Saturday 16 December 2006

BMJ

Influenza in elderly people in care homes

New evidence strengthens policy to vaccinate healthcare workers

Research p 1241

Influenza causes substantial mortality and morbidity in elderly people, particularly those with chronic diseases. Excess deaths during influenza epidemics are not limited to obvious causes such as influenza and pneumonia but also include circulatory and other respiratory causes.[w1] Elderly people in care homes and hospital wards are at particular risk, because high risk individuals are concentrated in an environment susceptible to the spread of respiratory pathogens. In this week's *BMJ,* Hayward and colleagues report the impact of vaccinating healthcare workers in elderly peoples homes on mortality in residents.[1]

Most developed countries offer elderly people vaccination against predicted influenza strains for the next season.[2] However, the age related decline of immune function reduces the ability of elderly patients to respond to the influenza vaccine,[3] and the vaccine is less effective in patients with chronic diseases.[4] Also, as most of the evidence in elderly people comes from database cohort studies, effects may have been overestimated because healthier people are more likely to be vaccinated and the reported estimates may not have been fully adjusted for confounding factors.[5] So even if all elderly people in residential care were vaccinated, the effect on reducing the risk of complications of influenza may be modest. It therefore makes sense to examine alternative strategies, such as vaccination of healthcare workers in elderly care establishments, which offer indirect protection by reducing the exposure of at-risk people.

Until now, the best evidence in support of vaccinating healthcare workers came from two related trials conducted in long term geriatric care wards in Scotland in the 1990s.[6 7] Both found that vaccination significantly reduced mortality in residents (in the larger trial 13.6% *v* 22.4% in the control arm[7]; in the smaller pilot study 10% *v* 17%[6]) in years when influenza activity was two to three times higher than recent years[8] and when the vaccine match to the circulating strain was good[7] or reasonable.[6] Assuming the estimates are robust, such a policy is likely to be cost saving or at the worst highly cost effective.[9]

However, the existing evidence has methodological limitations. The small number of clusters led to an imbalance in important confounding factors (patient vaccination rates and levels of disability) between the trial arms and uncertainty about the extent of benefit.[9 w2] This uncertainty was aired in a recent article published in the *BMJ,*[10] which has sparked debate about the value of influenza vaccination programmes, including vaccination of healthcare workers, by suggesting that the evidence does not justify the policy.

The current paper by Hayward and colleagues[1] provides robust evidence that vaccinating healthcare workers against influenza benefits elderly patients. The cluster randomised controlled trial was conducted over two seasons in 44 private care homes around the United Kingdom. Staff of 22 homes were offered influenza vaccination and those of 22 matched control homes were not (usual policy). During the 2003-4 periods of influenza activity, five fewer deaths occurred per 100 residents in intervention homes compared with control homes (95% confidence interval 2 to 7, $P = 0.002$). Episodes of influenza-like illness, consultations with general practitioners for influenza-like illness, and hospital admissions for such illness also decreased significantly. In the following season, influenza activity was much lower and no significant differences in patient morbidity or mortality were seen.

Despite an incomplete vaccine match,[4] in a year of modest influenza activity and vaccine uptake of around 50% for employees and more than 70% for patients, vaccinating healthcare workers significantly reduced patient mortality. Notably, in the following year of very low activity no effect was seen on outcomes.

Applying the uptake rates and mortality data from the new trial to our economic model[9] confirms the original conclusions that, even in the most pessimistic scenario, vaccination of healthcare workers costs as little as £274 (€407; $542) per life year gained. The trial therefore strengthens the case that vaccination of healthcare workers is the correct policy. Similarly, well designed studies in other settings and in years with different levels of circulating influenza, vaccine match, and vaccine uptake would help define best practice.

So should all healthcare workers in elderly care establishments be vaccinated? Evidence shows that healthcare workers themselves would benefit by reducing their risk of influenza with minimal adverse effects,[9] employers may benefit by reduced absenteeism,[9] and elderly people in care homes would benefit from reduced morbidity and mortality (although the quality of lives saved needs to be analysed).

Most countries in Europe and North America[2] have recommended for some years that healthcare workers should receive the influenza vaccine, but uptake remains poor—less than 25% in Europe.[11] Surveys suggest that

Extra references w1-w2 are on bmj.com

BMJ 2006;333:1229–30

the main reasons for refusing the offer are fear of side effects, fear that vaccinations will cause influenza, dislike of injections, being unaware that the vaccination is useful or available, and lack of time or forgetfulness.[9] The challenge to the health services is to overturn the misconceptions and provide an easy access service within which there are no reasons to refuse vaccination. Small studies suggest that mobile vaccination services can be beneficial,[9] but this—and other novel methods of delivery—needs to be tested in a well designed randomised controlled trial. It will also be interesting to view the progress of the new policy in the United States, which recommends that all healthcare personnel should be offered annual influenza vaccination, and those who decline for non-medical reasons should provide a signed decloration that they have declined.[12]

Rachel E Jordan *senior scientist*

(r.e.jordan@bham.ac.uk)

Health Protection Research and Development Unit, Health Protection Agency, Department of Public Health and Epidemiology, University of Birmingham, Edgbaston, Birmingham B15 2TT

Jeremy I Hawker *head of public health development*

Health Protection Agency, London WC1V 7PP

Competing interests: None declared.

1 Hayward AC, Harling R, Wetten S, Johnson AM, Munro S, Smedley J, et al. Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial. *BMJ* 2006;333:1241-4.
2 Van Essen GA, Palache AM, Forleo E, Fedson DS. Influenza vaccination in 2000: recommendations and vaccine use in 50 developed and rapidly developing countries. *Vaccine* 2003;21:1780-5.
3 Goodwin K, Viboud C, Simonsen L. Antibody response to influenza vaccination in the elderly: a quantitative review. *Vaccine* 2006;24:1159-69.
4 Herrera GA, Iwane MK, Cortese M, Brown C, Gershman K, Shupe A, et al. Influenza vaccine effectiveness among 50-64-year-old persons during a season of poor antigenic match between vaccine and circulating influenza virus strains: Colorado, United States, 2003-2004. *Vaccine* 2006 Aug 2; Epub ahead of print.
5 Jefferson T, Rivetti D, Rivetti A, Rudin M, Di Pietrantonj C, Demicheli V. Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. *Lancet* 2005;366:1165-74.
6 Potter J, Stott DJ, Roberts MA, Elder AG, O'Donnell B, Knight PV, et al. Influenza vaccination of health care workers in long-term-care hospitals reduces the mortality of elderly patients. *J Infect Dis* 1997;175:1-6.
7 Carman WF, Elder AG, Wallace LA, McAulay K, Walker A, Murray GD, et al. Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial. *Lancet* 2000;355:93-7.
8 Elliot AJ, Fleming DM. Surveillance of influenza-like illness in England and Wales during 1966-2006. *Eurosurveillance* 2006;11(10). www.eurosurveillance.org/em/v11n10/1110-224.asp.
9 Burls A, Jordan R, Barton P, Olowokure B, Wake B, Albon E, et al. Vaccinating healthcare workers against influenza to protect the vulnerable—is it a good use of healthcare resources? A systematic review of the evidence and an economic evaluation. *Vaccine* 2006;24:4212-21.
10 Jefferson T. Influenza vaccination: policy versus evidence. *BMJ* 2006;333:912-5.
11 Szucs TD, Muller D. Influenza vaccination coverage rates in five European countries—a population-based cross-sectional analysis of two consecutive influenza seasons. *Vaccine* 2005;23:5055-63.
12 Pearson ML, Bridges CB, Harper SA. Influenza vaccination of health-care personnel. Recommendations of the Healthcare Infection Control Practices Advisory Committee (HICPAC) and the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006;55:1-16.

doi 10.1136/bmj.39050.408044.80

Rehabilitation of traumatised refugees and survivors of torture

After almost two decades we are still not using evidence based treatments

In a 1988 BMJ editorial,[1] Marks and I reviewed the available knowledge on the mental health effects of torture and their treatment and presented a critical look at rehabilitation programmes for survivors. Eighteen years later, it is time to cast another look at the advances in our understanding of torture and its treatment and how this progress has translated into rehabilitation work with survivors. Such an update is timely: given the political developments of the last two decades, torture has become an ever more serious problem.

An important advance in the 1990s was the demonstration of an association between torture and post-traumatic stress disorder through controlled studies using standardised assessment instruments.[2] Further work provided insight into the psychological mechanisms that played a part in torture-induced post-traumatic stress. In a controlled study survivors who felt that those they held responsible for the torture did not receive the punishment they deserved were more likely to have a sense of injustice, anger, rage, distress, loss of meaning in life, demoralisation, desire for revenge, pessimism, fear, and loss of control over life.[3] Among these responses, however, only fear and loss of control were associated with post-traumatic stress disorder and depression. This implied that post-traumatic stress and depression could be effectively treated by psychological interventions designed to reduce fear and enhance the sense of control and that the sense of injustice associated with impunity would not necessarily impede recovery.

The 1990s also saw considerable progress in treating post-traumatic stress disorder. Controlled studies showed that it could be effectively treated with cognitive behavioural treatment, essentially a potent fear-reducing intervention. A consensus emerged among experts that cognitive behavioural treatment is the treatment of choice in post-traumatic stress disorder.[4] Recently, the National Institute for Clinical Excellence in the UK recommended cognitive behavioural treatment as an effective treatment for trauma survivors.[5] Such treatment is usually delivered in 8-10 weekly sessions, but a much briefer behavioural intervention has been developed in recent years. Randomised controlled studies with earthquake survivors showed that a single session of exposure treatment designed to enhance a sense of control over trauma-induced fear and distress is highly effective in reducing post-traumatic stress disorder and depression in over 85% of the cases.[6 7] Preliminary evidence suggests that exposure-based interventions are also useful in refugees[8 9] and survivors of torture.[10 11]

Such progress, however, appears to have had little impact on work with survivors of torture. Most psychological treatments used in rehabilitation programmes still appear to be a mixture of various psychotherapeutic elements, not based on a consistent theory, and

BMJ 2006;333:1230–1

lack evidence on their effectiveness. In 1988 we noted that lack of outcome evaluation makes it impossible to judge the effectiveness of these rehabilitation programmes in facilitating recovery from the trauma of torture. Unfortunately, evidence is still lacking. A recent report based on the work of the Rehabilitation and Research Centre for Torture Victims in Denmark is a sobering reminder of where we stand after two decades. The Danish centre is a pioneering organisation, serving as a model for more than 90 similar centres around the world. An outcome evaluation study based on 55 people admitted to the centre in 2001 and 2002 showed no improvement in post-traumatic stress disorder, depression, anxiety, or health-related quality of life after nine months' treatment.[12] These findings led the authors to conclude that future studies are needed to explore effective interventions for traumatised refugees, including cognitive behavioural therapy. This is indeed what we had recommended in1988.[1]

Lack of progress among torture survivors partly stems from the fact that scientific approaches to the problem are often dismissed as reductionist "medicalising." Many of those working with torture survivors advocate a solely political approach to the problem in the belief that recovery from trauma is only possible through eradicating impunity for the perpetrators of torture. Research evidence does not support this view.[3] Although advocacy against torture is certainly important, as long as the problem lasts rehabilitation centres also have a moral obligation to provide effective psychological treatment for their clients. After more than 30 years of work, those working with torture survivors need to confront the uneasy but important question of whether their approach is helpful. This issue can be addressed only by proper outcome evaluation. Given that there are now very brief and highly effective interventions available for survivors, the public have a right to know the justification behind lengthy and expensive rehabilitation programmes without demonstrable beneficial effects.

Funders of rehabilitation programmes are in an excellent position to promote progress here. They also need to adopt an evidence-based approach and consider the following questions in their review of funding applications: (*a*) is the proposed intervention based on sound theory; (*b*) is there is sufficient evidence on its effectiveness; and (*c*) does the work involve outcome evaluation? Making grant support conditional on such requirements would certainly enhance the quality of work in the field. Given the painfully slow progress this appears to be the only hope for change.

Metin Başoğlu *head of trauma studies unit*

(spjumeb@iop.kcl.ac.uk)

Institute of Psychiatry, King's College, London

This article was made possible by grant support from the Bromley Trust.

Competing interests: None declared.

1 Başoğlu M, Marks IM. Torture: research needed into how to help those who have been tortured. *BMJ* 1988;297:1423-4.
2 Başoğlu M, Jaranson JM, Mollica R, Kastrup M. Torture and mental health: A research overview. In: Gerrity E, Keane TM, Tuma F, eds. *The mental health consequences of torture*. New York: Kluwer Academic/Plenum Publishers, 2001.
3 Başoğlu M, Livanou M, Crnobarić C, Frančišković T, Suljić E, Đurić D, et al. Psychiatric and cognitive effects of war in former Yugoslavia. The relationship between lack of redress for trauma and posttraumatic stress reactions. *JAMA* 2005;294:580–90.
4 Ballenger JC, Davidson JR, Lecrubier Y, Nutt DJ, Foa EB, Kessler RC, et al. Consensus statement on posttraumatic stress disorder from the International Consensus Group on depression and anxiety. *J Clin Psychiatry* 2000;61:60-6.
5 National Institute for Clinical Excellence. Posttraumatic stress disorder: the management of PTSD in adults and children in primary and secondary care. *National Clinical Practice Guideline Number 26*. London: Gaskel and the British Psychological Society, 2005.
6 Başoğlu M, Şalcioğlu E, Livanou M, Kalender D, Acar G. Single-session behavioral treatment of earthquake-related posttraumatic stress disorder: a randomized waiting list controlled trial. *J Trauma Stress* 2005;18:1-11.
7 Başoğlu M, Şalcioğlu E, Livanou M. A randomised controlled study of single-session behavioural treatment of earthquake-related posttraumatic stress disorder using an earthquake simulator. *Psychol Med* (in press).
8 Neuner F, Schauer M, Klaschik C, Karunakara U, Elbert T. A comparison of narrative exposure therapy, supportive counselling and psychoeducation. *J Consult Clin Psychol* 2004;72:579-87.
9 Paunovic N, Öst GL. Cognitive-behaviour therapy versus exposure therapy in the treatment of PTSD in refugees. *Beh Res Ther* 2001;39:1183-97.
10 Başoğlu M, Aker T. Cognitive-behavioural treatment of torture survivors: A case study. *Torture* 1996;6:61-5.
11 Başoğlu M, Ekblad S, Bäärnhielm S, Livanou M. Cognitive-behavioral treatment of tortured asylum seekers: a case study. *J Anxiety Disord* 2004;18:357-69.
12 Carlsson JM, Mortensen EL, Kastrup M. A Follow-Up Study of Mental Health and Health-Related Quality of Life in Tortured Refugees in Multidisciplinary Treatment. *J Nerv Ment Dis* 2005;193:651-7.

doi 10.1136/bmj.39036.739236.43

The Cooksey review of UK health research funding

The art of being all things to all people

News p 1239

Prompted by concern that the drug industry might reduce its investment in research in the United Kingdom, the chancellor of the exchequer asked the distinguished venture capitalist Sir David Cooksey to lead a review. Widespread consultation showed that it is not only the Treasury that is concerned about the current state of health research funding, organisation, and performance.[1]

Four principal criticisms emerged. Firstly (confirming the Treasury's view), the drug industry is frustrated by what it sees as increasing obstacles to gaining access to patients and over-regulation leading to unacceptable delays and extra costs. Companies claim that developing products and conducting research in other countries is increasingly attractive and an inevitable consequence. Secondly, those responsible for providing health services—politicians, managers, clinicians—as well as research funders are concerned at the delays in translating advances in basic science into clinical applications and then translating such innovations into routine practice. This is seen as reflecting an unsupportive culture in the National Health Service, institutional barriers, and perverse incentives, such as greater regard and reward for basic research than for applied research. Thirdly, the distribution of research funds does not always reflect the burden of disease in the UK, which reflects the lack of a transparent mechanism for determining research priorities. This is partly

BMJ 2006;333:1231–2

explained by the final concern that Cooksey identified—the lack of coordination and a supposed resulting inefficiency between the principal funding bodies and, in particular, the two public funders, the Medical Research Council (MRC) and the NHS National Institute for Health Research (NIHR).

Together with criticisms came solutions. Faced with more than 300 responses from individuals and organisations, each with their own interests to defend and promote, the review team have constructed a strategy that tries to deal with the four principal concerns. Given the disparate nature of those concerns, the strategy is a masterful attempt at coherence.

The concerns of the drug industry (and the Treasury) are to be met by bringing new drugs to market faster, without compromising patient safety, and more cheaply. A new "drug development pathway" will include streamlining clinical trial procedures, "conditional licensing," earlier involvement of the National Institute for Health and Clinical Excellence (NICE), and ensuring NICE's recommendations are implemented. The aim is to "send a signal to industry that the UK is a world leader in research and development."

The challenge of promoting translation is to be met in several ways. The recently ring fenced budget for the NIHR is seen as a useful development though other funds, such as research training budgets for young clinicians, need to be brought inside the fence. More funding for the NHS Health Technology Assessment programme is proposed, together with the creation of a new Translational Medicine Funding Board, accountable to the NIHR and MRC. All of these initiatives are seen as part of creating a stronger research culture in the NHS that facilitates rather than discourages innovation.

To encourage greater attention to currently unmet health needs, research on neglected areas will be identified through burden of illness analyses, and designated topics will be labelled as UK Priority Health Research Projects. Public, private, and charitable research funders will hopefully respond to the institutional and procedural advantages that such priorities will benefit from, such as faster approval of trials and expedited approval from NICE.

The final criticism of the status quo, namely lack of coordination between public funders, is the one that has probably attracted the greatest interest, concern, and often heated debate. The proposed solution is to strengthen coordination by establishing an overarching Office for Strategic Coordination of Health Research (OSCHR, pronounced "Oscar") that is accountable to both the Department of Health and the Department of Trade and Industry. Its tasks include setting a health research strategy that both the MRC and NIHR must comply with, agreeing their funding needs, submitting those needs to the Treasury, and monitoring the results. To reduce duplication, some areas currently funded by MRC (including clinical research, health services research, and phase IV clinical trials) will become the sole responsibility of the NIHR so that the MRC can concentrate on basic and underpinning research. In addition, some structural changes are advocated—members of MRC boards are expected to become more representative of the broad spectrum of health research while the NIHR should become a real, rather than a virtual, institute and be separated from the Department of Health from 2009 as an executive agency.

Cooksey's proposals, which the government has welcomed and accepted, are in the great tradition of compromise solutions. The two major public funders, MRC and NIHR, are to work more closely, but a third public funding stream is to be created; more funding will be provided for translational research but funds for basic research will not be reduced; "blue skies" investigator led research will continue to be supported but national research priorities will be instigated. Anyone wanting and expecting more radical change to the structure and processes of research funding will be disappointed. Merger of the MRC and NIHR was rejected because of a fear that the larger MRC would dominate, and that this would jeopardise the development of translational and applied research.

Although, potentially, there is something for everyone in the overall package of proposals, for several reasons its success is not guaranteed. Firstly, the review is predicated on the view that we stand on the threshold of "a seismic shift in medical science" in which molecular medicine, gene therapy, stem cells, and other initiatives will revolutionise health care. Such faith in technology as the principal driver of improvements in people's health may prove over optimistic. Secondly, while the strategy shares much in common with reforms enacted in Canada in recent years, their success was facilitated by a 130% increase in research funds over five years, a level of investment not envisaged in the UK. Thirdly, key aspects depend on private industry responding to new incentives. On the one hand, the sorts of incentives that might motivate public researchers, such as those associated with Priority Health Research Projects, may be insufficient to influence private companies. On the other hand, there is a danger that incentives offered to private industry in which they can dictate the agenda of NICE and the Health Technology Assessment programme risks those bodies being co-opted and becoming adjuncts of the drug industry.[2] And lastly, while the strategy involves some straightforward structural changes that can be implemented from the centre, much of it relies on widespread cultural and behavioural changes within the NHS and research community, which will be hard to ensure take place.

Much also depends on the alignment of other policies such as those concerned with NHS finance, research assessment exercises, and postgraduate training. Perhaps it is for these reasons that Cooksey recognises the need to review progress in 2010.

Nick Black *professor of health services research*

(Nick.Black@lshtm.ac.uk)

London School of Hygiene and Tropical Medicine, London WC1E 7HT

Competing interests: NB is responsible for the NIHR National Coordinating Centre for Service Delivery and Organisation R&D and is a member of the MRC subcommittee on evaluation.

1 Cooksey D. *A review of UK health research funding*. London: Stationery Office, 2006.
2 Goodyear M. A model clinical trials agreement. *BMJ* 2006;333:1083-4.

doi 10.1136/bmj.39059.444120.80

Drug eluting stents

Dual antiplatelet therapy should not be discontinued without referral to a cardiologist

Last week an expert panel of the US Food and Drug Administration (FDA) recommended that the FDA should issue warnings to doctors and patients about drug eluting coronary stents. The safety of such stents is unclear except in low risk patients. Furthermore, patients with drug eluting stents should take antiplatelet therapy for at least one year after insertion.

Percutaneous coronary intervention is the dominant treatment for patients with coronary artery disease; 73 000 procedures were performed in the United Kingdom in 2005, compared with 25 000 coronary artery bypass operations. Drug eluting stents have been part of the procedure since 2002 as they reduce the risk of in-stent restenosis.

In-stent restenosis, caused by injury induced cell proliferation and scar tissue formation, requires repeat intervention in 12-20% of patients receiving a bare metal (non-drug eluting) stent.[1] Randomised trials have shown that drug eluting stents, which are coated with agents such as sirolimus or paclitaxel that inhibit such local smooth muscle proliferation, reduce the need for repeat procedures to about 5%.[2 3]

Do drug eluting stents have disadvantages? During percutaneous coronary intervention, balloon inflation and stent deployment injures the endothelial layer of the vessel wall. Endothelial recovery takes about four weeks with bare metal stents, but it can take several months with drug eluting stents because of bystander eluted drug inhibition. The risk of stent thrombosis may therefore increase because of prolonged exposure to the stent strut. Stent thrombosis may occur later with drug eluting stents than with bare metal stents, potentially many months after the procedure.[4] Though this happens in only about 2% of patients, up to half of these may die or have acute myocardial infarction.[5]

To reduce the risk of stent thrombosis, patients are given dual antiplatelet therapy with aspirin and clopidogrel.[6 7] With bare metal stents patients take aspirin for life, while clopidogrel is needed to cover the one month period of endothelial regrowth only. The duration of clopidogrel therapy is difficult to determine for drug eluting stents, however, as it is unclear how long endothelial healing takes, and the manufacturers of each drug eluting stent have in the past recommended different lengths of treatment (two to six months). Anecdotal cases[8] of late thrombosis—more than one year after the procedure—with drug eluting stents have raised many unanswered questions. Is stent thrombosis, particularly late thrombosis, more common with drug eluting stents? How long is the period of risk? Does antiplatelet therapy need to be continued for longer with drug eluting stents and if so, for how long?

Because the incidence of stent thrombosis and late thrombosis is small, large trials are needed for accurate measurement of excess risk. Meta-analyses of randomised studies and registries have shown either no significant difference in thrombosis rates with drug eluting stents compared with bare metal stents,[9 10] or non-significant trends towards excess rates of thrombosis with drug eluting stents (0.29%, 95% confidence interval −0.08% to 0.66%; P=0.13).[11] A recently presented but as yet unpublished meta-analysis by the European Society of Cardiology found significantly more stent thrombosis at three years with drug eluting stents (3.9% for bare metal stents *v* 6.3% for drug eluting stents; P=0.03), raising the possibility of ongoing cumulative risk and the need for long term dual antiplatelet therapy. However, independent clinical event committees who tried to reproduce the findings from patient level data found no excess adverse clinical events (acute myocardial infarction or death) associated with drug eluting stents at four years. Although this is reassuring, concern remains regarding the risk of excess stent thrombosis in the longer term.

Despite the paucity of current data, the British Cardiovascular Interventional Society has recently recommended that dual antiplatelet therapy should be continued for one year in all patients having drug eluting stents inserted. Thus, in the UK about 30 000 people who have drug eluting stents inserted each year will also need dual antiplatelet therapy for at least one year afterwards. This can be a problem if clopidogrel needs to be stopped within this time, either because of side effects or the need for non-cardiac surgical procedures. It is particularly important as the greatest risk factor for stent thrombosis at any time is premature discontinuation of clopidogrel (hazard ratio 89.8; 29.9 to 269.6; P<0.001).[12]

Interventional cardiologists can assess the risk of stent thrombosis associated with stopping the drug by taking into account the nature of the lesion, timing of the procedure, angiographic results, and other factors such as presence of renal failure and diabetes. Increasingly, patients treated with drug eluting stents are asked to carry an information or warning card that indicates the recommended length of clopidogrel therapy.[13] Antiplatelet therapy should not be discontinued at any time, but especially within the first six to 12 months after inserting a drug eluting stent, without discussion with an interventional cardiologist. If possible, non-cardiac procedures should be undertaken without stopping clopidogrel.

Ultimately, continued research into developing drug eluting stents that allow more rapid endothelial regrowth will reduce the need for prolonged dual antiplatelet therapy.[14 15] In the meantime, we recommend that the excess risk of stent thrombosis (up to 0.3% each year) balanced against a 60-70% reduction in the need for a repeat procedure with drug eluting stents compared with bare metal stents should be used as the basis for informed consent.

A H Gershlick *consultant cardiologist*
(agershlick@aol.com)
G Richardson *consultant cardiologist*
University Hospitals of Leicester, LE3 9QP

Competing interests: AHG is on the advisory board and is an educational adviser and panel speaker for all drug eluting

The full version, with extra references, is on bmj.com

BMJ 2006;333:1233–4

stent companies. GR is on the advisory board of Abbott Vascular.

1 Ellis SG, Bajzer CT, Bhatt DL. Real-world bare metal stenting: identification of patients at low or very low risk of 9-month coronary revascularization. *Catheter Cardiovasc Interv* 2004;63:135-40.
2 Colombo A, Iakovou I. Drug-eluting stents: the new gold standard for percutaneous coronary revascularisation. *Eur Heart J* 2004;25:895-7.
3 Moses JW, Stone GW, Nikolsky E. Drug-eluting stents in the treatment of intermediate lesions: pooled analysis from four randomized trials. *J Am Coll Cardiol* 20066;47:2164-71.
4 Wenaweser P, Rey C, Eberli FR. Stent thrombosis following bare-metal stent implantation: success of emergency percutaneous coronary intervention and predictors of adverse outcome. *Eur Heart J* 2005;26:1180-7.
5 Ong AT, Hoye A, Aoki J. Thirty-day incidence and six-month clinical outcome of thrombotic stent occlusion after bare-metal, sirolimus, or paclitaxel stent implantation. *J Am Coll Cardiol* 2005;45:947-53.
6 Stone GW, Aronow HD. Long-term care after percutaneous coronary intervention: focus on the role of antiplatelet therapy. *Mayo Clin Proc* 2006;81:641-52.
7 Urban P, Gershlick AH, Guagliumi G. Safety of coronary sirolimus-eluting stents in daily clinical practice: one-year follow-up of the e-Cypher registry. *Circulation* 2006;113:1434-41.
8 McFadden EP, Stabile E, Regar E, Cheneau E, Ong AT, Kinnaird T, et al. Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy. *Lancet* 2004;364:1519-21.
9 Bavry AA, Kumbhani DJ, Helton TJ, Bhatt DL. What is the risk of stent thrombosis associated with the use of paclitaxel-eluting stents for percutaneous coronary intervention? A meta-analysis. *J Am Coll Cardiol* 2005;45:941-6.

doi 10.1136/bmj.39058.554884.BE

Measles in developing countries

Vitamin A and antibiotics prevent complications, but vaccination remains the priority

Research p 1245

Widespread vaccination against measles and improvements in clinical care and socioeconomic status have reduced mortality due to measles in many countries.[1] Nevertheless, measles remains an important cause of global morbidity and mortality, with case fatality rates as high as 9.7% in some African children with measles in recent years.[1 2] Pneumonia, the most common cause of death due to measles, can be caused by the measles virus alone, secondary herpes simplex virus, adenoviruses, or bacterial infections.[1 3] Factors contributing to increased rates of pneumonia and other complications in developing countries include young age at infection, crowding, and malnutrition, especially vitamin A deficiency.[1 4]

Antibiotics are often given to children with measles without secondary bacterial infections, but evidence of benefit has been largely anecdotal. In this week's *BMJ*, a placebo controlled randomised trial by Garly and colleagues supports the effectiveness of co-trimoxazole for preventing pneumonia and secondary bacterial conjunctivitis in children with measles in Guinea-Bissau.[5] The trial found that children receiving co-trimoxazole were significantly less likely to develop pneumonia (odds ratio 0.08, 95% confidence interval 0 to 0.56), and had higher weight gain in the month after inclusion.

One limitation of the trial, however, is that the authors do not mention vitamin A therapy, which prevents pneumonia and mortality associated with measles.[6 7] The World Health Organization recommends that all children with measles should receive vitamin A at the time of diagnosis and a second dose the next day (table on bmj.com). Obviously, children with measles who have clinical signs of pneumonia should be treated with antibiotics; however, further studies need to determine whether antibiotics provide additional benefits to children who do not have clinical pneumonia and who receive vitamin A at the time of measles diagnosis.

Measles vaccination and vitamin A therapy are highly cost effective interventions for reducing mortality due to measles.[7] Although measles vaccines have been available since 1963, hundreds of thousands of children still die from measles every year. Fortunately, new strategies are proving to be highly effective in Africa, including large scale community based supplemental immunisation campaigns, which effectively eliminated endemic transmission of measles in Latin America.[9] These campaigns are being implemented in many African countries through the "measles initiative," an effort coordinated by the American Red Cross, the Centers for Disease Control, Unicef, WHO, and the United Nations Foundation, and have resulted in dramatic declines in the incidence of measles.[10 11]

The 2010 WHO/Unicef goal to reduce global mortality due to measles by at least 90% from the 2000 estimates has an excellent chance of being met.[11 12] Enthusiasm for declaring a goal for the global eradication of measles has been dampened by delays in meeting targets for polio eradication. Nevertheless, measles meets the criteria for diseases that could be eradicated.[11] Some day, clinicians will no longer need to ponder the therapeutic options for children with measles. In the meantime, doctors caring for children everywhere should support local and global immunisation programmes and optimise care of children with measles using vitamin A and antibiotics when necessary.

Neal A Halsey *professor*

(nhalsey@jhsph.edu)

Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21205, USA

Competing interests: NAH has received research grant support from GlaxoSmithKline, Sanofi Pasteur, and Merck, manufacturers of measles vaccines.

1 Perry RT, Halsey NA. The clinical significance of measles: a review. *J Infect Dis* 2004;189:S4-16.
2 Nandy R, Handzel T, Zaneidou M, Biey J, Coddy RZ, Perry R, et al. Case-fatality rate during a measles outbreak in eastern Niger in 2003. *Clin Infect Dis* 2006;42:322-8.
3 Hussey GD, Clements CJ. Clinical problems in measles case management. *Ann Trop Paediatr* 1996;16:307-17.
4 Caulfield LE, de Onis M, Blossner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. *Am J Clin Nutr* 2004l;80:193-8.
5 Garly ML, Balé C, Martins CL, Whittle HC, Nielsen J, Lisse IM, et al. Prophylactic antibiotics to prevent pneumonia and other complications after measles: community based randomised double blind placebo controlled trial in Guinea-Bissau. *BMJ* 2006;333:1245-7.
6 Hussey GD, Klein M. A randomized, controlled trial of vitamin A in children with severe measles. *N Engl J Med* 1990;323:160-4.
7 Edejer TT, Aikins M, Black R, Wolfson L, Hutubessy R, Evans DB. Cost effectiveness analysis of strategies for child health in developing countries. *BMJ* 2005;331:1177.

doi 10.1136/bmj.39058.361620.BE

P+ *The full version, with extra references and a table, is on bmj.com*