

# BMJ Chemoprophylaxis in the prevention of leprosy

W Cairns S Smith

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## EDITORIALS

### Improving uptake of MMR vaccine

Recognising and targeting differences between population groups are the priorities



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**Peter McIntyre** director  
[PeterM@chw.edu.au](mailto:PeterM@chw.edu.au)  
**Julie Leask** research fellow,  
National Centre for Immunisation  
Research and Surveillance of  
Vaccine Preventable Diseases, The  
Children's Hospital at Westmead,  
NSW 2145, Australia

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Almost a decade since the original report suggesting a link between the combined measles, mumps, and rubella (MMR) vaccine and autism or inflammatory bowel disease, we now have overwhelming evidence to refute such a link.<sup>1</sup> Some people, however, still refuse to have their children vaccinated for MMR, and sometimes replace the combined vaccine with single antigen vaccines. In the accompanying study, Pearce and colleagues report uptake of the combined MMR vaccine and single antigen vaccines and they discuss the factors influencing uptake in a three year follow-up of the UK millennium cohort.<sup>2</sup>

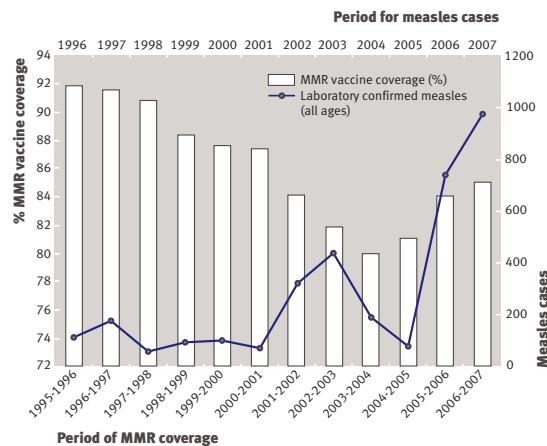
Low MMR vaccine coverage is not a trivial matter, because the accumulation of unvaccinated children will increase the risk of measles outbreaks. Confirmed cases of measles in England and Wales rose from 56 in 1998 to 971 in 2007 (figure).<sup>3</sup> In the United Kingdom, coverage for MMR at 24 months is lower than for other vaccines (85% versus about 94%).<sup>4</sup> Such a wide gap between coverage for MMR and other vaccines has not been seen in other countries. What do data from the UK and elsewhere on the characteristics of parents who refuse vaccines and their sources of advice tell us about the best ways to tackle their concerns at the individual and population level?<sup>1 2</sup>

Pearce and colleagues report that parents in the millennium cohort who sought single antigen vaccines were significantly more likely to be white, well educated, affluent, older mothers, and to have just one child, compared with parents who fully immunised their child. In contrast, families whose children had

not received MMR vaccine showed a less uniform pattern. They were more likely to have a larger family size and the mothers were more likely to smoke, be either younger or older than average, and have higher than average levels of education but not income. This may be because Pearce and colleagues did not differentiate between children lacking only MMR vaccine, those lacking some other vaccines, and those who had received no scheduled vaccines. This is probably important, because in the United States,<sup>5</sup> Australia,<sup>6</sup> and in this cohort at 9 months of age,<sup>7</sup> non-selective partial immunisation is associated with indicators of disadvantage, in direct contrast to vaccine refusal by choice.

A recent UK study differentiated two groups of people who are suspicious about vaccination into “reformists,” who were critical of vaccines but likely to support vaccination in at least some respects, and “radicals,” who followed alternative notions of health and questioned all vaccines.<sup>8</sup> Parents who seek out single antigen vaccines or those who selectively refuse MMR are more likely to fit the reformist definition, and may be receptive to approaches that deal with their concerns in an open and individualised way. Parents who refuse all vaccines are more likely to fit the radical definition. Even the best communication strategies are unlikely to change such people's opinions.

What can be done to reach the 95% or greater coverage with MMR needed to eliminate measles? Attitudes are key, because 14% of UK mothers in 2006 considered MMR a greater risk than the diseases it prevents, although this proportion had decreased from a peak of 24% in 2002.<sup>9</sup> At the individual level, efforts to persuade parents with deep seated philosophical or religious objections to all vaccines are likely to be futile. The main focus should be on parents of partially immunised children, who fall into two broad groups—those who are socially or materially advantaged and those who are not. Strategies to tackle late or partial immunisation (or both) in disadvantaged populations should focus on improving access. Families who selectively refuse MMR, usually on the basis of safety concerns,<sup>9</sup> are likely to have almost 95% coverage for other vaccines.<sup>5</sup> Communication needs to consider the experience and context of the individual families.<sup>10</sup> Pilot work with a detailed MMR decision aid for parents found that it has potential for influencing attitudes and knowledge.<sup>11</sup> The aid details rates of measles and its complications and adverse events related to MMR vaccination. This balance is useful because some parents in the UK think of official information as biased



MMR coverage at 24 months in the UK and laboratory confirmed cases of measles for all ages (England and Wales), 1995-2007<sup>3 4</sup>

and want information that is seen as “independent.”<sup>11 9</sup> At the population level, initiatives such as linking parental financial incentives or entry to school or childcare facilities to completion of immunisation have improved overall immunisation coverage but require legislative action and societal support.<sup>12</sup>

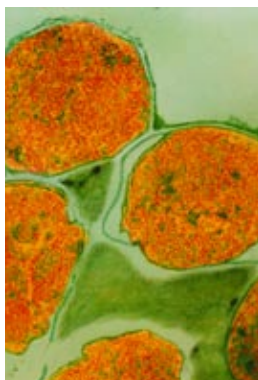
The goal of 95% immunisation coverage is a constant challenge, and the occurrence of disease outbreaks when coverage wanes is a salient reminder of the need for vigilance. Targeted strategies that recognise the different groups of people who contribute to low immunisation coverage are needed to achieve the best possible control of vaccine preventable diseases.

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## Chemoprophylaxis in the prevention of leprosy

National policies need to be reviewed in the light of new evidence supporting a single dose of rifampicin



KARILOUNATMAA/SPL

In the accompanying paper, Moet and colleagues report a randomised controlled trial of chemoprophylaxis using rifampicin in household contacts of patients with newly diagnosed leprosy.<sup>1</sup> The potential for chemoprophylaxis to reduce transmission of leprosy caused much interest in the 1960s and 1970s. A series of trials was conducted in household contacts and in highly endemic communities using dapsone, usually given twice weekly over a period of years. A meta-analysis based on 12 of these trials (six randomised controlled trials and six non-randomised controlled trials) showed that dapsone provided significant protection (relative risk 0.4, 95% confidence interval 0.29 to 0.55) against leprosy.<sup>2</sup> Although the efficacy rate in community trials was higher than in trials in household contacts the numbers needed to treat to prevent one new case were also higher.

Interest in chemoprophylaxis waned in the 1980s and 1990s with the introduction of short course multi-drug treatment in 1982 and the launch of the leprosy elimination strategy in 1991.<sup>3</sup> This strategy proved highly successful in reducing the prevalence of cases of leprosy registered for treatment to below the target of one in 10 000 by the year 2000, but it had little effect on the rate of detecting new cases.<sup>4</sup>

Interest in the role of chemoprophylaxis was renewed by community interventions in Micronesia and studies of chemoprophylaxis in communities and household contacts in remote islands in Indonesia, where rifampicin was used instead of dapsone.<sup>5 6</sup> As far as we know, Moet and colleagues’ trial is the largest randomised placebo controlled trial of chemoprophylaxis

using rifampicin in household contacts of patients with newly diagnosed leprosy. It randomised 21 711 contacts of 1037 patients with leprosy to either a single dose of rifampicin in the second month after the patient started treatment or to placebo. Rifampicin significantly reduced the incidence of leprosy in the first two years (absolute risk reduction 57%, 95% confidence interval 33 to 72; number needed to treat 265, 176 to 537). However, the difference was no longer significant in the third and fourth years. The efficacy of a single dose of rifampicin is similar to that achieved by a much longer duration of treatment with dapsone (60% reduction).

This new evidence raises important questions—how can the efficacy of chemoprophylaxis be improved and what is the place of chemoprophylaxis in the global strategy against leprosy? In some cases, the absorption of rifampicin may have been adversely affected by a transient gastrointestinal illness (which is common in Bangladesh), so it is possible that the protection rate of 57% in Moet and colleagues’ trial could have been improved by giving a second dose the next day. Treatment of the index case prevents further transmission from that source but there may be other sources of infection in the vicinity that remain untreated, so a second dose in the future would reduce re-infection with *Mycobacterium leprae*. This would explain why chemoprophylaxis in whole communities is more effective than in household contacts.<sup>2 6</sup>

BCG can help prevent leprosy, and it is used as immunoprophylaxis in household contacts in some South American countries.<sup>7</sup> Moet and colleagues found the lowest risk of leprosy in household contacts who

### RESEARCH, p 761

**W Cairns S Smith** professor of public health, University of Aberdeen, Public Health, Medical School, Aberdeen AB25 2ZD [w.c.s.smith@abdn.ac.uk](mailto:w.c.s.smith@abdn.ac.uk)

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received rifampicin and who had previously been vaccinated with BCG. BCG stimulates the host's immune response as opposed to killing *M leprae* so both treatments may act synergistically. Rifampicin cannot be given at the same time as BCG vaccination, however, because rifampicin would kill the BCG bacillus. Subgroup analysis in Moet and colleagues' trial suggests that chemoprophylaxis is less effective in household contacts who are genetically related to the index case. This is relevant to recent research on the genetic basis of host susceptibility to *M leprae* infection; genetically related people may need a full course of multidrug treatment rather than a single dose of rifampicin.<sup>8</sup>

Most new cases of leprosy have no history of household exposure, which is not surprising given the very long incubation period. This limits the overall effect of a chemoprophylaxis strategy restricted to household contacts on the incidence of leprosy. Exposure to the leprosy bacillus outside the household will be limited in countries with good leprosy control programmes and a reduced burden of disease, which strengthens the case for routine chemoprophylaxis of household contacts in these situations. The acceptability of chemoprophylaxis in household contacts needs to be explored because—although newly diagnosed patients may welcome the opportunity to protect the rest of their household with single dose rifampicin—they are faced with disclosing a diagnosis surrounded by stigma. The development of a test for latent or subclinical infection with *M leprae*, such as a leprosy specific T cell assay with unique antigens selected from the genome, would complement chemoprophylaxis by identifying contacts at greatest risk.<sup>9</sup>

So what is the future role for chemoprophylaxis in the global strategy for leprosy after this new and

robust trial? The current global strategy for leprosy for 2006-10 aims to sustain the control of leprosy and to reduce the burden of disease.<sup>10</sup> The strategy does not recommend universal chemoprophylaxis, and this may need to be reviewed in light of the new evidence.<sup>11</sup> However, any changes should be considered on a country by country basis, rather than as part of the overall global strategy for leprosy, because the decision must be based not just on the efficacy of the intervention but also on feasibility, cost effectiveness, and acceptability.

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## Effects of gender on performance in medicine

Men may have higher output than women, but this is possibly offset by litigation and disciplinary action

A recent study assessed the workloads of 7236 male consultants and 1048 female consultants in the 10 most common specialties using data from the hospital episode statistics for England 2004-5.<sup>1</sup> It found that, on average, male consultants completed 160 more episodes of care each year than their female colleagues. More women graduate from medicine than men, and the authors suggest that their finding could have financial implications beyond those of maternity leave. The authors point out possible flaws in the study, however, such as the accuracy and validity of the underlying hospital data. For example, if consultants work in teams, coders might allocate work to the most senior consultant in the team, who is more likely to be a man. Also, activities were limited to inpatient and outpatient settings, so other activities such as teaching and administration would have been ignored. More importantly, the findings may

reflect the way that women doctors work—perhaps they spend longer with their patients than their male colleagues and communicate differently.

Differences exist in the way that men and women work, in both medicine and other professions.<sup>2</sup> One meta-analysis has shown that women have longer consultations, are more patient centred, engage in more emotionally focused talk, counsel more psychosocially, and that their patients speak more.<sup>3</sup> Consequently, female consultants overall must conduct fewer patient episodes, unless they also work longer hours.

Rather than seeing the implications of this only in terms of cost to health services, economists and accountants must weigh this finding against the costs that arise from male doctors consistently experiencing more litigation and discipline than female doctors. For example, a recent report by the National Clinical Assessment Service (which assesses and makes recommendations

Jenny Firth-Cozens professor,  
London Deanery, London  
WC1B 5DN  
[jfirth-cozens@londondeanery.ac.uk](mailto:jfirth-cozens@londondeanery.ac.uk)

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for doctors and dentists in difficulties) found that significantly more male doctors were referred to the service than female ones.<sup>4</sup> Although women accounted for 42% of the general practitioner medical workforce and 37% of the medical hospital and community workforce in 2004, only 13% of general practitioners and 20% of hospital and community doctors referred to the National Clinical Assessment Service were female. These differences were not explained by an age cohort effect or by grade, and women were under-represented proportionally in all hospital and community specialties. For example, only 9% of surgical referrals were women, even though they form 20% of the surgical workforce.

The sex difference regarding disciplinary action is similar around the world. For instance, after controlling for all demographic factors, male doctors in the United States were three times more likely than women to have claims for malpractice made against them.<sup>5</sup> In England only six of the 49 career doctors with problems reported by Donaldson were women.<sup>6</sup> Although 31% of general practitioners in Norway are women, only 15% were referred to the Norwegian Board of Health.<sup>7</sup> Similarly, only a small proportion of doctors with alcohol problems are women,<sup>8</sup> and virtually none has been referred for sexual misconduct or fraud.<sup>9</sup>

Such findings do not suggest that male doctors as a group are inferior to female colleagues in terms of performance, but that the less favourable tail of the normal distribution curve is populated more by men, as it is in many other areas of life such as addiction, delinquency, and risky behaviour. For example, egoism, which relates to deviance in general, is lower in women,<sup>10</sup> whereas impulsivity is greater in men.<sup>11</sup> At a less extreme level, women's superior communication

skills<sup>3</sup> and greater emotional intelligence<sup>12</sup> may help them forge better relationships with patients and so make them less likely to be the subject of complaints, claims, or discipline.

Although the implications of the proportional rise of female doctors must be taken into account, it would be an error to tackle this simplistically. Several other differences between men and women may need to be considered, but undoubtedly any financial estimation that compares the costs of employing male or female doctors must also take into account sex differences in the costs of poor performance, litigation, re-education, and rehabilitation.

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## Follow-up of children who survive cancer

Should be individually tailored but may not be necessary for all

More than three quarters of children with cancer survive into adulthood, but cure is not the end of their journey. At least 60% have substantial morbidities as a result of their curative treatment. Most adults who survive cancer are discharged from active follow-up at five years, but historically children have been followed up for life; this is becoming unsustainable. A review published in the *BMJ* more than five years ago explored strategies for follow-up of children who have survived cancer.<sup>1</sup> Has anything changed since then?

Two large epidemiological studies—one in the United States and the other in the United Kingdom—have since been published.<sup>2 3</sup> More than 10 000 survivors in 26 centres participated in the US study, which found that 62% of survivors have some late effects of treatment (common terminology criteria for adverse events (version 3) grade 1-5), with 27% having severe or life threatening conditions (grade 3-5).<sup>4</sup> Data from the UK study of more than 10 000 survivors have just been collected and will be an important addition because the study is

population based rather than treatment centre based. Although these studies are limited by the data being collected from subjective patient questionnaires, the results are supported by a recent study.<sup>5</sup>

It is difficult to predict future healthcare needs from the results of these studies because the treatments given to the participants differ from those used today. For example, many of the late effects seen in these studies were caused by radiotherapy. Fortunately, this form of treatment is now used less frequently (for example, in leukaemia where universal prophylactic cranial irradiation is no longer used). Modern techniques are also more precise, which reduces the exposure of normal tissue to radiation. At the same time, the increased use of chemotherapy may lead to a new pattern of late effects. As new late effects are identified, a mechanism must be in place to recall patients when intervention is necessary. For example, all women who have had radiotherapy for Hodgkin's lymphoma in the UK must be actively identified and screened for breast cancer.<sup>6</sup>

**Meriel Jenney** consultant paediatric oncologist, Children's Hospital for Wales, Cardiff CF14 4XW  
meriel.jenney@cardiffandvale.wales.nhs.uk

**Gill Levitt** consultant in paediatric oncology and late effects, Great Ormond Street Hospital, London WC1N 3JH

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**If we keep calling patients back to the clinic some may never believe they have been cured**

So how can a service be developed for this growing and diverse group of patients? The UK government has recently launched a new initiative that explores methods of follow-up for (adult) survivors of cancer.<sup>7</sup> Also, the National Institute for Health and Clinical Excellence has recently published guidelines on improving outcomes in children and young people with cancer, which identified several important key points.<sup>8</sup>

The first is the need for information. A summary of the surgery, chemotherapy, and radiotherapy received—which is kept by the patient but can also be provided to the primary healthcare team—is key to understanding the late effects of treatment. The second is the need for a specialist multidisciplinary team with expertise in the late effects of treatment. This team might include an endocrinologist, psychologist, and specialist nurse. The third is the need for a key worker—who can be immediately accessed at any time—to be allocated to each patient. The key worker would be part of the multidisciplinary team, but the individual may change as the patient's needs change over time.

The move towards risk stratification of patients proposed in the previous review published in the *BMJ* remains appropriate but has not yet been universally implemented. Patients who are at high risk of late effects—for example, those who have received cranial radiotherapy, anthracyclines, or a bone marrow transplant—will require ongoing observation by skilled clinicians with an interest in the specific problems that these patients face. However, some patients may not need this service and other models for alternative follow-up have been proposed. For patients who are at low risk of late effects, a succinct accessible summary of the patient's previous treatment with a plan for any necessary investigations and likely late effects could be the solution. This could be managed by primary care doctors, providing they have access to expertise at the treatment centre. Other patients who may need closer surveillance may benefit from

ongoing contact with a specialist nurse who could refer them back to the multidisciplinary team if necessary. Only those with the highest risk of late effects should probably be brought back regularly to the clinic.

These models could also be extended to adults who have survived cancer, but further research is required to identify the extent of the problem, the need for support of both physical and psychological needs, and indeed the views of survivors, about which little is known.<sup>9 10</sup>

Although many patients will benefit from ongoing follow-up others must be allowed to move on—to leave the clinical setting and put the experience of cancer behind them. If we keep calling patients back to the clinic some may never believe they have been cured.

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## How should health professionals take action against climate change?

BMA report outlines the problems, but falls short in providing solutions

"The scientific evidence is now overwhelming: climate change is a serious global threat, and it demands an urgent global response." This was the unequivocal message of the Stern report, published by HM Treasury last year.<sup>1</sup> The time for debate is over—at least about whether climate change is potentially catastrophic and caused by human activity. But who should act and how? This week, the BMA Board of Science publish their report *Health Professionals—Taking Action on Climate Change*.<sup>2</sup> It outlines the basic facts and figures and points to copious sources of further information.

The report endorses Stern's conclusion that, "urgent action is needed now at an individual,

organizational, political and global level." It summarises evidence about cause and effect, then considers the health implications. A diagram (from the *Lancet*) points to floods, storms, and other forms of environmental damage leading to "impaired nutrition, health, survival."

Turning to how the effects of climate change can be reduced, the report says that the government's sustainable development strategy, *Securing the Future*, must be implemented.<sup>3</sup> Another diagram, from the International Panel on Climate Change (IPCC), lists "key mitigation technologies and practices that are currently commercially available" and those expected to be on tap by 2030.

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**Anna Coote** commissioner for health, UK Sustainable Development Commission, London SW1A 2HH  
[annacoote@hotmail.co.uk](mailto:annacoote@hotmail.co.uk)

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Next, carbon emissions and footprints are explained. In the United Kingdom, the average emission is equivalent to 10 tonnes of CO<sub>2</sub> each person each year. Most personal emissions come from household energy consumption and travel, with a sizeable chunk associated with purchases of consumable goods. A sustainable individual footprint is 2 tonnes of CO<sub>2</sub> each year. That means a staggering reduction of 8 tonnes per person.

So what solutions does the report propose? Several measures, it tells us, can reduce the amount of CO<sub>2</sub> that we emit. These include carbon offsetting, carbon trading, and “contraction and convergence.” Each solution is briefly explained, with references so that people can find out more. No effort is made to assess the relative merits of these very different strategies.

The report sets out what is being done globally, by the European Union and by the UK government to tackle climate change. It provides recommendations for health professionals. Measure your own carbon footprint; turn appliances off; improve ventilation and insulation; save water; reduce waste; buy fresh local produce; and cut down on meat, dairy products, and saturated fats. Avoid overly processed or packaged foods and bottled water. Use public transport, walk and cycle more, cut unnecessary flying and driving.



Health care organisations must take urgent action to reduce their carbon footprint

Of the NHS, the report says that—as the largest organisation in the UK, with an annual purchasing budget of more than £17bn (€21.5bn; \$34bn)—it must take urgent action to reduce its carbon footprint. It sets out examples of where such action might be taken—in building works and in managing energy, water, waste, and transport. It does not mention procurement, which accounts for the largest part of the NHS’s carbon footprint.

For health professionals who want to find out more, the report provides usefully referenced summaries of evidence. Hopefully, however, it will soon be followed by a more concerted effort to confront the heavily barbed challenges of climate change. It mentions, all too briefly, that climate change can affect mental health, and that measures to reduce greenhouse gases can help reduce the risk of cancer, heart disease, obesity, other chronic illnesses, and injuries caused by road traffic crashes. These are vital themes that must be paid closer attention by health professionals and policy makers.

It sits on the fence about methods of carbon reduction, as though they were equivalent options. Yet carbon offsetting is a highly controversial way of compensating for carbon emissions, rather than reducing them. And contraction and convergence is a profoundly radical strategy for each person on the planet to arrive at equitable and sustainable per capita greenhouse gas emissions.<sup>4</sup>

The report offers no view on what should happen if NHS trusts fail to cut their massive direct and indirect emissions. It makes no suggestions about how trusts can make sure that their contractors give priority to mitigating climate change. It points out that health professionals “have a responsibility to highlight the public health risks of climate change as well as the numerous health benefits associated with more environmentally friendly economic activities and lifestyles.” Yet it does not discuss where carbon reduction should stand in the hierarchy of clinical responsibilities. Nor does it suggest what health professionals should do if they find their government is dragging its feet—for example, in giving sufficient priority to its own sustainable development strategy.

Here, surely, is the crux of the matter for the BMA. We have the science. We have something approaching consensus about the causes and scale of the problem. Now what is required, from one of the UK’s most powerful trade associations that is well able to influence cabinet ministers and governments, is a sustained evidence based campaign to match the enormity of the risks to human health.

- 1 HM Treasury. *Stern review final report*. 2007. [www.hm-treasury.gov.uk/independent\\_reviews/stern\\_review\\_economics\\_climate\\_change/stern\\_review\\_report.cfm](http://www.hm-treasury.gov.uk/independent_reviews/stern_review_economics_climate_change/stern_review_report.cfm).
- 2 BMA Board of Science. *Health professionals—taking action on climate change*. 2008. [www.bma.org](http://www.bma.org).
- 3 Ministry of Justice. *Securing the future: proposals for the efficient and sustainable use of custody in England and Wales*. 2007. [www.justice.gov.uk/publications/securing-the-future.htm](http://www.justice.gov.uk/publications/securing-the-future.htm).
- 4 Global Commons Institute. *Contraction and convergence. A global solution to a global problem*. 2008. [www.gci.org.uk/contconv/cc.html](http://www.gci.org.uk/contconv/cc.html).