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bmj.com Scotland starts HPV vaccination programme

Bias could account for benefit attributed to flu vaccination

Jeanne Lenzer NEW YORK

The reduction in mortality seen among elderly people who have been given the flu vaccine could have more to do with a “healthy user” effect than any protective value of the vaccine itself, a study has found.

The researchers prospectively obtained clinical, laboratory, and functional status data and identified 1813 adults with community acquired pneumonia who were admitted to six hospitals in Alberta (*American Journal of Respiratory and Critical Care Medicine* 2008;178:527-33). Of these adults, 354 vaccine recipients met the inclusion criteria and were matched with 354 controls.

The outcome of in-hospital mortality was examined during the months before and after the flu season, when no benefit of the flu jab would be expected. The researchers replicated a 51% mortality difference between the groups found in previous observational studies (*JAMA* 1994;272:1661-5): 53 (15%) of the vaccinated control patients and 28 (8%) vaccine recipients died in hospital (unadjusted odds ratio 0.49 (95% confidence interval 0.3 to 0.79)).

The dramatic benefit shown of vaccination before and after the flu season could have been due only to a baseline imbalance or bias, say the researchers.

The study's principal investigator, Sumit Majumdar, associate professor in the department of medicine at the University of Alberta, said, “There is no possible mechanism for reducing deaths from influenza when there's no influenza circulating.”

He added, “What we did was exactly the opposite of what researchers have been doing for the past 20 years. They throw away all results during the summer.”

By examining results from outside the flu season, he and his team were able to show that the difference in mortality most likely represents a “healthy user effect” in which healthier people who tend to watch what they eat, exercise regularly, and don't smoke are also the people who are most likely to comply with drug and vaccine regimens.

Cite this as: *BMJ* 2008;337:a1550

European paediatric clinical trials miss priority needs

Michael Day MILAN

Key studies that are needed to assess the efficacy and safety of medicines in children are not being done, according to a major review of clinical trials in Europe which shows that few studies are carried out in priority areas.

A research group at the Mario Negri Pharmacological Research Institute in Milan, Italy, reviewed all paediatric clinical trials carried out from 2004 to 2007, after identifying them from a literature search.

The 379 paediatric trials being carried out in the European Union during this period dealt with only four of the 25 priority conditions identified by the European Medicines Agency (EMA). The most common of these were “malignant diseases” (18.2% of trials) and “asthma” (3.2%) (*Acta Paediatrica* 2008;97:1232-7).

The results “reveal a lack of overlap between therapeutic needs and research,” the researchers said. They noted, in particular, that “few trials in the EU address the precise, high-priority therapeutic areas identified by the EMA as lacking necessary information.”

One of the researchers, Dr Chiara Pandolfini, from the Laboratory for Mother and Child Health, Mario Negri Pharmacological Research Institute, told the *BMJ*: “Doing this research is very important. Physicians need this information so that they're not guessing, for example, what doses to use in children. With this extra knowledge children will be spared unnecessary side effects and get more effective treatments.”

Even when the priority diseases were studied, often the most pertinent aspects of these conditions and their treatments were not considered, the researchers found. Only four of the 10 completed or ongoing trials in asthma investigated the specific drugs and factors outlined by EMA as priorities, collecting data on β_2 agonists or on the long term safety of inhaled or oral steroids.

Dr Pandolfini said that the findings highlighted the need for a list of key off-patent treatments, including medications for asthma and cancer, that should be subjected to new



SALLY AND RICHARD GREENHILL/ALAMY

Clinical trials in children are not focusing on priority conditions or areas of need

paediatric trials to provide more information on their use in children. Such a list is being produced by the EMA. The final version should be published by the end of October.

The findings also underline the need for the EMA to ensure that recent European legislation is acted on, the researchers said. This law, Regulation (EC) No 1902/2006 of the European Parliament and the Council on Medicinal Products for Paediatric Use, which entered into force in January 2007, calls on medical research institutes and industry to give greater priority to key areas of medicine in which paediatric drug data are lacking.

“Until now paediatric clinical trials have not been done much for fear of testing drugs on children and for commercial considerations—drug companies know that they're looking at relatively small paediatric markets with some drugs. But with the new EMA drug lists and the new regulation, hopefully this is going to change,” Dr Pandolfini said.

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IN BRIEF

Red Cross increases supplies to Georgia:

The International Committee of the Red Cross has increased provisions of medical supplies for the thousands of people displaced by the conflict in Georgia. Supplies include surgical equipment for seriously injured patients, a mobile clinic in Gori to provide basic care to elderly and chronically ill people, and materials for obstetric care.

NICE issues guidance on ventilator associated pneumonia:

The National Institute for Health and Clinical Excellence has recommended that patients on ventilators and who are intubated should be positioned with their upper body elevated, if possible, to reduce the risk of pneumonia. (See www.nice.org.uk/PatientSafetyPilot.)

Another US university rejects drug company funds:

Stanford University in California has joined other US universities in stopping drug companies' sponsorship of continuing medical education, which most US doctors are required to undergo. Drug companies can contribute to a funding pool, and the university will decide how to use the money.

Study shows costs of UK vascular surgery lawsuits:

The cost of litigation concerning vascular surgery was around £17m (€21m; \$31m) from 1995 to 2007 in the UK, says a new report (*European Journal of Vascular and Endovascular Surgery* doi:10.1016/j.ejvs.2008.06.018). Out of 395 claims 303 had been settled, with compensation given in 160 cases. Varicose vein surgery was involved in 48% of successful claims.

Incense increases risk of respiratory cancer:

Long term use of incense is associated with an increased risk of squamous cell carcinoma of the respiratory tract, concludes new research that involved 61 320 Singaporean Chinese people (*Cancer* doi:10.1002/cncr.23788). The relative risk, in comparison with not using incense, was 1.8 (95% confidence interval 1.2 to 2.6).

C difficile deaths are on the rise in England and Wales:

The number of deaths involving *Clostridium difficile* rose by 28% from 2006 to 2007, the latest figures from the Office for National Statistics show. *C difficile* was mentioned on 8324 death certificates in 2007 and on 6480 in the previous year.

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FRANCES M. ROBERTS/ALAMY

A total knee replacement operation: cemented knees are least likely to need revision

Traditional hip and knee replacement are less likely to need revision

Zosia Kmietowicz LONDON

People who have hip replacement surgery are nearly three times more likely to need a revision operation within three years if their joint is resurfaced rather than fully replaced and cemented, shows a review of procedures carried out by the NHS in England.

Patients whose knee replacement operation involves a unicondylar prosthesis also fare worse than patients given a traditional knee prosthesis, concluded the study, which linked records from the National Joint Registry and the Department of Health's hospital episode statistics (*PLoS Medicine* doi:10.1371/journal.pmed.0050179).

The study tracked more than 150 000 people who underwent a hip or knee replacement between April 2003 and September 2006 in the NHS in England—more than half of all such operations in this period—to study the performance of joint replacements according to the type of prosthesis used.

It found that, overall, only one in 75 patients (1.4%) needed revision of their hip or knee operation in the three years after initial surgery, but the percentage needing

revision varied with the procedure used.

Among patients who underwent the newer hip resurfacing technique, where only the diseased components of the hip are replaced rather than the entire joint, 2.6% (95% confidence interval 2.1% to 3.1%) needed a revision operation. The need for a second operation was particularly high among women who had this newer procedure, with 3.7% needing further surgery within three years.

Patients who had cemented hips were the least likely to need further surgery, with 0.9% needing revision within three years (0.8% to 1.1%); the percentage for cementless hips was 2% (1.7% to 2.3%) and that for "hybrid" prostheses—those in which cement is used for some parts of the joint but not for others—was 1.5% (1.1% to 2%).

In knee patients the three year revision rates were 1.4% (1.2% to 1.5%) with cemented, 1.5% (1.1% to 2.1%) with cementless, and 2.8% (1.8% to 4.5%) with unicondylar prostheses ($P < 0.001$). The revision rate after knee replacement strongly decreased with age and was lowest in the over 75s.

Cite this as: *BMJ* 2008;337:a1520

Low cost intervention helps to reduce suicide rate in poorer countries, study shows

Susan Mayor LONDON

A brief, low cost intervention followed by contact reduces the number of deaths from suicide among people who have attempted suicide in low and middle income countries, an international study shows.

From January 2002 to October 2005 the

study followed up 1867 people who had attempted suicide identified by medical staff in the emergency units of eight collaborating hospitals in five culturally different sites: Campinas, Brazil; Chennai, India; Colombo, Sri Lanka; Karaj, Iran; and Yuncheng, China.

The participants were randomised to

Cutting price of alcohol leads to higher mortality, study shows

Roger Dobson ABERGAVENNY

Lowering the price of alcohol is associated with an increase in alcohol related mortality, a study of the effects of substantial price cuts in Finland indicates.

Alcohol related mortality rose by 16% among men and 31% among women after a series of changes in the law in 2004 reduced the price of alcoholic drinks in Finland (*American Journal of Epidemiology* doi:10.1093/aje/kwn216).

"These results imply that a large reduction in the price of alcohol led to substantial increases in alcohol related mortality, particularly among the less privileged, and in chronic diseases associated with heavy drinking," the authors, from the population research unit of the University of Helsinki's Department of Sociology, wrote.

In January 2004 it became legal in Finland to import virtually unlimited amounts of alcoholic drinks from other European Union countries

for buyers' own consumption. On 1 March taxes on alcohol were reduced by an average of 33%. The price of spirits in retail outlets fell by an average of 36%, the price of wine by 3%, the price of beer by 13%, and the price of other alcoholic drinks by 17% to 25%.

In 2003, says the study, the estimated total annual alcohol consumption in Finland was 9.4 litres per inhabitant. The increase in consumption was estimated to be 10% in 2004 and a further 2% in 2005.

The authors used mortality data for all Finns aged over 15 for two periods before and after the price drop. Their results showed that between 2001-3 and 2004-5 the number of alcohol related deaths rose by about 16% (95% confidence interval 12% to 19%) among men (equivalent to 22 deaths per 100 000 person years) and by 31% (22% to 40%) among women (eight deaths per 100 000 person years).

Chronic diseases accounted for 82% of the



Finns drank 12% more alcohol in 2005 than they did in 2003, when they drank 9.4 litres each

total increase in alcohol related mortality, and alcoholic liver diseases alone accounted for 39%. Deaths from alcoholic liver diseases rose by 38% in men and 41% in women.

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Doctors issue warning that OTC antibiotics will increase resistance

Lisa Hitchen LONDON

Plans to make two antibiotics for treating urinary tract infections available to buy over the counter in the United Kingdom rather than being prescription only are governed by commercial rather than public health concerns, say doctors and pharmacists.

The Medicines and Healthcare Products Regulatory Agency (MHRA) is currently considering reclassifying trimethoprim and nitrofurantoin for the treatment of uncomplicated urinary tract infections, such as cystitis.

The move follows the agency's approval earlier this month of a

similar switch for the antibiotic azithromycin, for the treatment of chlamydia infection.

But members of the British Society of Antimicrobial Chemotherapy oppose the move, the GPs' magazine *Pulse* reports (www.pulse-today.co.uk, 28 Aug, "Fury over decision to make first mainstream antibiotic OTC"). In a letter to health ministers they express concerns that "approvals of this type are determined commercially and not on the basis of medical need."

One of the authors of the letter, Jonathan Cooke, director of medicines management and pharmacy at University Hospital South Man-

chester NHS Foundation Trust, said: "This is a mechanism for commercial companies to change the licensing opportunities."

The society's main concern is the effect that such a move will have on antimicrobial resistance.

"If [these drugs] are routinely used in pharmacies, GPs will inevitably start to use more broad spectrum antibiotics for [urinary tract infections]," Professor Cooke told the *BMJ*.

"This would include quinolones and cephalosporins. These are real problem antibiotics for the genesis of community associated MRSA [meticillin resistant *Staphylococcus aureus*] and *Clostridium difficile*," he said.

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OTC trimethoprim: will it increase resistance?

receive either treatment as usual or to the standard treatment together with a one hour, individual information session as close as possible to the time of discharge from hospital and nine follow-up contacts, by phone or in the form of visits from a person with clinical experience (*Bulletin of the World Health Organization* 2008;86:703-9, doi:10.2471/BLT.07.046995). Whenever an interviewer realised that a patient needed more intensive treatment the patient was referred for more

intensive treatment if this was available. Overall, 91% of the participants completed the study.

The results showed fewer deaths from suicide at 18 months' follow up in the intervention group than in the usual treatment group (0.2% versus 2.2%; $\chi^2=13.83$, $P<0.001$).

"People who make attempts at suicide often end up in emergency rooms," explained the lead author, Alexandra Fleischmann, from the Department of Mental Health

and Substance Abuse at the World Health Organization, Geneva. "But in low to middle income countries, if there are no complications, patients are discharged after being treated for their injuries with no referral to mental health services.

"By providing the patient with information and following up with telephone calls, further attempts can be prevented and lives can be saved."

Cite this as: *BMJ* 2008;337:a1524

Deaths from drug poisoning in English and Welsh men increase

Adrian O'Dowd MARGATE

Almost 2000 men died from drug poisoning last year in England and Wales, the highest number for five years, the latest statistics from the Office for National Statistics (ONS) show.

Deaths linked to heroin and morphine accounted for the largest amount of the total number of 2640 deaths from drug poisoning in men and women in 2007, but one of the sharpest rises in deaths involved methadone.

The figures showed that 1914 deaths of men were related to drug poisoning, the highest recorded number since 2002—and a rise of 7% from the 1782 deaths recorded in 2006.

Deaths among women, however, were at their lowest recorded annual number since the ONS drug poisoning database was begun in 1993. The number of drug poisoning deaths among women fell by 8%, from 788 deaths in 2006 to 726 in 2007.

Overall the number of deaths from drug poisoning has remained stable—2623 in 2003 and 2640 in 2007. The number of deaths involving heroin and morphine rose by 16% from 2006, going up from 713 to 829. An even bigger increase was noted in deaths

involving methadone, which rose to 325, a rise of 35% on the 2006 figure, reaching the highest level since 1999.

The long term upward trend in the number of deaths involving cocaine continued, reaching 196 deaths in 2007, the highest recorded number since 1993. In contrast, the numbers of deaths involving antidepressants, paracetamol, and aspirin were all at their lowest since records began.

Among men, those aged 20-29 had the highest rate of deaths related to substance misuse between 1993 and 2002, but the pattern is changing: from 2003 men aged 30-39 were the group with the highest deaths.

Harry Shapiro, director of communications for the drug information charity Drugscope, said, "It looks as if we have an ageing heroin population, but nevertheless it also underlines the fact that just because somebody has been using heroin for a long time doesn't necessarily mean they are immunised against drug death."

The report is at www.statistics.gov.uk/downloads/theme_health/HSQ39.pdf.

Cite this as: *BMJ* 2008;337:a1521

Refused asylum seekers can get free NHS care, says BMA

Zosia Kmietowicz LONDON

Doctors deciding whether refused asylum seekers are entitled to free NHS care should judge each case on its own merits and not according to how long the patients have lived in the United Kingdom, the BMA says in new guidance.

The new advice has been issued after a recent ruling by the High Court that guidance on this matter from the Department of Health was unlawful (*BMJ* 2008;336:849), which caused confusion among doctors.

The department's guidelines, issued in 2004, instruct trusts to charge for the treatment of failed asylum seekers who did not meet the legal definition of "ordinarily resident." Those who had been in the UK for a period of less than 12 months did not meet this criterion, the guidelines state.

But in a test case in April a refused asylum seeker challenged the guidance in the High Court after his local NHS trust denied him free treatment for a liver condition. The judge ruled that the interpretation of "ordinarily resident" status had no legal basis.

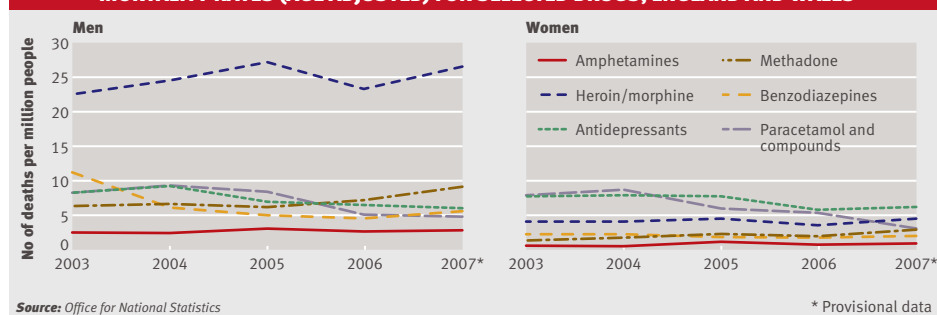
The government's appeal against the ruling is due to be heard in mid-November, but unless and until the decision is overturned the judge's interpretation is effectively the law, say the BMA.

"The resultant ruling makes it possible for asylum seekers whose application for asylum has been unsuccessful to be considered 'ordinarily resident' in the UK and therefore entitled to free NHS hospital treatment," says the BMA.

The guidance can be found at www.bma.org.uk.

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MORTALITY RATES (AGE ADJUSTED) FOR SELECTED DRUGS, ENGLAND AND WALES



New vaccines and screening can reduce cervical cancer rate in

Rory Watson BRUSSELS

New vaccines and screening tests can help to achieve a major reduction in the incidence of cervical cancer in developing countries, concludes research presented last week at the world cancer congress of the International Union Against Cancer.

Francesc Xavier Bosch of the Catalan Institute of Oncology in Barcelona, Spain, coordinated a

monograph that brings together research analysing the cost effectiveness of introducing human papillomavirus (HPV) vaccination and new screening methods into poorer countries in the world (www.kaizo.net/releases/cervicalmonograph/).

"The discovery of HPV as the cause of cervical cancer has shaken a field that was stagnating," he said, "and we are now in a new era

where developing countries no longer have to be left behind."

Every year, 510 000 diagnoses of cervical cancer are made around the world. Around half die from the disease—and about 80% of these women are in developing countries.

If the present trends continue, developing countries could face a 75% rise in the number of cases of cervical cancer, as a result of ageing and growing populations over the

next two decades, unless effective preventive action is taken.

The research concludes that vaccination at a cost of \$10 (£6; €7) to \$25 per vaccinated girl would be cost effective in the Asia-Pacific region. To be financially viable in Latin America and the Caribbean the cost would need to be less than \$25 per girl.

However, the authors point out, for large scale vaccination



The police are often the first people to deal with a person undergoing a mental health crisis

Charity calls for better training of police in handling mentally ill people

Lynn Eaton LONDON

Police officers need more and better training in how to handle people with mental illness, says a briefing paper from the Sainsbury Centre for Mental Health. And healthcare and social services could do more to help with this process, it says.

The police, the centre's report says, are often the first people to deal with a person who is experiencing a mental health crisis. They have powers under the Mental Health Act 1983 to remove a person to a place of safety and to gain enforced entry, with a warrant, to a person's home.

But the report says that the police have very little training in awareness or recognition of mental ill health, although they often deal with people who are mentally ill or very distressed.

"The police are often the first point of contact for a person in a mental health crisis," said Rob Fitzpatrick, the Sainsbury

Centre's project manager and a coauthor of the report. "Yet police officers rarely have mental health training, and there are too few opportunities to divert people from police stations to health and social care services."

Opportunities to build a closer relationship between the police and healthcare and social services now exist, Mr Fitzpatrick said. "Safer Neighbourhood teams could, for example, work closely with mental health teams and other local services to help people who need support to keep out of the criminal justice system," he said.

The report advocates joint agency training, including probation and prison officers and court staff. The involvement of service users and voluntary groups is also essential. *The Police and Mental Health* is available at www.scmh.org.uk. For details of the mental health first aid training programme see <http://mentalhealthfirstaid.csip.org.uk>.

Cite this as: *BMJ* 2008;337:a1531

poor countries

programmes to go ahead the cost of the vaccine, which is currently \$120 per dose in the private sector, or \$360 per girl, would have to be considerably reduced.

The monograph also details the advances being made in effective new screening methods.

One method involves visual inspection of the uterine cervix after application of acetic acid.

Cite this as: *BMJ* 2008;337:a1545



Human papilloma viruses: vaccines could be cost effective

German insurance companies agree to doctors' pay rise

Annette Tuffs HEIDELBERG

Health insurance companies in Germany have been forced to agree a 10% pay rise for community based doctors, averting the threat of strike action.

The €2.7bn (£2.2bn; \$3.9bn) settlement is the minimum that the country's 150 000 family doctors and community based specialists were prepared to accept without going on strike. The profession had originally demanded €4.5bn. The Ministry of Health is yet to formally agree the deal but has signalled its consent.

Andreas Köhler, head of the National Association of Statutory Health Insurance Physicians, which negotiated on the profession's behalf, said that the pay rise was a first step towards nationwide guaranteed care of patients outside hospitals.

But the health insurance companies, which had been forced to settle after the intervention of an external mediator, said that they might now have to put up their membership fees by 15%.

"This massive pay rise will unfortunately be felt in everybody's purse," said Johann-Magnus von Stackelberg, principal negotiator for the health insurance companies.

About 90% of people in the German population are members of one of the 200 statutory health insurance companies; the remainder have private health insurance.

Doctors have long argued that in many cases low and unequal pay threatened their existence. The average GP or community based specialist in Germany earns about €126 000 a year before tax, which is higher than the average income. But doctors often have to service debts from buying or investing in a practice.

And not everyone is paid the same, because budgets are agreed with regional health insurance companies. Doctors in northern and eastern Germany earn considerably less than their colleagues in the south. The pay rise should even out these regional differences.

The health ministry, which welcomed the deal, said that the new system was fairer and more transparent and would strengthen the doctor-patient relationship. Doctors would also be able to calculate their income better, because they will be paid fixed rates for medical procedures and services.

Cite this as: *BMJ* 2008;337:a1533

US proposal protects healthcare workers objecting to abortion

Janice Hopkins Tanne NEW YORK
The US Department of Health and Human Services has issued a draft proposal to protect healthcare workers from discrimination if they object to abortion.

The regulation would apply to 584 000 employers in the healthcare sector that receive federal funding from programmes such as Medicare (which provides health insurance for elderly and some disabled people), Medicaid (which provides insurance for poor people), those that offer reproductive health services to poor

people, and biomedical research projects. It applies to doctors and nurses and workers in "any activity with a reasonable connection" to the particular service.

Hospitals, doctors' offices, nursing homes, and other facilities would have to certify in writing that they do not discriminate against employees who have religious or moral objections to abortion. Facilities could lose federal funding, face penalties, or be forced to return funds if they were found to discriminate.

The proposal is open for a 30 day

comment period, after which it may be modified.

Although the regulation focuses on abortion, its broad wording might apply to provision of contraceptives or care at the end of life or to any procedure that an employee objected to. Healthcare workers who object to abortion need not provide information or refer a patient to a healthcare provider that does offer abortions.

The new proposal was presented by Mike Leavitt, the US secretary of health and human services. He said that it would protect medical

practitioners' rights. "People should not be forced to say or do things they believe to be morally wrong," he said.

The *Salt Lake Tribune*, the major newspaper in Utah, where Mr Leavitt was formerly governor, said in an editorial, "This proposed rule goes far beyond the abortion issue. It could mean a woman who visits a federally funded clinic might not receive information about contraceptive options, including emergency contraceptives."

See www.hhs.gov/news/.

Cite this as: *BMJ* 2008;337:a1509

Case suggests peanut allergy may be passed on by transplant

Roger Dobson ABERGAVENNY

A case of peanut allergy possibly being transferred between a donor and recipient of a lung transplant has been reported.

The 12 year old donor had died from anaphylactic shock after eating peanut related food. Seven months after the transplantation the 42 year old recipient, who had no prior history of allergy, had an anaphylactic reaction after eating food containing peanuts, which she survived (*Journal of Heart and Lung Transplantation* doi:10.1016/j.healun.2008.07.015).

"This case emphasises the importance of considering donor allergy transfer when caring for all solid organ transplant recipients in order to avoid a life threatening event," write the authors of the case report, from Detroit, Michigan. "It is imperative that physicians take extra caution when solid-organ donors are known to have severe food allergy."

The lung recipient was a woman with sarcoidosis and pulmonary hypertension. On the fourth day after the transplantation she ate a chocolate bar that contained peanuts. Soon afterwards she became short of breath. She was treated with nebulised bronchodilators, and her symptoms improved, and this incident was not linked to the transplantation. Two other similar incidents occurred in the next few weeks.

Seven months after the transplantation the patient ate a peanut butter biscuit and immediately had severe shortness of breath



with wheezing, followed by swelling of her lips, urticaria, and dizziness, and she went into severe respiratory distress.

She was visiting the hospital at the time of the episode and was treated with adrenaline (epinephrine), oxygen, nebulised

salbutamol, intravenous methylprednisolone, ranitidine, and diphenhydramine, and her condition improved.

She later underwent skin prick testing with various nuts and foods and was found to test positive only to peanuts. Before the operation foods containing peanuts had been part of her diet without any problem.

The authors, who say that the initial allergic reactions may have been less severe because of the high dose of corticosteroids she was given after the transplantation, say it is very difficult to determine the precise mechanism by which allergy may have been transferred.

Because the initial reaction occurred in the patient four days after the operation, it is possible, they say, that passive transfer of anti-peanut IgE may have occurred from donor to the recipient via donor mast cells.

"Although mast cells bind IgE with high affinity, the large burden of transplanted mast cells could degranulate with release of mediators in the recipient after peanut exposure, causing the observed symptoms," they wrote.

Cite this as: *BMJ* 2008;337:a1512

NICE introduces cost sharing scheme for blindness drug

Roger Dobson ABERGAVENNY

Patients in England and Wales with one of the most common causes of blindness will be able to be treated with injections of ranibizumab (Lucentis) on the NHS under a cost sharing scheme announced by the National Institute for Health and Clinical Excellence (NICE).

The final guidance states that the NHS should pay for the first 14 injections of ranibizumab for patients with the wet form of age related macular degeneration (AMD), with the manufacturer picking up the bill for any more that are needed. The drug costs more than £10 000 (£12 400, \$18 280) for each eye treated with 14 injections.

A second drug for the condition, pegaptanib (Macugen), has not been recommended by NICE, a decision that has been criticised by the Royal College of Ophthalmologists.

The new guidance recommends the use of ranibizumab, which blocks vascular endothelial growth factor and stops abnormal blood vessel growth and bleeding beneath the macula, as long as a number of conditions are met, including evidence of recent progression of the disease.

"Lucentis is an expensive drug, costing more than £10 000 for each eye treated," said Andrew Dillon, chief executive of NICE. "But that cost needs to be balanced against the likely cost savings. It has been estimated that the costs related to sight impairment for patients treated with Lucentis

Two doses of chickenpox vaccine needed, report shows

Janice Hopkins Tanne NEW YORK

Two doses of varicella vaccine protect better than one, confirms a US report on the national vaccination programme published this week.

The United States introduced vaccination of children against chickenpox in 1995. One dose was recommended for children aged 12 months to 12 years and two doses for susceptible adolescents and adults. The vaccine policy was changed in 2006 to recommend a second vaccination for all.

The review by researchers at the Centers for Disease Control and Prevention (CDC) and Tufts University Medical School in Boston found that the vaccination programme had resulted in “a dramatic decline in disease” (*Pediatrics* 2008;122:744-51).

It added: “Even with high vaccination coverage, the effectiveness of one dose of vaccine did not generate sufficient population immunity to prevent community transmission.”

Before the vaccine was introduced the US had about four million cases of chickenpox each year, of which more than 90% were in children under the age of 15 years. By the early 1990s, when more children were in day care, the highest incidence was in children aged 1 to 4 years.

It is estimated that before the vaccination programme began the US had more than 10 000 hospitalisations attributed to chickenpox every year.

Children aged less than a year old and people over 20 years were at especially high risk. The most common reasons for hospital

admissions were infections of the skin and soft tissue, pneumonia, dehydration, and encephalitis. About 105 people died every year from chickenpox, and a further 40 had the disease listed as a contributory factor in their deaths.

After the vaccination programme was introduced, vaccine coverage among children aged 19 to 35 months rose—to 89% in 2006. Morbidity and mortality from chickenpox were “dramatically reduced,” the authors say. The number of hospitalisations fell by 75%, and their associated costs fell by 88%.

However, one dose of vaccine did not generate enough herd immunity to prevent the transmission of the virus, especially in settings such as schools. Outbreaks of the infection occurred in groups where a high number of children had had a single vaccination. Some index cases and contributors to disease transmission had been vaccinated.

About 15% to 20% of children who had received only one vaccination did not develop antibody levels high enough to protect them fully. As adolescents or adults they might be exposed to the disease when it was likely to be more severe.

“A second dose of varicella vaccine among children produces an improved humoral and cellular immune response that correlates with improved protection against disease,” the authors note.

Since 2006 it has been recommended that the second dose be given between the ages of 4 and 6 years.

Cite this as: *BMJ* 2008;337:a1534



US health and human services secretary, Mike Leavitt, has proposed the new abortion legislation

are around £8000 cheaper than for patients who receive best supportive care over a 10 year period.”

The decision was welcomed by the Royal National Institute for the Blind. “NICE’s guidance will finally bring an end to a cruel post-code lottery,” said Steve Winyard, head of campaigns with the charity. “We’ve been waiting for this for over two years. It is a victory for thousands, bringing overwhelming relief to desperate people across the country.”

The manufacturer of ranibizumab, Novartis, said that the arrangement whereby the NHS would pay for only the first 14 injections would benefit patients. “This reimbursement scheme is an important collaboration that will ensure patients living with wet AMD in England and Wales receive the best possible care,” said Trevor Mundel, head of global development functions with Novartis.

The Royal College of Ophthalmologists also welcomed the decision but said it was concerned that NICE had dismissed an appeal by Pfizer to allow treatment with pegaptanib.

“NICE has decided not to allow treatment with Macugen—even where patients are sensitive or allergic to Lucentis,” said Winfried Amoaku, chairman of the college’s scientific committee. “This, in our view, unfairly penalises the 3% of wet AMD patients who may be allergic to Lucentis. This can result in severe inflammation in the eye that lasts several weeks. This type of reaction to the drug in itself can cause additional damage to the retina with further sight loss unrelated to AMD.”

NICE technology appraisal guidance 155 is available at www.nice.org.uk/TA155.

Cite this as: *BMJ* 2008;337:a1487



US chickenpox vaccination figures show that two doses of the vaccine are needed for herd immunity