Saturday 27 September 1997

BMJ

Optimising the investigation of meningococcal disease

Early treatment with benzylpenicillin is important and doesn't jeopardise diagnosis

See p 774

The incidence of meningococcal disease in England and Wales has remained at high levels over the past two winters, as has the proportion of cases caused by strains of serogroup C (M Ramsay, E Kaczmarski, personal communications). Clusters, also caused mainly by serogroup C strains, have increased considerably, particularly among students at schools and universities (A Rushdy, J Stuart, personal communications). While effective vaccines are awaited, current priorities are to optimise recognition, diagnosis, and management.

Administration of benzylpenicillin to suspected cases before admission to hospital reduces mortality[1] and is advocated by the United Kingdom's chief medical officers. Though now used more widely, continuing failure to implement this simple measure[2] may be due to a misplaced fear of obscuring the diagnosis and thereby jeopardising management.

After an injection of benzylpenicillin blood culture is rarely positive and, though cerebrospinal fluid may still yield meningococci,[3] lumbar puncture is an increasingly controversial investigation in suspected meningococcal disease. Occasional deaths due to brainstem herniation, together with the recognition that negative initial results are often misleading,[4] have focused attention on alternative diagnostic methods. Using a few simple alternative investigations greatly improves the chances of confirming the diagnosis.[5]

In about half of patients with systemic disease meningococci can be isolated from the posterior pharyngeal wall, preferably accessed through the mouth (or through the nose if the patient is unconscious or delirious); this proportion is unaffected by prior benzylpenicillin treatment.[3] In as many as two thirds of patients tissue fluid aspirated from skin affected by haemorrhagic rash may show Gram negative diplococci on a stained smear or yield meningococci on culture.[6] Serological diagnosis is also available, though paediatricians may be reluctant to recall and rebleed a small child recovering from the combined traumas of recent meningococcal disease and hospital admission.

Polymerase chain reaction (PCR) amplification of bacterial DNA to detect meningococci in peripheral blood or cerebrospinal fluid is now used widely in England and Wales. Performed on peripheral blood, this can be much more sensitive than blood culture,[7] but specificity has yet to be evaluated in large, clinically relevant populations. New primers designed by the PHLS Meningococcal Reference Unit now permit serogrouping of meningococci in over half of cases with a positive result on PCR screening,[8] providing important information for management of contacts. The most suitable specimens for PCR are cerebrospinal fluid or the residue of the first blood sample taken on admission for haematological evaluation; later blood samples are less satisfactory because of clearance of meningococcal DNA. The admitting clinician should either take two samples into EDTA tubes or ask the microbiology department to retrieve a single sample from the haematology department. Retrieval must be swift; routine samples for blood counts are normally discarded rapidly.

As the use of lumbar puncture declines, the microbiology department is less likely to be aware of newly admitted cases. Clinicians must ensure robust lines of communication between ward and laboratory. Furthermore, all cases of meningococcal disease, whether suspected or confirmed, must be reported immediately to the consultant in communicable disease control (or the consultant in public health medicine), who is responsible for identifying close contacts and organising prophylaxis. Regular joint audit of cases helps to reinforce good diagnostic, clinical, and reporting practice.

Current British guidance for managing close contacts is to offer advice and information, a chemoprophylactic antibiotic, and vaccine if appropriate. Chemoprophylaxis must be given speedily as the risk of secondary cases, though small, is highest in the days immediately after the admission of the index case to hospital. In their *BMJ* leading article last year Kristiansen and Knapskog proposed that close contacts aged under 15 years should be offered protective penicillin treatment in addition to chemoprophylaxis.[9] However, they offered no evidence to support this additional measure, which is not national policy in Norway. We do not recommend it for Britain.

The same authors also proposed that in outbreaks with three or more linked cases chemoprophylaxis should be restricted to proved nasopharyngeal carriers. This is unwise. A single negative throat swab is unreliable in predicting freedom from meningococcal carriage; moreover, during the two to three days it takes to carry out swabbing and obtain culture results the risk is at its highest. Paradoxically, the contacts at greatest risk of disease are those who have yet to acquire the pathogenic strain. Management of clusters is complex and has been considered recently by a working group commissioned by the Public Health Laboratory Service.[10]

Clinical evaluation of promising conjugated serogroup C meningococcal vaccines is now well advanced, and development work at an earlier stage continues on candidate vaccines for serogroup B disease. Prospects for a reduction, and ultimately, elimination of meningococcal disease are good.

Keith Cartwright *Secretary PHLS meningococcus working group*

PHLS South West Directorate Office, Gloucestershire Royal Hospital, Gloucester GL1 3NN

Simon Kroll *Professor of paediatrics and molecular infectious diseases*

Imperial College School of Medicine, St Mary's Hospital, London W2 1PG

1 Cartwright K, Strang J, Gossain S, Begg N. Early treatment of meningococcal disease. *BMJ* 1992;305:774.
2 Irwin D, Miller JM, Cornell SJ. GPs often fail to give early parenteral benzylpenicillin in suspected meningococcal infection. *BMJ* 1996;312:1538.
3 Cartwright K, Reilly S, White D, Stuart J. Early treatment with parenteral penicillin in meningococcal disease. *BMJ* 1992;305:143-7.
4 Wylie PAL, Stevens D, Drake III W, Stuart J, Cartwright K. Epidemiology and clinical management of meningococcal disease in Gloucestershire: retrospective population-based study. *BMJ* 1997;315:774-9.
5 Kaczmarski EB, Cartwright KAV. Control of meningococcal disease: guidance for microbiologists. *Commun Dis Rep Rev* 1995;5:R196-8.
6 van Deuren M, van Dijke BJ, Koopman RJJ, Horrevorts AM, Meis JFGM, Santman FW et al. Rapid diagnosis of acute meningococcal infections by needle aspiration or biopsy of skin lesions. *BMJ* 1993;306:1229-32.
7 Newcombe J, Cartwright K, Palmer WH, McFadden J. Polymerase chain reaction of peripheral blood for the diagnosis of meningococcal disease. *J Clin Microbiol* 1996;34:1637-40.
8 Borrow R, Claus H, Guiver M, Smart L, Jones DM, Kaczmarski EB, et al. Non culture diagnosis and serogroup determination of meningococcal B and C infection by a sialyltransferase (siaD) PCR ELISA. *Epidemiol Infect* 1997;118:111-7.
9 Kristiansen B-E, Knapskog A-B. Secondary prevention of meningococcal disease. *BMJ* 1996;312:591-2.
10 Stuart JM, Monk PN, Lewis DA, Constantine C, Kaczmarski EB, Cartwright KAV. Management of clusters of meningococcal disease. *Commun Dis Rep Rev* 1997;7:R3-5.

Climate change—thinking widely, working locally, acting personally

Health workers have a crucial role

See p 805

One of the aims of public health is to seek the tools with which we can implement policies to improve the health of our populations. But the potential health effects of climate change spelt out in papers by McMichael and Haines in this issue (p 805)[1] and next week's seem so remote that implementing change is difficult. The rich populations of the north are not sufficiently exercised by the plight of small island states that may not exist by 2050, by the aggravation of the food crisis in Africa, or, indeed, by the spread of vector borne diseases. Notably, President Bill Clinton is not ready to commit America to reduce emissions of carbon dioxide, a major contributor to global warming, by 20% by 2010.

The underlying pressure causing climate change—the unsustainable pattern of consumption in the world's rich countries— also has other, more immediate consequences. Changes in technology, social organisation, and lifestyles that have accompanied the changes in consumption are associated with chronic diseases, including coronary heart disease, diabetes, respiratory disorders, and osteoporosis. Unfit, obese populations with a high prevalence of coronary heart disease are a product of the same unsustainable consumption as drives climate change.

Unsustainable development affects health in many ways. Take, for example, food production. Most food consumed in the developed world is grown under intensive, often polluting, conditions remote from where it is consumed. Many products travel thousands of miles to the consumer, their transport contributing via carbon dioxide emissions to global warming.[2] In the long term this contributes to wide ranging hazards to human health. In the short term it does little to improve the nutrition and health of millions living in deprived areas of developed nations without the incomes and cars to reach out of town supermarkets. Thus unsustainable development helps widen the gap between rich and poor. This not only damages the health of the poor[3-5]; it also undermines the "social capital" of the whole society— derived from a sense of shared participation in society's activities and decisions—a key determinant of the population's health.[6 7]

The recognition that unsustainable development underlies both climate change and much ill health is helpful in that policies aimed at reducing the impact of climate change will also help prevent illness. We suggest four areas for action nationally and locally.

Firstly, we need to create integrated transport systems, emphasising walking, bicycling, and public transport and rerouting commercial freight from road to rail. About a quarter of Britain's production of carbon dioxide comes from vehicle exhaust.[8] Measures to make walking and cycling safer will make these modes of transport more acceptable and increase social capital as people feel less threatened on the streets. Increased levels of physical activity and reduced levels of vehicle pollutants will have health benefits.

Secondly, production of carbon dioxide should be reduced by decreasing the use of fossil fuels. Improvements in energy efficiency, including home insulation and energy efficient appliances, are particularly important for people suffering fuel poverty (eight million in Britain).[9] The potential for renewable energy is vast and underexploited. For example, it has been estimated that a wholesale application of solar photovoltaic technology could generate up to two thirds of Britain's electricity.[10]

Thirdly, we should move towards a more locally based agriculture, encouraging retailers to stock locally sourced food and developing links between growers and consumers. As well as cutting transport this encourages more environmentally responsible agriculture and healthier eating. Fourthly, we should

*A form to help you calculate your contribution to carbon dioxide production is available on the *BMJ*'s website

promote tree planting since growing trees absorb and recycle carbon dioxide, as well as stabilising ecosystems.

Imaginative solutions in each of these policy areas could be piloted in the new Health Action Zones proposed by the government within existing resources. For instance, if local authorities in these zones invested in energy efficient houses, the cost of the work could be recouped relatively quickly by savings on energy bills.

Finally, while locally implemented public policy along these lines is important, personal example is a powerful ally. The carbon dioxide for which each one of us is responsible comes mainly from travelling, heating, and eating. Each of us can measure the amount of carbon dioxide for which we are responsible* and try to reduce it by making changes which are for the most part life and health enhancing as well as environmentally beneficial. For instance 75% of all car journeys are under five miles, and walking or bicycling even a quarter of these would be powerful medicine. Insulating our houses and installing radiator specific thermostats, buying locally produced food, and cooking with lids on the pan, are all simple measures anyone can take. Protecting the environment is an essential public health function. If we act now we will reap benefits now and long into the future.

Cathy Read *Registrar in public health medicine*
Robin Stott *Consultant physician andChairman*

MEDACT: Medical Action For Global Security, London N19 4DJ

1 Intergovernmental Panel on Climate Change. Contribution of working group 1 to the second assessment report of the intergovernmental panel on climate change. In: Houghton JT, Meira-Filho LG, Callandar BA, eds. *Climate changes, 1996: the science of climate change.* New York: Cambridge University Press 1996.
2 Paxton A. *The food miles report: the danger of long distance food transport.* London: SAFE Alliance, 1994.
3 Marmot MG, Bosma H, Hemmingway H, Brunner E, Stansfield S. Contributors of job control and other risk factors to social variations in coronory heart disease incidence. *Lancet* 1997;350:235-9.
4 Wilkinson R How can secular improvements in life expectancy be explained? In: Blane D, Brunner E, Wilkinson R, eds. *Health and social organisation.* London: Routledge, 1996.
5 Syme L.S. Explaining inequalities in coronary heart disease. *Lancet* 1997;350:231.
6 Putnam RD. *Democracy and the civic community: tradition and change in an Italian experiment.* Princeton: Princeton University Press, 1993.
7 Mustard JF. Health and social capital. In: Blane D, Brunner E, Wilkinson R, eds. *Health and social organisation.* London: Routledge, 1996.
8 Department of the Environment. *Climate change: UK Programme.* London: Department of the Environment, 1997.
9 Boardman B. *Fuel Poverty: from warm homes to affordable warmth.* London: Belhaven, 1991:206.
10 Department of Trade and Industry. *The potential generating capacity of PV-clad buildings in the UK.* London: DTI, 1992 (ETSU 1365 - P1).

Peer review: reform or revolution?

Time to open up the black box of peer review

See p 766

As recently as 10 years ago we had almost no evidence on peer review, a process at the heart of science. Then a small group of editors and researchers began to urge that peer review could itself be examined using scientific methods. The result is a rapidly growing body of work, much of it presented at the third international congress on peer review held in Prague last week. The central message from the conference was that there is something rotten in the state of scientific publishing and that we need radical reform.

The problem with peer review is that we have good evidence on its deficiencies and poor evidence on its benefits. We know that it is expensive, slow, prone to bias, open to abuse, possibly anti-innovatory, and unable to detect fraud. We also know that the published papers that emerge from the process are often grossly deficient. Research presented at the conference showed, for instance, that reports of randomised controlled trials often fail to mention previous trials and do not place their work in the context of what has gone before; that routine reviews rarely have adequate methods and are hugely biased by specialty and geography in the references they quote (p 766); and that systematic reviews rarely define a primary outcome measure.

Perhaps because scientific publishing without peer review seems unimaginable, nobody has ever done what might be called a placebo controlled trial of peer review. It has not been tested against, for instance, editors publishing what they want with revision, and letting the correspondence columns sort out the good from the bad and point out the strengths and weaknesses of studies. Most studies have compared one method of peer review with another and used the quality of the review as an outcome measure rather than the quality of the paper. One piece of evidence we did have from earlier research was that blinding reviewers to the identity of authors improved the quality of reviews,[1] but three larger studies presented at the congress found that it did not. The new studies also found that blinding was successful in only about half to two thirds of cases. One of those studies—by Fiona Godlee from the *BMJ* and two colleagues—might also be interpreted as showing that peer review "does not work." The researchers took a paper about to be published in the *BMJ*, inserted eight deliberate errors, and sent the paper to 420 potential reviewers: 221 (53%) responded. The median number of errors spotted was two, nobody spotted more than five, and 16% didn't spot any.

How should editors—and those deciding on grant applications—respond to the growing body of evidence on peer review and the publishing of scientific research? The most extreme sometimes argue that peer review, journals, and their editors should be thrown into the dustbin of history and authors allowed to communicate directly with readers through the internet. Readers might use intelligent electronic agents ("knowbots" is one name) to help them find valid research that meets their needs. This position is being heard less often, and at the conference Ron LaPorte—an American professor of epidemiology who has predicted the death of biomedical journals[2] —took a milder position on peer review. He sees a future for it. Readers seem to fear the firehose of the internet: they want somebody to select, filter, and

purify research material and present them with a cool glass of clean water.

Peer review is unlikely to be abandoned, but it may well be opened up. At the moment most scientific journals, including the *BMJ*, operate a system whereby reviewers know the name of authors but authors don't know who has reviewed their paper. Nor do authors know much about what happens in the "black box" of peer review. They submit a paper, wait, and then receive a message either rejecting or accepting it: what happens in the meantime is largely obscure. Drummond Rennie—deputy editor (West) of *JAMA* and organiser of the congress—argued that the future would bring open review, whereby authors know who has reviewed their paper. Such a proposal was floated several years ago in *Cardiovascular Research*, and several of the editors who were asked to respond (including Dr Rennie; Stephen Lock, my predecessor; and me) said that open review would have to happen.[3] Indeed, several journals already use it. The argument for open review is ultimately ethical—for putting authors and reviewers in equal positions and for increasing accountability.

Electronic publishing can allow peer review to be open not only to authors but also to readers. Most readers don't care much about peer review and simply want some assurance that papers published are valid, but some readers, particularly researchers, will want to follow the scientific debate that goes on in the peer review process. It could also have great educational value. With electronic publishing we may put shorter, crisper versions in the paper edition of the journal and longer, more scientific versions on our website backed up by a structured account of the peer review process.

The *Medical Journal of Australia* and the Cochrane Collaboration have already made progress with using the internet to open up peer review. The Australians have been conducting a trial of putting some of their accepted papers on to their website together with the reviewers' comments some two months before they appear in print. They invite people to comment and give authors a chance to revise their paper before final publication. Contributors, editors, reviewers, and readers have all appreciated the process, although few changes have been made to papers. The *Medical Journal of Australia* now plans to extend its experiment and begin to use the web for peer review of submitted manuscripts. The Cochrane Collaboration puts the protocols of systematic reviews on the web together with software that allows anybody to comment in a structured way—so long as they give their names. Protocols have been changed as a result. The collaboration also invites structured responses to published reviews. These are particularly important because those who have contributed reviews are committed to keeping them up to date in response to important criticisms and new evidence. Dr Rennie predicted a future in which the such a commitment to the "aftercare" of papers would apply also to those publishing in paper journals. At the moment papers are frozen at publication, even when destroyed by criticism in letters columns.

I believe that this conference will prove to have been an important moment in the history of peer review. The *BMJ* now intends to begin opening up peer review to contributors and readers and invite views on how we should do this. Soon closed peer review will look as anachronistic as unsigned editorials.

Richard Smith *Editor, BMJ*

1 McNutt RA, Evans AT, Fletcher RH, Fletcher SW. The effects of blinding on the quality of peer review: a randomized trial. *JAMA* 1990;263:1371-6.
2 LaPorte RE, Marler E, Akazawa S, Sauer F, Gamboa C, Shenton C, et al. Death of biomedical journals. *BMJ* 1995;310:1387-90.
3 Fabiato A. Anonymity of reviewers. *Cardiovascular Reseach* 1994;28: 1134-9.

Diagnostics in developing countries

Time for an essential diagnostics programme

Diagnostics are big business in developing countries. In Lahore private clinics advertise magnetic resonance imaging on public billboards, diagnostic clinics abound, and ultrasound examination on demand costs $2.50 to $10. In Bangkok there is one computed tomographic scanner for every 62 000 people, and 90% of private hospitals with more than 50 beds own one.[1] While some of these changes might be anticipated as government policies shift towards enabling provision of private care,[2] there is some evidence that governments themselves are spending public money to expand diagnostic services. For example, one provincial government in Pakistan borrowed $8m to upgrade basic healthcare facilities by providing medical equipment—mainly *x* ray machines, ultrasound scanners, and microscopes[3]; in Lesotho plans to upgrade basic health centres included the purchase of *x* ray facilities and laboratories[4]; and similar large expenditures are being considered by donors or governments in countries from Peru to Palestine. The investment is sometimes large: in Pakistan, for example, the Network for the Rational Use of Medication estimated that in 1995 the value of the market for medical equipment in Pakistan was $0.25bn, while the pharmaceutical market in the same year was $0.91bn.

The trend towards providing better diagnostic equipment is partly driven by the desire to make diagnostic tests more accessible—something that the World Health Organisation has promoted.[5] However, there are other pressures at work. Gleaming equipment and laboratories provide a professional veneer that is attractive to both doctors and patients. Some private practitioners own their own laboratories, and commercial laboratories in some countries pay doctors for patients referred. In some instances, unscrupulous equipment manufacturers encourage purchase of equipment through incentives for the administrators who sign the requisitions forms. Sometimes overseas aid programmes use funds to stimulate their own industrial base, including the manufacture of medical

equipment. Yet it is expensive to install, staff, maintain, and buy consumables for any diagnostic equipment, particularly *x* ray and ultrasound machines, microscopes, spectrophotometers, and kit assays. Therefore, ministries need to be sure the investment is likely to benefit patients, and good science and technical support should help here.

Technical advice from the WHO and other aid and donor agencies generally focuses on efficient delivery of medical tests by ensuring that equipment is regularly serviced, gives accurate measurements, and is supplied with consumable materials.[6] This is clearly a prerequisite if a test is to have any potential impact. But we need to step back a little. Providing *x* ray machines and basic laboratory equipment for a 100 bed district hospital seems sensible, but will such investigations mean better primary care at smaller, less sophisticated, walk-in clinics?

This can be answered by addressing three questions. Firstly, will the tests actually result in altered decision making, change the timing or type of treatment, and thus result in a better outcome?[7] To answer these questions, we would need to evaluate the skills of the clinical staff at these facilities and the case mix of the patients. Secondly, given the additional information provided by the test and its potential to improve outcomes, can the healthcare system as a whole provide the care that will result in these better outcomes? Thirdly, "Is this location the most cost effective for this test?" Economies of scale mean that low throughput results in high unit costs, so that an *x* ray unit at an urban primary health facility seeing 25 general outpatients a day is unlikely to be a sensible use of scarce resources.

These are difficult questions. In the face of specialist clinical demand and strong commercial pressures, healthcare planners need support and information. We propose an essential diagnostics programme that promotes the rational and effective use of diagnostic tests in the developing world. Such a programme could refine a series of basic tests linked to symptom complexes in standard treatment regimens. Methods for doctors and managers to audit diagnostic practice should be developed and disseminated, and the effectiveness of tests should be debated in the public arena, along the lines of the WHO's excellent essential drugs programme. In the meantime, ministries and donors aiming to improve the quality of primary health care should examine carefully whether buying medical equipment for primary care centres is an efficient or effective use of scarce resources.

This collaborative work is part of the Effectiveness of Health Care in Developing Countries Project, supported by the Department for International Development (UK) and the European Union. However, these organisations can accept no responsibility for any information provided or views expressed.

Paul Garner *Head*

International Health Division, Liverpool School of Tropical Medicine, Liverpool L3 5QA

Ayyaz Kiani *Project coordinator*

Association for Rational Use of Medication in Pakistan, Islamabad, Pakistan

Anuwat Supachutikul *Senior research fellow*

Health Systems Research Institute, Bangkok, Thailand

1 Tangcharoensathien V, Kongsawad S, Urchaikun C, Uppamayun Y. [The diffusion of medical devices in Thailand in 1994]. Bangkok: Health Systems Research Institute, 1995.
2 Word Bank. *World development report 1993: investing in health*. Oxford: Oxford University Press, 1993.
3 Haque I. Health care facilities for NWFP: plan approved. *Dawn Sunday* 1996 Jan 7:1.
4 Pepperall J, Garner P, Fox-Rushby J, Moji N, Harpham T. Hospital or health centre? A comparison of the costs and quality of urban outpatient services in Maseru. *Int J Health Plann Manage* 1995;10:59-71.
5 World Health Organisation. *The role of health centres in the development of urban health systems*. Geneva: WHO, 1992:1-38. (Technical Report Series No 827.)
6 Temple-Bird C, Mhiti R, Bloom G. *Medical equipment in Botswana: a framework for management development*. Geneva: World Health Organisation, 1995. (WHO/SGS/NHP/95.)
7 Eddy DM. *A manual for assessing health practices and designing practice policies: the explicit approach*. Philadelphia: American College of Physicians, 1992.

Determining prognosis after acute myocardial infarction in the thrombolytic era

Non-invasive investigations still have a place

The most appropriate and cost effective approach to assessing prognosis in patients who survive an acute myocardial infarction in the thrombolytic era remains controversial. Prognosis is determined mainly by the degree of left ventricular dysfunction and the extent of residual jeopardised myocardium, both generally and in the distribution of the infarct related artery. The extent of myocardial damage and inducible ischaemia can be assessed with non-invasive stress imaging and the extent of coronary artery disease with angiography. The issue is whether "routine" coronary angiography performed soon after infarction in patients reperfused early and with an uncomplicated course yields better prognostic information than exercise or pharmacological stress perfusion imaging.

Outcome studies in America and Canada have yielded unexpected findings about the value of routine invasive investigations in patients with uncomplicated courses. Rouleau et al reported that, although coronary angiography was more often performed in America than in Canada (68% *v* 35%), as was revascularisation after infarction (31% *v* 12%), no difference in mortality (23 *v* 22%) or rate of reinfarction (13% *v* 14%) was observed at a mean follow up of 42 months.[1] In the GUSTO-1 trial, despite a much higher rate of angiography (72% *v* 25%) and angioplasty (43% *v* 14%) in America than in Canada, there was no difference in survival at 1 year (90.7% *v* 90.3%).[2] The GUSTO-2 trial and a more recent one have confirmed the same picture,[3 4] and other studies in American centres suggest that merely the presence of a cardiac cath-

eterisation laboratory in a hospital is one of the strongest predictors of catheterisation in patients with acute infarction.

Studies in the 1980s showed that submaximal exercise or pharmacological stress myocardial perfusion imaging performed before discharge successfully distinguished patients at high risk of subsequent cardiac events and did so better than exercise electrocardiographic testing alone. Perfusion imaging was better at detecting and localising ischaemia at submaximal exercise heart rates; identifying multivessel coronary artery disease and residual ischaemia within the zone of infarction; and measuring infarct size. Gibson et al reported that about half of patients who were 65 or younger with an uncomplicated myocardial infarction who showed major defects on imaging subsequently experienced cardiac death, recurrent infarction, or class III-IV angina requiring admission to hospital.[5] These defects were either multiple perfusion defects in more than one coronary vascular supply region on submaximal exercise scintigraphy with thallium-201, reversible ^{201}Tl defects (ischaemia) within or outside the infarct zone, or abnormal lung thallium uptake. The cardiac event rate was only 6% in patients with normal scans or only persistent defects in the supply region of the infarct related artery. Studies published in the prethrombolytic era showed that stress perfusion had a sensitivity of about 70% and a specificity of 85% for detecting patients with multivessel disease.[6] Similar findings were reported with dipyridamole or adenosine stress in conjunction with perfusion imaging.[7 8]

In the thrombolytic era, however, it is hard to show the worth of stress perfusion. Patients who are eligible for thrombolysis comprise a relatively low risk group, and many asymptomatic patients undergo routine angiography before stress testing. Those with multivessel disease or a residual high grade infarct related stenosis are often referred straight for revascularisation. Most of these high risk patients would have been identified by stress imaging but underwent the invasive strategy first. Also, many patients who do initially undergo stress testing are referred for coronary angiography and revascularisation as a result. This reduces the future cardiac event rate in these cohorts, resulting in a low positive predictive value of non-invasive imaging variables for predicting cardiac death or reinfarction (post test referral bias).[9]

Nevertheless, data are now emerging which show the continuing value of non-invasive stress imaging for risk stratification after acute myocardial infarction. Dakik et al recently reported that quantitative exercise ^{201}Tl imaging performed in patients who had received thrombolysis provided extra prognostic information over and above clinical findings and ejection fraction data; coronary angiographic variables did not further improve prognostic information.[10] Again, other studies have shown similar findings, with both exercise and pharmacological stress.[11-13]

Although the negative predictive value of a low risk stress perfusion scan for predicting a low event rate is excellent, the positive predictive value of an ischaemic response for predicting subsequent cardiac death or infarction is only 40-50%. A cost effective approach therefore may be to categorise patients clinically into high risk, intermediate risk, or low risk groups before determining which investigations to use. Clinically high risk patients (those with postinfarction angina, history of infarction, rales in over a third of the lung field on admission, hypotension and sinus tachycardia on admission) could go directly to coronary angiography with a view to coronary revascularisation. Patients at intermediate or low risk could undergo an initial non-invasive investigation with angiography performed in those with significant ischaemia or a scan pattern on perfusion imaging that suggests multivessel disease. Patients with a depressed left ventricular ejection fraction but without clinical manifestations of heart failure could also undergo a non-invasive investigation to determine both myocardial viability within the zone of dysfunction and extent of inducible ischaemia. Those whose depression of left ventricular function is caused by jeopardised myocardium could be referred for angiography followed by revascularisation of arteries with important stenoses; those in which it is caused predominantly by myocardial scar would be treated with angiotensin converting enzyme inhibitors, aspirin, and β blockers. To validate the worth of this approach, however, we need a clinical trial comparing it with "routine" angiography.

George A Beller *Chief*

Cardiovascular Division, Department of Internal Medicine, University of Virginia Health Sciences Center, Charlottesville, VA 22908, USA

1 Rouleau JL, Moyé LA, Pfeffer MA, Arnold JMO, Bernstein V, Cuddy TE, et al for the SAVE Investigators. A comparison of management patterns after acute myocardial infarction in Canada and the United States. *N Engl J Med* 1993;328:779-84.
2 Van de Werf F, Topol EJ, Lee KL, Woodlief LH, Granger CB, Armstrong PW, et al for the GUSTO Investigators. Variations in patient management and outcomes for acute myocardial infarction in the United States and other countries. Results from the GUSTO trial. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. *JAMA* 1995;273:1586-91.
3 Armstrong PW, Granger CB, Knight D, Sutherland W, Clapp-Channing N, Hlatky M, et al. Temporal trends in the process of myocardial infarction management; Canadian/US GUSTO experience. *Circulation* 1996;94 (suppl 1):I-28.
4 Tu JV, Pashos CL, Naylor CD, Chen E, Norman S-L, Newhouse JP, et al. Use of cardiac procedures and outcomes in elderly patients with myocardial infarction in the United States and Canada. *N Engl J Med* 1997;336:1500-5.
5 Gibson RS, Watson ED, Craddock GB, Crampton RS, Kaiser DL, Denny MJ, et al. Prediction of cardiac events after uncomplicated myocardial infarction: a prospective study comparing predischarge exercise thallium-201 scintigraphy and coronary angiography. *Circulation* 1983;68:321-36.
6 Gimple LW, Beller GA. Assessing prognosis after acute myocardial infarction in the thrombolytic era. *J Nucl Cardiol* 1994;1:198-209.
7 Brown KA, O'Meara J, Chamber CE, Plante DA. Ability of dipyridamole-thallium-201 imaging one to four days after acute myocardial infarction to predict in-hospital and late recurrent myocardial ischemic events. *Am J Cardiol* 1990;65:160-7.
8 Bosch X, Magriñá J, March R, Sanz G, Garcia A, Betriu A, et al. Prediction of in-hospital cardiac events using dipyridamole-thallium scintigraphy performed very early after acute myocardial infarction. *Clin Cardiol* 1996;19:189-96.
9 Miller TD, Gersh BJ, Christian TF, Bailey KB, Gibson RJ. Limited prognostic value of thallium-201 exercise treadmill testing early after myocardial infarction in patients treated with thrombolysis. *Am Heart J* 1995;130:259-66.
10 Dakik HA, Mahmarian JJ, Kimball KT, Koutelou MG, Medrano R, Verani MS. Prognostic value of exercise ^{201}T1 tomography in patients treated with thrombolytic therapy during acute myocardial infarction. *Circulation* 1996;94:2735-42.
11 Mahmarian JJ, Mahmarian AC, Marks GF, Pratt CM, Verani MS. Role of adenosine thallium-201 tomography for defining long-term risk in patients after acute myocardial infarction. *J Am Coll Cardiol* 1995;25: 1333-40.
12 Pirelli S, Moreo A, Piccalò G, Corato A, Sara R, Danzi GB, et al. Dipyridamole thallium-201 imaging very early after uncomplicated acute myocardial infarction in patients treated with thrombolytic therapy. *Eur Heart J* 1997,18:925-30.
13 Basu S, Senior R, Dore C, Lahiri A. Value of thallium-201 imaging in detecting adverse cardiac events after myocardial infarction and thrombolysis: a follow up of 100 consecutive patients. *BMJ* 1996;313:844-8.