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bmj.com Costs of complying with new directive threaten paediatric trials

Isotope shortage is cutting nuclear medicine capacity across Europe by more than half

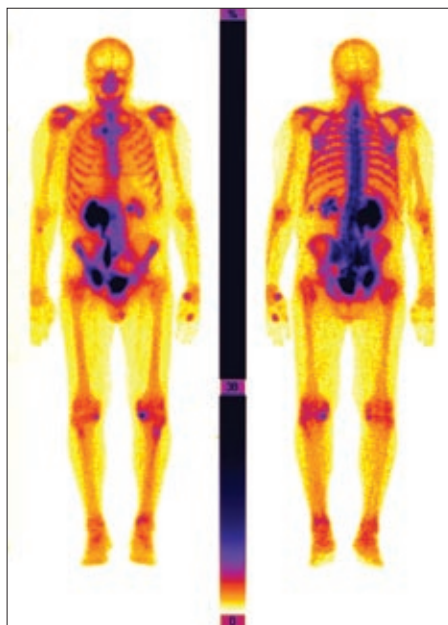
Ned Stafford HAMBURG

A worldwide shortage of medical isotopes used as radiotracers in molecular imaging will persist at least until the end of September, limiting European hospitals to between 20% and 40% of their usual nuclear medicine activities, the European Association of Nuclear Medicine warned this week.

In a letter to the *BMJ* this week (2008;337:a1577) Alan Perkins, honorary secretary of the British Nuclear Medicine Society and professor of medical physics at University Hospital Nottingham, and colleagues said that UK hospitals were receiving less than 50% of expected supplies and that rations are expected to drop further in the coming weeks. The matter received wide coverage in the UK press at the weekend.

Wolfram Knapp, the association's president elect, said that with three of the five global nuclear reactors supplying medical isotopes still shut down, it is too early to determine when supplies will return to normal. But he cautioned: “The end of September is a best case scenario.”

In the meantime drug companies will have to ration deliveries of isotopes. Most hospitals receive isotope deliveries once a week, Dr Knapp said, but deliveries around Europe



EDWARD KINSMAN/SPL

Only prioritised patients are getting bone scans

this week were generally about half of the normal quantities, and levels next week are expected to be even lower.

Although 80% of molecular imaging investigations are not urgent and can be postponed by one to three weeks, others must be done

within days, and these cases will be at the top of the priority list, said Dr Knapp, director of nuclear medicine at the University of Hanover Medical School in Germany.

Professor Perkins said that in some non-urgent cases doctors will have the option to use alternative tracers or alternative imaging methods, such as magnetic resonance tomography. “But some patients will receive suboptimal diagnostic observation,” he said. “It will slow up the system.”

Liselotte Højgaard, director of clinical physiology, nuclear medicine, and positron emission tomography at University Hospital, Copenhagen, said that supplies of medical isotopes at her hospital this week were 50% of normal but will drop to 16% of normal next week.

The hospital is one of the most active in nuclear medicine in northern Europe, with 30 000 investigations each year. Because of the isotope shortage she has cancelled plans to attend a conference this weekend so as to be involved in deliberations over which patients should be at the top of the priority list for nuclear medicine.

“It is a bit like having a restaurant without enough food,” said Dr Højgaard.

Cite this as: *BMJ* 2008;337:a1575

Academics draw up protocol for handling research misconduct

Caroline White LONDON

The UK body responsible for advising academic institutions and NHS trusts on how to deal with research misconduct has launched a protocol to try to standardise the procedure for investigating allegations and ensure that cases are handled fairly.

The protocol is a step by step guide to investigating and acting on allegations of research misconduct brought by other colleagues or external bodies, from the types of documentary evidence required, to

who should be involved and over what time frame.

It is targeted at all employers of people engaged in research who rely on funds from government bodies, charities, and commercial ventures, within and outside the United Kingdom.

The protocol was devised by the UK Panel for Research Integrity in Health and Biomedical Sciences, part of the UK Research Integrity Office. This was set up in 2006 after almost a decade of pressure from biomedical scientific

editors, ethicists, and publishers, spearheaded by the Committee on Publication Ethics (COPE).

Michael Farthing, vice chairman of the Research Integrity Office board, said that everyone would gain from a standard “purpose built” procedure.

“Those accused of misconduct can have confidence that the matter raised will be investigated appropriately and that they will receive a fair hearing,” he said, adding, “We hope that organisations that have already

adopted an approach may choose to review their systems and adopt the procedure in full or in part.”

The protocol specifies that every organisation should nominate a knowledgeable individual charged with the task of looking into cases when they arise and that this person should not be the head of the institution, or the research or human resources departments. Procedure for the Investigation of Misconduct in Research is at www.ukrio.org.

Cite this as: *BMJ* 2008;337:a1612

IN BRIEF

African health ministers commit to meningitis vaccine: Health ministers meeting in Yaoundé have agreed to prepare meningitis control plans, including the introduction of the new vaccine, and to improve information exchange for epidemic response. The new product, conjugate meningococcal A vaccine (MenAfriVac) will be priced at \$0.40 (£0.23; €0.28). It was developed through the Meningitis Vaccine Project set up in 2001, with core funding from the Bill and Melinda Gates Foundation.

Patients need nutrition plans, says safety agency: All NHS patients should have access to food and drinks 24 hours a day, says guidance from the National Patient Safety Agency. They have produced four factsheets that cover nutritional screening for patients in hospital and argue that patients should have a nutritional care plan. For details see www.npsa.nhs.uk.

GMC to consult on patient confidentiality: The General Medical Council has started a three month consultation on patient confidentiality, including how to deal with appropriate disclosure of information in the case of infectious diseases or whether to tell the police if a patient arrives at hospital with a gun or knife wound. For details see www.gmc-uk.org.

China takes action on drug regulatory body: China's Ministry of Health has taken over the supervisory role of the scandal ridden State Food and Drug Administration to become the sole source of drug regulation, safety investigation, and quality monitoring. The move was proposed in March this year and came into effect on 1 September.

Postcode lottery continues: Some primary care trusts spend far more than others per head of population, a report from the King's Fund shows. Islington, for example, spends £332 (£409; \$579) per head of population on mental health compared to £114 by East Riding in Yorkshire. Such wide variation shows spending on different diseases has remained relatively unchanged for three years, says the report. NHS Spending Local Variations in Priorities is available at www.kingsfund.org.uk.

Cite this as: *BMJ* 2008;337:a1624

Uganda to double use of antiretrovirals in people with HIV

Henry Wasswa KAMPALA

Uganda has introduced a programme to increase the number of people infected with HIV who are treated with antiretroviral drugs, setting a new CD4 cell count of 350 cells $\times 10^6/l$ at which patients will be given this treatment.

The country's original national antiretroviral programme targeted people with a much lower CD4 cell count of 200 cells $\times 10^6/l$, and infected patients with more CD4 cells were told to take co-trimoxazole tablets as prophylaxis. The higher cut off is estimated to more than double the number of people infected with HIV in Uganda who will be treated with antiretrovirals, from about 125 000 to 300 000.

The government run Uganda AIDS Commission estimates that the number of children aged 7-12 years who are treated with antiretrovirals will rise from 13 000 to 50 000.

Ugandan health officials say that the project, which is being supported by the World Health Organization, has been introduced in response to the rising number of new cases of HIV infection in the country each year.

"Uganda is implementing the new WHO recommendations of treating HIV/AIDS patients with a minimum CD4 count of 350 [cells $\times 10^6/l$] from the current count of 200 [cells $\times 10^6/l$]. This is because of increasing new infections," said David Kihumuro-Apuuri, the director general of the commission.

Statistics show that an average of 80 000 new cases of HIV infections were registered in Uganda each year before 2001. The annual number of new infections then began to increase steadily, from 100 000 a year in 2005 to the latest figure of 130 000. New infections are more common in women aged 30-34 years and in men aged 40-45 years.

Uganda has been running a widely acclaimed and ambitious AIDS control programme, but health officials attribute the rise in new HIV infections to laxity in infection prevention measures among people who thought that taking antiretrovirals had cured their infection and so resumed having unprotected sex.

Health officials also say that the increase in the new infections has been caused by a lack of funds to purchase the antiretroviral drugs.

Dr Kihumuro-Apuuri told the *BMJ*, "We have to scale up treatment because the new infections are on the rise. Unless we do that, we will be chasing a mirage."

Cite this as: *BMJ* 2008;337:a1610



Ugandan boy with AIDS receives care including antiretroviral drugs from nurses attending his village

SEAN SPRAGUE/STILL PICTURES

Deaths from lung cancer in people who

Jacqui Wise LONDON

The death rate from lung cancer among life-long non-smokers is higher in men than in women, a large data review has found. The research contradicts assertions that the risk of lung cancer in people who have never smoked is growing and that the incidence of the cancer is higher among non-smoking women than non-smoking men.

The study pooled information from 13 large cohort studies that included more than 630 000 people for incidence analyses and 1.8 million people for mortality

analyses (*PLoS Med* 2008;5(9):e185).

The studies spanned 1960 to 2004 and were based in North America, Europe, and Asia. They were supplemented with data from 22 cancer registries from 10 countries reported to have a low prevalence of smoking among women.

The results showed that in people of European descent who had never smoked the cumulative probability of dying from lung cancer before the age of 85 years was 1.1% for men and 0.8% for women. The equivalent figures for smokers were 22.1% in

WHO says cluster approach improves impact of disaster aid

Peter Moszynski LONDON

A "cluster" approach, in which different aid organisations work together with shared goals, made for a better coordinated response to Cyclone Nargis, which hit Burma (Myanmar) in May this year, a report from the World Health Organization states.

The response used innovative forms of assessment and distribution to overcome political constraints in responding to the disaster, which claimed more than 160 000 lives.

Rudi Coninx, WHO's coordinator for emergency relief efforts, was one of the first specialist staff from a United Nations agency on the ground in the wake of Cyclone Nargis and helped to ensure that a cluster approach was adopted at the start to provide a "coordinated, predictable response."

Dr Coninx explained that the idea of a group of relevant UN agencies and charities coordinating specific areas in an emergency is the result of reforms born out of recent experience, such as the tsunami that hit Indian Ocean countries in 2004. He said, "The tsunami of 2004 made clear the need for a coordinated approach that is predictable and accountable to donors and that doesn't duplicate the efforts of different organisations."

WHO co-chaired the healthcare cluster in Burma together with the British medical charity Merlin, the first time that a charity has taken the lead in such circumstances.

"This relationship was extremely beneficial, as it allowed for the sharing of staff, technical and strategic expertise, and the administrative burden," said Yves-Kim Creac'h, head of



HLAHLA HTAY/STRINGER/AF/GETTY IMAGES

Relief after Cyclone Nargis was better than expected

Merlin's emergency response team.

The Post-Nargis Joint Assessment is at www.searo.who.int/LinkFiles/Myanmar-Cyclone_PONJA.pdf.

Cite this as: *BMJ* 2008;337:a1571

Most children with vaccine allergies can be revaccinated

Janice Hopkins Tanne NEW YORK

Children who have had allergic reactions to previous vaccinations can usually be safely revaccinated, say new guidelines from a US team of experts in vaccine safety.

When considering revaccinating a child, especially one who has had an immediate reaction, doctors should take a history and use skin testing or serum IgE testing, or both, to try to identify the cause of the reaction, advise the authors, led by Robert Wood of the Johns Hopkins Children's Center, Baltimore.

This is "particularly helpful in assessing risk regarding future immunisation and thereby minimising the risk for anaphylaxis," they write (*Pediatrics* 2008;122:e771-7).

Unless a severe anaphylactic reaction has occurred, the authors say, a series of skin tests can be done, moving from a skin prick test to intradermal tests at progressively higher concentrations of the vaccine or its individual components. Whenever possible, testing should use the same vaccine from the same manufacturer that was thought to have caused the initial reaction.

The authors advocate case by case decision making about revaccination, by using an algorithm that they have developed.

If patients have serological evidence of immunity, are at low risk of disease or its

complications, or are at high risk of life threatening complications, the vaccine can be withheld. Otherwise, such patients can be revaccinated with minimal precautions if they did not have an immediate hypersensitivity reaction. Other choices include revaccination with alternative vaccines that do not have the component to which the patient is allergic or revaccination with special precautions for patients who have incomplete immunity and are at risk of the disease.

If a patient tests positive on a skin test for the vaccine or one of its components, revaccination should be done in a well equipped clinic or possibly in the intensive care unit, the authors say.

Cite this as: *BMJ* 2008;337:a1609

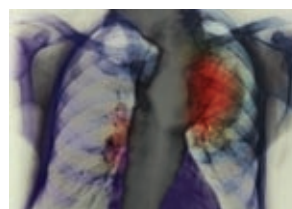
have never smoked are higher in men than in women

men and 11.9% in women. Rate ratios comparing death rates in non-smokers showed a higher death rate in men than in women in people of European descent (rate ratio 1.3 (95% confidence interval 1.2 to 1.5) and people of Asian descent (2 (1.4 to 2.7)) at all ages over 40.

The lead author, Michael Thun, head of epidemiological research at the American Cancer Society in Atlanta, Georgia, said, "Dispelling myths is important. There has been a lot of publicity that women are more at risk from lung cancer than men, and

this study clearly shows the opposite."

The question of whether women are more susceptible to lung cancer than men has been debated since the early 1990s, when reports from case control studies showed higher odds ratios in women than in men for broadly similar levels of cigarette smoking. These reports were not, however, replicated in large prospective studies.



Women who don't smoke are less likely than men to get lung cancer

Up to 90% of deaths from lung cancer are caused by exposure to cigarette smoke, and on average people who currently smoke are 15 times more likely to die from lung cancer than lifelong non-smokers. However, this still means that factors other than cigarette smoking account for at least 16 000 deaths from lung cancer each year in the United States, said the authors.

Cite this as: *BMJ* 2008;337:a1597

DR P MARAZZI/SPL

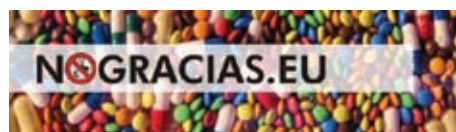
Spanish doctors say “no thank you” to pressure from drug industry to prescribe their products

Miguel Jara MADRID

Healthcare professionals in Spain are beginning to fight back against the pressure that the drug industry exerts on them to prescribe particular products.

Professionals from a wide range of medical fields have created the No Gracias (“No thank you”) group, part of the international No Free Lunch movement, a network of non-profit organisations that aim to “encourage health care providers to practise medicine on the basis of scientific evidence rather than on the basis of pharmaceutical promotion” (www.nofreelunch.org).

One of the organisers of the recently launched Spanish group, Carlos Ponte, head of the intensive care unit at Asturias Central Hospital, in Oviedo, northern Spain, said, “This platform aims to impact on, and to change, the relations between the drug industry, public sector health bodies, healthcare professionals, and patients and citizens.”



Many professionals who have joined the group wear a “No Gracias” badge on their white coats to promote discussion with patients about the group’s aims.

Juan Gervás, a GP in Madrid, said, “The No Gracias platform is an effort to promote relations between the industry and doctors that are based on transparency, independence, and proportion. It would be a positive step if No Gracias were to be seen as a necessary movement, even by the industry itself.”

No Gracias was an initiative of the Federation of Associations for the Defence of Public Health (Federación de Asociaciones para la Defensa de la Sanidad Pública).

It was established after several instances over the past few months of leading Spanish media outlets, including the *Discovery Salud* global health news magazine and Informativos Tele 5 (Channel 5 news), reporting cases of multinational drug companies offering incentives to doctors to prescribe their products. These incentives have included not only gifts, meals, and travel but also cash.

The group’s main objective is to put an end to such practices. It warns: “The penetration of the drug industry into health care has

resulted in a complex network of interests and collusion that affects the whole sector. The industry finances professional training, an area severely neglected by the public sector, by offering free courses, meetings, trips, meals, and presentations. Health centres open their doors to company sales representatives who, with their gifts of greater or lesser value (presented as “educational opportunities”), generate a sponsorship culture that damages the autonomy of the professional and the rationale behind the prescription.”

Patients and the drug industry have conflicting interests, the group argues. At a meeting launching the No Gracias group, Joan-Ramon Laporte, professor of pharmacology at Barcelona Autonomous University, said that other consequences of industry influence on prescribing is an increase in the number of prescribing errors and in the cost of drugs to the public sector health service.

No Gracias is steadily building support among healthcare professionals. Since the group’s launch less than four months ago 1200 people have signed up to its manifesto (www.nogracias.eu).

Cite this as: BMJ 2008;337:a1579

Vatican newspaper reopens debate on defining the end of life

Michael Day MILAN

A front page editorial in the Vatican newspaper, *L'Osservatore Romano*, has reopened the debate on what constitutes the end of life, 40 years after the widely accepted Harvard report that established the concept of brain death.

The editorial, in the 2 September issue, declares that life might continue after the brain dies. It says that the current, almost universally accepted definition published by Harvard doctors in 1968 “is in contradiction to the concept of the person according to Catholic doctrine.” Before the influential US report was published, death was defined by the absence of a heart beat and breathing.

The change brought by the Harvard report (*JAMA* 1968;205:337-40) enabled the church to sanction the switching off of life support machines. However, the key beneficiary of the definition of the end of life as brain death, the newspaper article says, has been organ transplantation. It notes, too, that the Vatican had only accepted the definition of brain death with reservations and that it

was not used within Vatican City.

The Pope’s spokesman, Federico Lombardi, said that the editorial, signed by Lucetta Scaraffia, a historian and bioethics expert, was a personal opinion rather than the official Vatican line. He said, however, that the article was “interesting and authoritative.”

The Vatican’s leading spokesman on health issues, Javier Lozano Barragan, was reported in *La Repubblica* newspaper as saying that he agreed “completely” with the article.

As evidence that a person might not die after irreversible brain death, Professor Scaraffia cited the 1992 case of a pregnant woman who was declared brain dead and whose pregnancy proceeded normally until she aborted spontaneously.

Vincenzo Carpino, president of the Association of Italian Anaesthetists, said, however, that the definition of brain death “remained at the moment the only valid one in the absence of new scientific evidence for defining the death of an individual.”

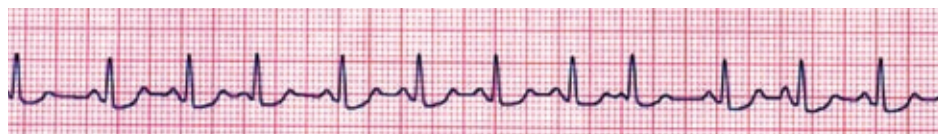
Vicenzo Passerelli, president of the Italian

Association of Organ Donors, said he was perplexed by the article. “We’re talking about a philosophical argument,” he said. “Here in the scientific world, on the other hand, nobody doubts the value of brain death in allowing transplantation to happen.”

Carlo Alberto Defanti, a neurologist at Milan’s Niguardia Hospital, said that the editorial was more likely to represent a “generic defence of life,” in line with the Catholic church’s philosophy. He noted that this line of thought could ultimately bring the church into conflict with organ transplantation.

In recent years the Catholic church in Italy has clashed with the medical establishment in several high profile cases over the right of terminally ill patients to refuse treatment or care. In one such case the church refused to allow a religious funeral for the artist Piergiorgio Welby, who had muscular dystrophy, after he successfully campaigned to have his ventilator switched off in December 2006 (*BMJ* 2007;334:9).

Cite this as: BMJ 2008;337:a1602



Electrocardiogram of atrial fibrillation: most patients receive no or inadequate doses of anticoagulants

Most patients at risk of stroke fail to get adequate anticoagulation therapy

Janice Hopkins Tanne NEW YORK

Only 10% of patients with atrial fibrillation who were admitted with a stroke to centres in Ontario, Canada, had warfarin concentrations in the therapeutic range, warns a study that demonstrates the high risk associated with inadequate anticoagulation.

The researchers reviewed data from the registry of the Canadian Stroke Network, which had information on 597 patients who had known atrial fibrillation or who were classified as being at high risk of systemic emboli and who had no contraindications to anticoagulation. They were admitted with a first acute ischaemic stroke to 12 stroke centres across Ontario between 2003 and 2007.

Overall only 29% of patients were taking any antithrombotic prophylaxis, and of those who were taking warfarin three quarters were taking an inadequate dosage (*Stroke* doi:10.1161/STROKEAHA.108.516344).

Of 323 patients with atrial fibrillation and who had had a transient ischaemic attack or stroke, nearly two thirds (57%) were taking warfarin, but only 18% had warfarin concentrations at the recommended level (international normalised ratio of ≥ 2). Just over a third (39%) had warfarin concentrations below the recommended level, and 15% were taking no antithrombotic treatment.

The authors, from the University of Toronto's Sunnybrook Health Sciences Center, said that, despite 29 trials in the past three decades showing the benefit of warfarin, the drug was underused in patients who would benefit from anticoagulation to prevent stroke. They noted that cardioembolism as a result of atrial fibrillation causes about one in six ischaemic strokes—increasing to one in four in elderly people—and is “a potentially preventable cause of stroke related disability, dementia, and death.” Such strokes are usually severe, they write, and mortality at one year has been estimated at 50%.

Warfarin is highly effective for preventing strokes in people with atrial fibrillation, reducing the relative risk of ischaemic stroke by 67% and death by approximately 25%, the authors say.

The strokes that patients in the study had were serious, being disabling in 60% of cases and fatal in 20%. If thromboembolic control were better, about one in 10 strokes could have been prevented, the researchers argue.

They note that guidelines recommend warfarin to prevent stroke in patients with persistent or paroxysmal atrial fibrillation who are older than 75 or who have high risk factors for thromboembolism.

Cite this as: *BMJ* 2008;337:a1529

African ministers adopt plan to reduce threats to health

John Zarocostas GENEVA

Health and environment ministers from African countries adopted a declaration during a conference sponsored by the United Nations in Gabon last week, creating a strategic alliance to reduce environmental threats to human health.

The declaration “is the first step towards saving the lives of millions of people from harmful effects of changes in the environment,” said Luis Sambo, director of the World Health Organization's Africa regional office. “I am delighted that we have managed to secure political commitment to catalyse institutional changes.”

WHO says that over 23% of all deaths in Africa, estimated at more than 2.4 million each year, are attributable to avoidable environmental risk factors.

The emergence of new environmental risks such as climate change—resulting in desertification and a higher frequency of natural disasters—and Africa's poor capacity to adapt, contaminated water supply, lack of sanitation, prevalence of vectorborne diseases, exposure to toxic chemicals, and poor waste management are issues of major concern.

The Libreville declaration agreed on 29 August, at the end of the ministerial conference on health and environment in Africa, commits governments to implement the necessary policy measures, investment, and institutional changes to maximise cooperation in health and environment initiatives.

Cite this as: *BMJ* 2008;337:a1547

Patients are less satisfied with robot assisted prostatectomy

David Spurgeon QUEBEC

Men who opt for robot assisted laparoscopic radical prostatectomy are around four times as likely to be dissatisfied with their decision as men who choose open retropubic surgery, new research indicates.

The study, which assessed the emotional effects on patients of the two approaches to prostatectomy, involved cross sectional surveys of 400 patients (with a 61% response rate) who underwent radical

prostatectomy between 2000 and 2007 (*European Urology* doi:10.1016/j.eururo.2008.06.063).

Results showed that men who had undergone the robot assisted laparoscopic procedure were about three to four times more likely to be regretful and dissatisfied than those who underwent the open retropubic procedure. Overall, most (84%) of the respondents were satisfied, but almost one in five (19%) regretted their

choice of treatment.

Multivariate logistic regression analysis showed that lower income (odds ratio 0.08 (95% confidence interval 0.03 to 0.23)), shorter follow-up (0.63 (0.41 to 0.98)), retropubic rather than robot assisted laparoscopic radical prostatectomy (4.45 (1.9 to 10.4)), higher urinary domain scores (indicating better urinary function) (2.7 (1.6 to 4.54)), were independently associated with satisfaction.

Cite this as: *BMJ* 2008;337:a1557



Men having radical prostatectomy preferred open surgery to robot assisted laparoscopy