuberculosis and Malaria beyond the three diseases. This is a promising idea, but the agency, and its donors, will have to learn to

overcome their mistrust of developing country governments if they really hope to meet the Millennium Development Goals for health.

The Global Fund, GAVI, the US Government, and other donors have tended to avoid direct investments in government national health plans,² perhaps on the grounds that African governments lack accountability. But recent scandals such as the theft of Global Fund cash in Uganda³ have shown that parallel funding mechanisms are no solution to this problem.

Meanwhile, large sums have been spent on vertical programmes that bypass national plans and budgets. The effectiveness of such programmes has in many cases owed much to government health systems, especially in Africa. For example, WHO's Integrated Management of Childhood Illness programme succeeded in reducing child deaths only in two districts of Tanzania where a government-run health systems strengthening programme was already underway.⁴ Similarly, UNICEF's Accelerated Child Survival and Development Program was most effective in Ghana's upper east region, where the Ghana Health Service's Community Health Planning and Services programme was fully functioning.⁵

In many African countries, government health budgets at the district level are largely consumed by salaries (paid by the government) and vertical programmes (paid by donors), leaving nothing for programmes that donors aren't interested in, which often includes maternal health. The solution is not to funnel more money into maternal health in particular, but to strengthen the capacity of African governments to meet all basic health needs, and to strengthen the capacity of African civil society to demand that they do so.

I declare that I have no conflicts of interest.

Helen Epstein
helenepstein@yahoo.com

424 West 144th Street, New York, NY 10031, USA