

Science vs “scaremongering” over measles-mumps-rubella vaccine

The British government has been forced to mount a US\$ 4.4-million information campaign to reassure doctors and parents about the safety of the measles-mumps-rubella (MMR) vaccine. Fears about the combination vaccine arose most recently after a London hospital physician claimed in January that it had not been adequately tested before being put into wide use in the United Kingdom. In 1998, the same physician claimed that the vaccine may be linked to autism and bowel disease. Both claims received massive nationwide media coverage and have been vigorously refuted by government health officials as “scaremongering”.

The information campaign will include distribution of leaflets and posters to the public and information packs to health professionals, as well as advertising on national television. The campaign has been mounted against a background of falling uptake of the vaccine amongst two-year-olds in the UK — from around 92% in early 1995 to around 88% today. In some, mainly inner-city, areas coverage has dropped to around 75%, sparking fears of localized measles outbreaks. WHO recommends vaccine coverage rates of around 95% to prevent outbreaks.

David Salisbury, head of the UK government’s immunization programme, told the *Bulletin* that the 88% coverage level has remained steady for the past 18 months. Among children starting school at five years of age coverage hovers around the 93% mark. However, he admits this is still not high enough. “So far we have not had any significant emergence of measles but there is a danger that parents will worry because of all the adverse media coverage and we will get a self-fulfilling prophecy of falling immunization rates.”

The controversy over the MMR vaccine was first triggered by a study on 12 children reported in the 28 February 1998 issue of the *Lancet* by Andrew Wakefield and his colleagues at the Royal Free Hospital in London. All 12 children had intestinal abnormalities and nine were judged to have autism. The study merely concluded that “gastrointestinal disease and developmental regression was associated in time with possible environmental triggers”. The

authors admitted that the study “did not prove an association between MMR vaccine and the syndrome described”. However, Dr Wakefield suggested at a press conference that there might be a link. The study was widely criticized at the time because of the small numbers involved and because of the lack of evidence of a causal association between MMR and autism or bowel disorders.

The following year, the 12 June issue of the *Lancet* carried a report of a large epidemiological study reported by a different team, headed by Brent Taylor from the same hospital, that found no causal association between the MMR vaccine and autism: MMR coverage was the same in children with autism as in the general population and there was no clustering of cases of autism arising shortly after MMR vaccination.

On 6 April 2000, media interest was aroused once again when Dr Wakefield and John O’Leary, director of pathology at Coombe Women’s Hospital, Dublin, Ireland, presented unpublished data to the US Senate’s Congressional Oversight Committee in Washington. Dr Wakefield told the committee he had now studied more than 150 children with “autistic enterocolitis” and that gut biopsy material from 24 of 25 children with autism, vs 1 of 13 controls, was positive for measles virus. These data have been presented at scientific meetings but have never been published in full in a peer-reviewed journal.

Dr Wakefield and others have called for the combination vaccine to be replaced by separate vaccines against measles, mumps and rubella, on the assumption that this might be a safer vaccination policy. However, Mary Ramsay from the UK’s Public Health Laboratory Service, says that switching to single vaccines “would completely undermine the solid evidence base that MMR is very safe. It could lead to serious erosion of the current coverage of the MMR vaccine and render outbreaks of disease more, rather than less, likely.”

Japan is the only country that uses single (*monovalent*) measles and rubella vaccines and the country suffers from endemic and epidemic measles. Between 1992 and 1997 there were 79 measles deaths in Japan.

The most compelling evidence for continued use of the combined vaccine comes from a large prospective Finnish study reported by Annamari Patja of the

Helsinki University Hospital for Children and Adolescents in the 19 December 2000 issue of the *Pediatric Infectious Disease Journal*. The study followed 1.8 million children for 14 years and detected no cases of inflammatory bowel disease or autism reported as short-term consequences of the vaccination. In a previous study, the same authors had followed up all children reported to have gastrointestinal symptoms after MMR vaccination. None had developed autism or inflammatory bowel disease. The authors concluded that serious adverse events with MMR are rare and greatly outweighed by the risks of disease.

Dr Wakefield’s latest claim, advanced in the 21 January 2001 issue of *Adverse Drug Reactions and Toxicological Reviews*, is that the MMR vaccine was prematurely licensed for use. Two independent expert groups that advise the UK government, the Joint Committee on Vaccination and Immunisation and the Committee on Safety of Medicines (CSM), reviewed the Wakefield paper. The CSM also conducted a detailed review of MMR safety. Both committees strongly endorsed the use of MMR, rejected calls for single vaccines and severely criticized Dr Wakefield’s claims. At the end of January, the British Medicines Control Agency and the Department of Health published a detailed rejection of these claims (www.doh.gov.uk), which they say rests on “highly selective” and “flawed” data. “It is easy for scaremongering to sap public confidence by biased presentations,” they write. Before the MMR vaccine was introduced in the UK in 1998, they note, the vaccine had been “extensively tried and tested in Scandinavia and the USA.” Moreover, several hundred million doses have been administered worldwide and “extensive data demonstrate [the vaccine’s] safety”.

The current controversy appears to be confined to the UK. Ana-Maria Henao-Restrepo, medical officer with the Expanded Programme of Immunization at the World Health Organization, says: “WHO is not aware that fears over safety have affected the uptake of the vaccine anywhere other than the UK.” ■

Jacqui Wise, *London*

In Brief

Outbreak readiness a priority after India earthquake

Respiratory infections are the main health dangers confronting survivors of the earthquake that on 26 January hit Gujarat state in north-western India, according to WHO's South-East Asia regional office. Among the estimated 700 000 buildings damaged or destroyed are a number of hospitals.

"Destruction of buildings is forcing people to sleep in the open, despite low night-time temperatures," says Eigil Sorensen, an on-the-spot WHO adviser, "and is making respiratory infections one of the most acute dangers (in the area)" About 1 million people in Gujarat state are believed to be without shelter. A 12-member WHO team in Ahmedabad and Bhuj, cities close to the quake's epicentre, is coordinating the work of local health officials and agencies working in the area. It is also helping them take stock of the situation, restore severely disrupted health services in the area and set up an outbreak early warning and prevention system. As the *Bulletin* went to press on 14 February, the latest on-the-spot reports gave the human toll as 16 480 confirmed deaths and 144 927 injuries. ■

New hormone, a link between obesity and diabetes?

US researchers report in the 18 January issue of *Nature* their discovery of a hormone that is secreted in large amounts by fat cells in obese mice and that produces signs of adult-onset, or type 2, diabetes when given to healthy mice. In type 2 diabetes, blood sugar levels are abnormally high despite high levels of insulin. The problem is that the patient's tissues are *resistant* to the insulin. Hence, the name "resistin", with which the researchers have dubbed the new-found hormone. They also found that antibodies to the hormone improve the action of insulin in obese mice. These findings, if confirmed in humans, may explain the strong but hitherto unexplained link between obesity and type 2 diabetes. ■

Study quantifies children's risk from passive smoking

A study of 5400 US children aged 4 to 16 years, reported in the January issue of the *Archives of Pediatrics & Adolescent Medicine*, found that exposure of children to tobacco smoke in the home and public places nearly doubled their risk of respiratory problems, such as impaired lung function and wheezing. Children in the 4- to 6-year-old age-group, in addition, were at an over fivefold



Photograph: Harsaran Pandey, WHO

Dr Luis Jorge Perez from the Pan American Health Organization and Dr Paul Francis, from WHO's South-East Asia Regional Office, assessing the damage in Bhuj, the city closest to the Gujarat earthquake's epicentre.

risk of asthma from exposure to tobacco smoke compared with unexposed children. Unlike previous research that has relied on parents' recall to identify children's exposure to tobacco smoke, this study, conducted by the National Center for Environmental Health in Atlanta, Georgia, used children's blood levels of cotinine, a metabolite of nicotine, as a marker of exposure. ■

Genetically modified tobacco loses nicotine but not taste

Vector Group Ltd announced on 15 January that it had produced a cigarette from genetically modified tobacco that contains "virtually no nicotine" and no cancer-causing nitrosamines. Unlike previous attempts to make nicotine-free cigarettes, which failed to win consumer approval, Vector's product, the company claims, retains its original taste and could be used to wean people off smoking. Whether or not it will pass muster with WHO will depend on whether the organization's scientific advisory committee on tobacco product regulation believes the new product will really help people quit smoking. The cigarettes are expected to be on sale early next year. ■

An artificial protein blocks HIV

A synthetic protein made by a US team from the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, appears in cell culture experiments to prevent HIV from attaching to its target T cells, the team reported in the 12 January issue of *Science*. The protein, which the researchers call 5-Helix, jams the "grappling hook" that HIV uses to attach to T cells. It seems to

work on a wide range of HIV strains. The researchers, who hope soon to start monkey tests on their protein, see it as a possible first step in designing drugs for HIV/AIDS patients in whom current medications are not effective or tolerated. ■

More Gates' money for health

Microsoft chairman Bill Gates announced on 27 January at the World Economic Forum in Davos, Switzerland, that the Bill & Melinda Gates Foundation would give US\$ 100 million over the next five years to the New York-based International AIDS Vaccine Initiative. IAVI, which over the past three years has already received US\$ 26.5 million from the Foundation, plans to use the new funds to launch clinical trials of three promising AIDS vaccines currently in the R&D pipeline. In a separate development, the Foundation announced on 6 February a US\$ 1 million grant over the next two years to the Geneva-based Global Forum for Health Research to boost its efforts to get public-private partnerships to make drugs and vaccines available to poor countries. ■

WHO to explore health risks in Gulf and Balkans war zones

WHO wants to carry out a US\$ 20-million, four-year investigation into environmental risk factors, including depleted uranium and other radioactive metals, which may have led to alleged increases in cancers and other illnesses in the Balkans and the Gulf. In the shorter term, WHO is looking for US\$ 2 million to fund operations in the two emergency areas over the next six months.

The two regions have been the scene of violent conflict over the past 10 years and WHO will investigate the health status of civilian populations and humanitarian personnel who have been working there. Europe has been in the grips of a panic since 30 Balkans veterans became ill, among them five who died from leukaemia.

The media have concentrated on depleted uranium (DU) as the likely cause of the purported increase in disease. More recently, the focus has widened to include other radioactive metals, such as plutonium, neptunium and americium, found in shells used by the US military in Kosovo, according to press reports. But Xavier Leus, Director of WHO's department of emergency and humanitarian action, says the current speculation about possible health risks of DU is "unacceptable". "Evidence on the incidence of cancers needs to be strengthened in communities within Iraq and the Balkans in order to draw any epidemiological conclusions," he said. "There is also very little information on other possible risk factors for civilians and the military that may be equally important."

Over the next four years, WHO will attempt to find out first of all whether or not there has been a true increase in cancers, including leukaemia, and in other noncommunicable diseases, and if so what environmental factors in the region might be to blame.

Possible risk factors include, for the Balkans, pollution from heavy industry and mining activities in the region and, for the Gulf, environmental pollution and chemicals which may have been used in the Gulf War and the Iran-Iraq War. Radioactive metals are just one category of possible agents being considered, WHO says.

WHO has appealed to the international community for US\$ 2 million to cover its investigations in Iraq and the Balkans over the next six months and says about

US\$ 20 million will be needed over the next four years to carry out in-depth studies. The immediate needs include field surveys, the strengthening of national surveillance systems for noncommunicable diseases, including cancers, and the deployment of toxicologists, and radiation and chemical experts.

WHO has invited experts from Iraq to a meeting in Geneva, at a still unspecified date, to help draw up guidelines for the investigation into the possible health effects of environmental contamination in the Gulf Region. The Iraqi government maintains that exposure to DU is responsible for an increase in cancers and congenital malformations among the civilian population. Since 1995, WHO has been working with the ministry of health in Iraq to rebuild the country's cancer registries, so that trends in cancer incidence can be recorded and verified.

In late January, WHO sent a team of environmental health experts to Kosovo to make an initial assessment of the data available on population exposure to DU and other contaminants and its possible damage to health. It is currently reviewing hospital data on cancer incidence and has made recommendations for improved surveillance and environmental safety measures.

WHO is currently completing a thorough review of the scientific evidence for health effects from exposure to DU. "This report should be completed in March and will form a reference from which health risk assessments can be made for different exposure situations," Mike Repacholi, who is coordinating the production of the WHO scientific review, told the *Bulletin*.

Meanwhile, samples of DU found at 8 of the 11 sites in Kosovo inspected by the United Nations Environment Programme (UNEP) during a field assessment in November 2000 are currently being analysed at five European laboratories. The UNEP team collected samples of soil, water, milk, and vegetation, and carried out smear tests on buildings, vehicles, and weapons. Some 340 samples are currently being examined for both radioactivity and toxicity. The results are due in early March.

Most studies to date — mainly involving uranium workers and people affected by the Chernobyl disaster — suggest that, at low exposure rates, the health risks from exposure to DU are low. However, WHO

maintains that the evidence available is too limited to be conclusive.

What is known is that the heavy metal component of uranium can cause kidney damage in experimental animals. And some studies suggest that long-term exposure could cause similar damage in humans. The radiological risks include a possible increased risk of lung cancer if DU particles are inhaled and an elevated risk of other cancers, including leukaemia, only if DU is absorbed into the blood or other organs.

However, it is thought unlikely that DU could be responsible for the leukaemia cases reported among military personnel who served in the recent conflict in Kosovo, since the disease normally takes at least five years to develop after exposure to radiation. ■

Sheila Davey, *Geneva, Switzerland*

WHO's Executive Board tackles tricky topics

At its 107th meeting, held throughout the third week of January, the delegates of the 32 countries making up WHO's Executive Board had some thorny issues to discuss. A sampling: Should WHO continue to recommend exclusive breastfeeding for the "first 4 to 6 months" of a baby's life or switch to the first 6 months? Should the organization continue to rank the health systems of its 191 member states, as it did for the first time in its *World Health Report 2000*? How good a job is WHO doing in responding to epidemics?

Breastfeeding

WHO currently recommends that babies should be exclusively breastfed "from birth to 4 to 6 months". Some countries, particularly in the developing world, want that statement to read: "from birth to 6 months"; others, particularly in the industrialized world, want to keep WHO's vaguer wording. At issue is how early in life babies could safely be given foods other than breast milk. Related to that issue is what to do about manufacturers and distributors of industrially prepared infant food who do not abide by the International Code of Marketing of Breast-milk Substitutes that WHO issued 20 years ago to combat "inappropriate sales promotion of infant foods".

The Board passed a resolution calling for strengthening of "national mechanisms to ensure [their] global compliance" with the international code.

On the age issue, the Board decided to let the forthcoming May meeting of the World Health Assembly decide. By then a WHO-mandated literature review on the topic will have been completed and a group of experts will have met to discuss the review's findings.

Ranking of health systems

Last year's *World Health Report* erupted onto the international health scene with a ground-breaking table ranking the 191 member states of the organization according to how their health systems were performing. As WHO Director-General Gro Harlem Brundtland admitted in her opening statement to the Board, this exercise provoked not only "considerable public interest" but also "significant debate ... including critical remarks". Some countries were unhappy with the methodology or the data used. Others felt they should have been more involved in the process. Yet others questioned the usefulness of the table. Responding to these criticisms, Dr Brundtland said that the next ranking of health systems — scheduled for 2002, and every two years thereafter — would be based on a broad consultative process conducted at national, regional and global levels. The Board expressed satisfaction at Dr Brundtland's response and called for continuation of the health system assessments.

Outbreak surveillance and response

WHO is stepping up its outbreak surveillance and response capability. It is taking a leading role in a powerful new "network of networks" that scans the Internet for rumours of outbreaks, investigates suspected cases and verifies outbreaks of international concern. WHO announces confirmed outbreaks on its web site (<http://www.who.int/cha/disasters/>), together with advice on any travel or trade restrictions. A long-standing problem has been the reluctance of some countries to acknowledge outbreaks and thereby risk a negative impact on tourism and trade. The new procedures being put in place, which are implemented in close collaboration with the affected country, are contributing to prompt notification of outbreaks, mobilization of international assistance and rapid containment of epidemics.

The Board called on the Director-General to provide support to countries to bolster "their capacity to detect and respond rapidly to communicable disease threats and emergencies". ■

John Maurice, *Bulletin*, with reporting by Mary Kay Kindhauser, *WHO*

In Brief

WHO opens new office in France

On 8 February, WHO announced the opening in Lyon, a French city 150 km from the organization's Geneva headquarters, of an office that will coordinate activities aimed at bolstering the capability of developing countries to tackle epidemics, emerging diseases and drug resistance. The office, which will be part of WHO's communicable disease, surveillance and response department, will help train specialists from all over the world in epidemic control techniques. ■

Diary

Healthy water for all



WHO

"Water and health" is the theme of World Water Day 2001, which falls this year on 22 March. The theme also explains why this year WHO is the event's lead agency, among a large congregation of UN or UN-related bodies with an interest in water. The day will be marked by activities around the world aimed at reminding people of the vital link between safe water and health. Visit www.worldwaterday.org for further information. ■