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NEWS

Former BMA chairman faces misconduct and deficiency charges

Clare Dyer **BMJ**

The former chairman of the BMA, James Johnson, faces charges of professional misconduct and deficient professional performance in his work as a surgeon, in a two month hearing at the General Medical Council that opened on 20 September.

In seven cases between June 2006 and January 2008 Mr Johnson, a vascular surgeon at Halton General Hospital in Runcorn, Cheshire, is accused of failing to make patients aware of the potential risks and benefits of surgery. Some operations are also alleged not to have been surgically appropriate, not in the patients’ interests, performed incorrectly, or done without proper preoperative assessment.

He is also charged with failing to involve himself in postoperative care and on one occasion shouting at a patient and at staff members who were assisting him in a gastroscopy that he was attempting, the GMC alleges, when he knew that the patient had not signed the required consent form.

Mr Johnson, 64, was chairman of the BMA during part of the period covered by the allegations. He resigned as chairman in May 2007 after protests over a letter he wrote to the *Times* supporting the then chief medical officer, Liam Donaldson, during a bitter row over the government’s attempt to reform the organisation of junior doctors’ training.

He told his local newspaper that leading the BMA while doing his hospital work was “like a full time job, with another full time job at the hospital. It was about a 100 hour week.”

The GMC imposed conditions on his practice in July, including not performing any vascular surgery except varicose vein operations, having a workplace supervisor, and informing the GMC if he applies for medical work outside the UK.

In one operation he is accused of failing to treat his colleagues in the operating theatre with respect, failing to arrange for the administration of heparin before cross clamping the aorta, and closing the patient’s wounds knowing a surgical clip was missing and leaving the clip inside the patient’s leg.

Mr Johnson denies the allegations.

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Protesters call for more spending on HIV and AIDS to fulfil the sixth UN millennium development goal

SETH WENIG/AP/PA

UN chief urges world leaders to put MDGs back on track

Peter Moszynski **LONDON**

Only one of the United Nations’ eight millennium development goals, agreed at a meeting of world leaders in New York in 2000, is on target to be met by 2015, the latest UN summit meeting heard this week.

But the UN’s general secretary, Ban Ki-moon, insisted that the other seven goals were still within reach. “Despite the obstacles, despite the scepticism, despite the fast approaching deadline of 2015, the millennium development goals are achievable,” he told the meeting of 140 world leaders in New York.

He said that “there is no global project more worthwhile” and called on the leaders to provide the necessary investment, aid, and political will to ensure that the goals are achieved. “The clock is ticking, with much more to do,” he added.

A number of countries have achieved major successes in fighting poverty, improving school enrolment and child health, expanding access to clean water, strengthening control of malaria and tuberculosis, and widening access to treatment for HIV.

But progress has been uneven, and without additional efforts the goals are likely to be missed in many countries, the UN’s latest figures show. The only goal on track is that of halving global poverty.

Around 1.4 billion people still subsist on less than \$1.25 (£0.80; €0.95) a day. Almost one billion people suffer from hunger. Each year almost nine million children die before they reach their fifth birthday and hundreds of thousands of women die from complications of pregnancy or childbirth.

The United Kingdom’s

international development secretary, Andrew Mitchell, said, “We don’t want to balance our budgets on the backs of the poorest countries of the world.” Calling on donors to fund the GAVI Alliance’s drive against pneumonia and rotavirus, Mr Mitchell said it was a “global scandal” that a million children a year were still dying from diseases that could be prevented by vaccination.

The target to halve the proportion of people living without adequate sanitation will not be met globally until 2049 and in sub-Saharan Africa not until the 23rd century, at current rates of progress, the charity WaterAid has said.

The Millennium Development Goals Report: 2010 is available at www.un.org/millenniumgoals.

See **NEWS**, p 629

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NHS publishes data on patient reported health outcomes

Jacqui Wise LONDON

The first study of patient reported outcome measures (PROMs) for four surgical procedures in NHS hospitals in England has been published.

PROMs are self completed questionnaires that measure a patient's health status or health related quality of life. Since April 2009 it has been a requirement for all providers of NHS funded hip replacements, knee replacements, groin hernia surgery, or varicose vein surgery to collect these data from patients before and after the procedures.

The data, from April 2009 to April 2010, have now been published by the NHS Information Centre.

The system uses five different questionnaires to evaluate patients' health: three specific to hip replacement, knee replacement, and varicose veins and two that apply across all four surgical procedures and reflect general health status.

Data on 258 415 eligible hospital episodes and 155 018 preoperative questionnaires were returned, an overall participation rate of 60%. Of the 99 203 postoperative questionnaires sent out, 70 946 were returned (72%). The statistics are termed experimental as they are new official statistics that are still undergoing evaluation.

The data show that patients undergoing hip replacements reported the worst level of general health before their surgery but the biggest gain in general health afterwards.

Eighty seven per cent of patients undergoing hip replacements and 77% of those undergoing knee replacements reported better general health after their procedure than before. The data also show that 96% of hip replacement patients and 91% of knee replacement respondents recorded joint related improvements after their operation. Some

84% of those having varicose vein surgery said their condition had improved.

Just under half (49%) of patients undergoing hernia surgery and 55% of those undergoing varicose vein surgery reported better general health after their procedure, but both these groups had a substantially higher level of general health before the operation than the other patients.

John Appleby, chief economist at the healthcare think tank the King's Fund, told the *BMJ*: "This is going to be hugely valuable for a variety of reasons. It can contribute to patient choice. It will also be very useful for commissioners of health care, as it will give a strong measure of the quality of care. The information can also be used in contracts to set goals for providers."

The former health minister Ara Darzi highlighted PROMs in his final report on NHS reform, *High*

Pool resources to lift children's health services out of "mediocre state," review recommends

Zosia Kmiotowicz LONDON

Health services for children in England are designed too much around the needs of organisations, buildings, and professionals rather than the people they are intended to serve, a review has found.

Children and their parents are given fourth priority when it comes to the NHS, said Ian Kennedy, an expert in health law and chairman of the Healthcare Commission from 2003 to 2009, at the launch of his review on 16 September.

To better meet the needs of children and young people the money spent on children's health from the NHS, social services, and education budgets should be pooled and administered under a new government department for children's wellbeing.

An integrated system of care is needed, says the review, with hospital and community based doctors, nurses, health visitors, social workers, and school nurses working collaboratively with GPs at the centre acting as navigators.

"Professionals must be able to say 'I exist to provide for you' rather than 'this is what I as a professional do,'" said Professor Kennedy.

He was asked in autumn 2009 to review children's health services by David Nicholson, chief executive of the NHS, after a series of tragic cases, such as the death of Baby P (Peter Connelly), in



CRISTINA PEDRAZZINI/SPL

Better training in paediatrics is a top priority, said Professor Kennedy

2007, which suggested that services for children and young people were not good enough in several ways.

His review, which involved visiting different services across the country, showed that "when [services] are good they are very, very good, but too often they are mediocre."

Training in paediatrics is woefully inadequate, said Professor Kennedy. Up to half of GPs have no formal training in paediatrics and child health despite the fact that a quarter of GPs' patients are children and up to 40% of GP consultations are with children and families. The low priority given to children by general

practice means that emergency departments have become the "default option" with 26% of visitors now children, said Professor Kennedy.

Parents of children with disabilities complained that they had to fight for services rather than being offered them routinely. One parent said that in 18 years of looking after a disabled child she had never been able to see two consultants on the same visit despite being under the care of orthopaedic, neurological, spinal, and general practitioner services.

Professor Kennedy said, "No 21st century health system should require parents and children to go from place to place or even worse to go to multiple appointments to tell the same story."

His review makes 39 recommendations in all. Training and engagement across all the professions was crucial, he said. In addition, GPs' system of payment (the Quality and Outcomes Framework) and revalidation needed to recognise expertise in paediatrics, says the review.

Importantly, investment should be shifted towards the early years of a child's life and concentrate on those most at risk of not having the opportunity to flourish.

Professor Kennedy's review can be seen at www.dh.gov.uk.

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Data showed that 96% of hip replacement patients and 91% of knee replacement patients recorded joint related improvements, while 84% of those having varicose vein surgery said their condition had improved

Quality Care for All, as an important way to assess effectiveness of care from the patient's perspective. The aim is for such data to help patients make informed decisions about their health care.

Provisional Monthly Patient Reported Outcome Measures (PROMs) in England: April 2009 to April 2010 is at www.ic.nhs.uk.

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NICE recommends more flexible antenatal services

Susan Mayor LONDON

Antenatal services need to be more flexible in their care to meet the needs of women with complex social problems during pregnancy and to reduce the higher risk of death in these women and their babies, says new guidance.

Gillian Leng, deputy chief executive of the National Institute for Health and Clinical Excellence (NICE) and executive lead for the new guideline, said, "Expectant mothers need support throughout their pregnancy, but some groups of women do not access, or maintain contact with, traditional antenatal services because of issues such as domestic violence, teenage pregnancy, or not having English as a first language."

She warned: "These factors are consistently associated with a lack of antenatal care and, as a consequence, poor birth outcomes."

Data for England show that the risk of dying during pregnancy or after childbirth among women who live in areas of high deprivation is five times higher than among women who live in affluent areas. Babies born to women in these circumstances are twice as likely to be stillborn or to die shortly after birth.

NICE, together with the Social Care Institute for Excellence, has developed the new guideline to improve access to antenatal services for these women in England, Wales, and Northern Ireland. It recommends that antenatal staff should ask the few women with complex social problems who do attend clinics how services

can be reorganised to attract more women with similar needs.

Rhona Hughes, lead obstetrician at NHS Lothian and chairwoman of the guideline development group, said, "Commissioners and social care services have a vital role in ensuring that pregnant women with complex social factors get the right kind of support, but we need to know how to achieve this."

Antenatal services should become more flexible, the guideline suggests. This may include working with social care providers and charities if women—such as those who misuse substances—prefer to access their care outside traditional clinics.

Women who become pregnant before the age of 20 are at particularly high risk of adverse outcomes, the guideline warns. It suggests that the NHS consider commissioning a specialist antenatal service for this age group. This service may include providing antenatal care in schools or colleges.

The guideline also calls for better support for women who suffer domestic abuse during pregnancy, a time when abuse commonly starts. It suggests that health services develop local protocols jointly with social care providers, the police, and voluntary agencies.

Women with complex social problems sometimes find healthcare professionals to be judgmental, Dr Hughes said. To overcome this, the guideline recommends training staff working in antenatal services to be more sensitive to the needs of such women and to help them feel safer and better understood.

The NICE Guideline on Pregnancy and Complex Social Factors is available at www.nice.org.uk/CG110.

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Keeping a diary in intensive care halves the risk of PTSD

Zosia Kmietowicz LONDON

Patients who have spent more than three days in intensive care are less likely to develop post-traumatic stress disorder (PTSD) if staff and relatives make a diary of their stay and go through it with them afterwards, a study has found.

Out of 162 patients randomised to review their diaries with a health professional one month after discharge from intensive care, just eight (5%) developed PTSD, compared with 21 of 160 (13%) patients who did not review their stays with the help of a diary, shows the study published in the open access journal *Critical Care* (2010;14:R168).

Richard Griffiths, professor of medicine (intensive care) at the University of Liverpool and one of the study's authors, said that, although there are costs associated with keeping diaries, "compared with providing formal therapy to all patients struggling to cope with their experiences, diaries are likely to be highly cost effective."

Previous research indicates that about 1 in 10 patients who stay in intensive care for more than 48 hours develop PTSD. Professor Griffiths explained that the fragmentary nature of patients' memories and the high proportion of delusional memories, such as nightmares and hallucinations, make it difficult for patients to make sense of what happened to them.

"These memories are frequently described as vivid, realistic, and frightening and may even involve patients thinking that nurses or doctors tried to kill them," he said. "Hard evidence of what really happened, in the form of a diary filled out by the treatment staff, may help to allay these fears."

As well as reducing the incidence of PTSD, going through the diary with a nurse seems to help recovery. PTSD symptoms improved significantly among patients who went through their diaries compared with those who did not.

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About 1 in 10 patients who stay in intensive care for more than 48 hours develop PTSD

IN BRIEF

New campaign will alert people to early signs of cancer: The Department of Health for England is giving £9m (€11m; \$14m) to 59 local campaigns aimed at raising awareness of the early symptoms of breast, bowel, and lung cancer. NHS Leeds is using its share of the money to advertise new services to reduce deaths from lung cancer, such as self-referral for chest radiography, on major bus routes.

Vaccine funding shortfall leaves millions at risk: A funding gap of \$4bn (£2.6bn; €3bn) is threatening new and ongoing immunisation programmes that could save 4.2 million lives between now and 2015, the GAVI Alliance and Red Cross and Red Crescent societies have warned. The funds are urgently needed to ensure the introduction of new vaccines against pneumococcal bacteria and rotavirus.

Study will track health effects of oil spill: The US National Institutes of Health is planning a \$10m (£6.4m; €7.6m) study to track the long term effects on health of the Deepwater Horizon oil well blowout in the Gulf of Mexico.

The research project will prospectively track the health of about

50 000 adult workers and volunteers who helped clean up the oil spill. It will include pulmonary and neurological function tests, mental health monitoring, DNA damage analyses, and immunological assessment.

Younger women are most likely to stop hormone therapy after breast cancer: Only half (49%) of nearly 9000 women with hormone sensitive breast cancer who were followed up in a study took adjuvant therapy for the full duration recommended, researchers have found (*Journal of Clinical Oncology* 2010;28:4120-8). Younger women were most likely to not adhere, but non-adherence was also linked to lumpectomy and comorbidities.

Former president calls for world summit on legalising drugs: Felipe Gonzalez, former president of Spain and current chairman of the European Union's reflection group on the challenges facing Europe until 2030, is calling for an international summit to debate the possibility of legalising the consumption of recreational drugs worldwide. He has the support of other international leaders such as the former presidents of Brazil, Mexico, and Colombia and the former EU commissioner Emma Bonino.

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European Union leads way on e-health, but obstacles remain

Rory Watson BRUSSELS

The European Union is leading the world in the development of new technology in health care, such as electronic patient records and telemedicine, but serious political, legal, and practical obstacles to its wider use remain. This is among the preliminary findings of a study conducted for the European Commission.

The study, which is due to be formally launched next month, notes that overall there is strong momentum behind the planning and implementation of national and regional e-health infrastructure. But responsibility for e-health strategies in EU member states is not uniform. In most countries this responsibility lies largely with health ministries, but in others—notably Ireland, the Netherlands, Italy, Hungary, and Estonia—it is spread across government departments and agencies dealing with new technologies and innovation. In federal countries this dispersal is even greater.

The use of electronic health records shows how practices can vary greatly. Only a few countries have rolled out patient summaries nationally. Denmark, which launched its first electronic record strategy in 1996, is one, and here almost all GPs' clinics are computerised. Scotland's central Emergency Care Record, which covers nearly all its five million citizens, has been in place since 2007 and is updated twice a day. Regional systems exist or are being established in Sweden, Italy, Finland, and Spain.

Similarly, electronic prescriptions are used

routinely at a national level only in Denmark, Iceland, and Sweden. Countries that are expected to launch nationwide electronic prescribing in the near future include Belgium, the Netherlands, France, and the United Kingdom. In Spain, Andalusia has a workable solution that operates throughout the region, and the Spanish government plans to extend the facility to the entire national health service. Pilot schemes are also under way in the Czech Republic, Finland, Italy, and Poland.

Small, local telemedicine pilot projects exist across the continent; but only in Denmark, Sweden, Norway, and Finland is the technology widely used nationally. Poland is planning to move to a larger scale programme next year, while Slovakia, Romania, and Spain are developing national telemedicine strategies.

The draft report, presented to a symposium on e-health in Brussels on 16 September, notes that almost all EU countries have a national body responsible for overseeing the development and implementation of e-health standards.

Despite the progress made, the report points out that implementing e-health strategies "has almost everywhere proven to be much more complex and time-consuming than initially anticipated." Exchanging experience in this area could be highly beneficial, it suggests.

The authors also recommend that terminology be more precise and goals and objectives more concrete. However, among the main challenges are data protection and the absence of "a governance structure and leadership which provides the framework for legitimate uses of individual medical data," the report notes.

Monitoring National eHealth Strategies is at www.ehealth-strategies.eu.

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New threat of antibacterial resistance emerging from India attracts international attention

Bob Roehr BOSTON

Researchers and clinicians are troubled by a new genetic segment that confers resistance to virtually all of the β lactam class of antibiotics. The plasmid, called New Delhi metallo- β -lactamase-1 (NDM-1), was first identified in *Escherichia coli* and *Klebsiella pneumoniae* and seems to be readily exchanged between a variety of bacteria.

It was the focus of talks at the 50th inter-science conference on antimicrobial agents and chemotherapy in Boston on 12-15 September.

NDM-1 was first detected in a patient in the United Kingdom who had gone to India for surgery. Other examples of infection with the plasmid have since been identified in Canada,

Australia, Kenya, and other European countries, all with some link to countries on the Indian sub-continent, usually because those infected had travelled there for treatment.

A study in *Lancet Infectious Diseases* in August (2010;10:597-602) describing the emergence of the mechanism created an international furore. Initial charges were that the paper was an attempt to undermine the Indian medical establishment and the income generated by "medical tourists." Predominantly from Western countries, nearly half a million people visited India last year seeking medical procedures that were cheaper than in their home countries.

Patrice Nordmann, with the Bicêtre Hospital in France, told a news conference that overuse

Industry lobbying and trade pacts threaten India's role as major supplier of generic drugs



Naz Care Home in Delhi was able to look after 45 HIV positive orphans because of access to cheap drugs

Ganapati Mudur NEW DELHI

Indian manufacturers have supplied more than 80% of antiretrovirals to developing countries since 2006, a new study has shown, amid concern that trade negotiations and industry lobbying threaten to restrict this flow of affordable generic drugs.

The study also shows that Indian generic drugs accounted for 91% of all antiretrovirals for children supplied to developing countries in 2008 (*Journal of the International AIDS Society* 2010;13:35). Of 100 countries surveyed, 96 relied on Indian generic drugs; and 99% of antiretrovirals used by DR Congo, Mozambique, and Namibia came from India.

Indian generic formulations accounted for 65% of the \$463m (£295m; €353m) purchases of

antiretrovirals in 2008, while non-Indian generics made up 13% and brand name drugs made up 22%, the study found.

Suerie Moon, from the Harvard Kennedy School of Government in Cambridge, Massachusetts, and one of the study's authors, said, "Indian generic antiretrovirals have cost consistently and significantly less than other generics."

The most common first line regimen of generic antiretrovirals from India for adults cost \$74 per person per year in 2008, while brand name regimens reported to the agency Médecins Sans Frontières cost up to eight times this amount.

However, the study warns that the free trade agreements that India is currently negotiating with the European Union may create new obligations that will increase the prices of antiretrovirals

and delay access to new and improved versions of generic formulations.

The closed door negotiations have sparked concerns about India accepting fresh restrictions that may block progress in generics. "When India introduced product patents on medicines in 2005, the space for generic production was seriously curtailed. Any further restrictions would add insult to injury," Ms Moon said.

Leaked documents released by non-government health organisations in India last week suggest that multinational drug companies have contacted the top echelons of the Indian government bureaucracy in their attempts to seek fresh changes in intellectual property rules. The documents show that senior officials from five companies met bureaucrats in the office of the Indian prime minister earlier this year to make a presentation on intellectual property enforcement and data protection.

The prime minister's office had subsequently forwarded notes from the Organisation of Pharmaceutical Producers of India, a group seen as representing foreign drug companies, with suggestions relating to intellectual property rights to the Indian health ministry seeking its comments.

Anand Grover, director of Mumbai's Lawyers Collective, who has campaigned for the rights of people with HIV for two decades, said, "This suggests that sections of the multinational pharmaceutical industry are trying to change Indian laws in an insidious, non-transparent manner."

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of antibiotics, poor sanitation, limited access to clean water, and a high prevalence of diarrhoea among a large portion of the subcontinent's nearly two billion people are "all of the ingredients that may spread this bug" within the local population and then worldwide.

"These plasmids can be quite promiscuous," Timothy Walsh, a professor at Cardiff University and a coauthor of the *Lancet Infectious Diseases* paper, told the *BMJ*. He said it is unusual in that it contains "14 or more mobile elements of resistance," some of which are well known but others that haven't been seen before. Many of the clinical isolates recovered are resistant to all the β lactam drugs; but tigecycline, a new antibiotic approved for use in 2009, and colistin, an old drug that is not widely used, have shown some effectiveness.

See **EDITORIAL**, p 615.

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Knit wit

Zosia Kmiotowicz LONDON

No, it's not a new character from a children's television programme but a knitted interpretation of the bacterium *Clostridium perfringens*, which can cause gangrene.

Gavi Levy Haskell, a high school student planning to study physics at university, came up with the idea of knitting the bacterium in honour of the annual Ig Nobel prize awards, whose theme this year is bacteria. Gavi's mother, Susan, and Geri Sullivan, a colleague at

Improbable Research, the group behind the awards, joined in.

The Ig Nobel award ceremony takes place at Harvard University on 30 September. The competition honours achievements that first make people laugh then make them think. The prizes are intended to celebrate the unusual, honour the imaginative, and spur people's interest in science, medicine, and technology.

BMJ papers on coitus



in a magnetic resonance imaging machine (*BMJ* 1999;319:1596-600) and on

sword swallowing (*BMJ* 2006;333:1285) have been previous winners.

"Knitting bacteria is a lot more fun than being infected by them," Ms Sullivan said.

The 20th annual awards will introduce 10 new Ig Nobel Prize winners and will be covered in a news item in the *BMJ* on 9 October.

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WHO officials press Russia to consider needle exchanges to reduce spread of HIV and AIDS

Andrew Osborn MOSCOW

The World Health Organization is urging Russia to change its controversial approach to tackling HIV and AIDS, suggesting that it consider embracing methods such as needle exchange programmes for injecting drug users.

WHO officials made the suggestion in private meetings with Russian officials at the annual conference of the organisation's regional committee for Europe, held in Moscow last week. The event, which was attended by Vladimir Putin, the Russian prime minister, heard how Russia

has the highest incidence of HIV among the 53 countries that make up the WHO's European Region, with about 50 000 new cases each year.

"Russia has one of the fastest growing HIV epidemics in the world," said Martin Donoghoe, programme manager for HIV and AIDS at WHO's Copenhagen office. He said that in 2004 the incidence of HIV in Russia was 20 cases per 100 000 people but by 2009 this had more than doubled to 44 per 100 000.

"By the end of 2008 Russia had contributed to 36% of all cases ever registered in the entire WHO European region," he said.

"[The incidence] is probably growing faster than anywhere else in the world," added Mr Donoghoe. Experts said that most new cases resulted from injecting drug users sharing dirty needles, and the female partners of male drug users were also increasingly becoming infected.

Despite an increase in the overall number of patients in Russia taking antiretrovirals, WHO officials said they were concerned by the "abysmal" access of drug injectors there to antiretrovirals and the lack of action to increase the number of needle exchanges. Russia's continued ban on the use of opioid substitution

therapy with methadone and buprenorphine was also something that WHO would like to see lifted.

"The problem is that the epidemiological data are not being transformed into meaningful action," warned Mr Donoghoe. "There is still a lot of public and professional opposition to addressing the problem in a proper way."

Although WHO officials had nothing but praise for the quality of the data on HIV and AIDS collected by Russia, they said they were trying to reach an agreement with Moscow to restart the annual process of formally notifying WHO about new cases. Officials said that the process was halted some two years ago and should now restart.

But though problems persisted, WHO officials said they saw grounds for optimism, not least because Mr Putin personally attended the conference and spoke about HIV and AIDS. Russian campaigners were more pessimistic, however. During the conference they protested on Moscow's Red Square against what they said was a severe lack of antiretrovirals in Russia before being swiftly detained by the police.

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Russia does not allow opioid substitute therapy with methadone and buprenorphine

DIMA KOROTAYEV/REUTERS

Researchers describe how melanoma drug blocks key cancer pathway

Susan Mayor LONDON

An investigational new drug has a "remarkably" high response rate (81%) in patients with metastatic melanoma, says a recent report in *Nature*, which describes how the drug inhibits a key signalling pathway in tumour development.

The drug, PLX4032, inhibits B-RAF kinase, an enzyme that regulates signalling pathways in cells to control cell division and differentiation. B-RAF kinase is the most frequently mutated protein kinase in human cancers.

The researchers report that it selectively blocks a particular pathway in cells with mutations of the BRAF gene, known to be associated with the development of cancer (*Nature*, doi:10.1038/nature09454). When a growth factor binds to its receptor on the surface of the cells, this pathway—made up of a chain of kinase enzymes (RAF, MEK, and ERK)—communicates a signal from the surface to DNA in the cell's nucleus.

Once the signal reaches the DNA it triggers production of further proteins that control cell division and differentiation. If any of these proteins are mutated, they can be stuck in the "on" or "off" position. This can result in uncontrolled cell growth,

leading to tumour development.

"The finding that oncogenic mutations in BRAF are common in melanoma, followed by the demonstration that these tumours are dependent on the RAF/MEK/ERK pathway, offered hope that inhibition of B-RAF kinase activity could benefit melanoma patients," said the researchers, led by Gideon Bollag, senior vice president of research with Plexxikon, the company developing the drug.

In their report in *Nature* the group, which includes scientists working in US cancer centres as well as in industry, explains how it developed PLX4032 specifically to inhibit mutated B-RAF. During their early work the scientists found that at very low concentrations it also inhibited several other kinases.

"Preclinical experiments demonstrated that the investigational drug selectively blocked the RAF/MEK/ERK pathway in BRAF mutant cells and caused regression of tumours in BRAF mutant xenograft models," they explain.

Phase I clinical trials showed that using high doses of PLX4032 that achieved >80% inhibition of ERK phosphorylation in tumours of patients

with malignant melanoma correlated with a clinical response. The results showed that the ERK signalling pathway, which is downstream of B-RAF, needs to be almost completely blocked for the drug to be clinically effective. This means that a high concentration is needed.

"Phase I clinical data revealed a remarkably high 81% response rate in metastatic melanoma patients treated with an oral dose of 960 mg twice daily," the research group reports. "These data demonstrate that BRAF-mutant melanomas are highly dependent on B-RAF kinase activity," the group concludes.

Andrew Futreal, codirector of the Cancer Genome Project at the Wellcome Trust Sanger Institute, Cambridge, considers that the new information on how PLX4032 works is an important step forward. "It provides strong biochemical evidence that melanomas with BRAF mutations are very dependent on this mutant activity and that the drug has its major clinical effects through inhibiting this activity."

He added, "This sounds perhaps straightforward, but establishing target dependence on a mutant gene and showing that a drug developed against that mutant gene is how the drug is working in patients

Australia's supervised injecting centre has a more certain future

Melissa Sweet SYDNEY

After operating on a trial basis for more than nine years, Australia's only medically supervised injecting centre is to become a regular health service.

The centre opened in May 2001 in Sydney's Kings Cross area as an 18 month trial and has since needed endorsement by the New South Wales parliament every four years to continue (*BMJ* 2008;337:a732). However, the state government has announced plans to make the centre an ongoing health service that will be subject to regular evaluation and monitoring, "as would any other government programme or treatment regime."

Many groups, including the Royal Australasian College of Physicians, the New South Wales branch of the Australian Medical Association, and the Public Health Association of Australia, have welcomed the move.

Marianne Jauncey, the centre's medical director, said that reports from five reputable organisations undertaken at various times in the centre's history had shown the service to be cost effective and achieving its goals.

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Data in phase I trials revealed a high 81% response rate in metastatic melanoma patients

really solidifies the approach of targeting agents to the specific genetic lesions found in cancer genomes."

Dr Futreal also considers the development of PLX4032 to be important for the clinical management of metastatic melanoma. "It's a very difficult disease to treat in the metastatic setting, with no other agents in trials past or present showing efficacy of this sort. They really do open the door to the possibility of effective therapy in this otherwise very grim diagnosis. To achieve complete or partial regression of tumours in this group of patients with a single agent is unprecedented."

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Malawian Joyce Folias passed HIV on to her younger daughter despite attending a clinic in Lilongwe

Global elimination of mother to child HIV transmission is now achievable

Peter Moszynski LONDON

For the first time the elimination of transmission of HIV from mothers to their babies is considered a realistic goal, according to a presentation at a summit in New York on the United Nations' millennium development goals.

On 21 September the heads of Unicef, the World Health Organization, UNAIDS, and the Global Fund to fight AIDS, Tuberculosis and Malaria, together with representatives of donor governments and most affected countries, jointly launched a new initiative to promote intensified efforts to reach all mothers and children with the most effective interventions.

Unicef says that although the delivery of proved interventions "has effectively eliminated MTCT [mother to child transmission] in affluent countries, every day more than 1000 children in low and middle income countries are newly infected with HIV via transmission during pregnancy, labour and delivery, and breast feeding."

However, new evidence has shown that reducing transmission from a background rate of 30% to less than 5% is now "achievable in resource constrained settings, even where breast feeding is the norm."

Using new data, WHO issued revised guidance on HIV and infant feeding in June, which it says can "significantly improve outcomes in both mothers and their babies and greatly reduce disparities." The new data show that giving antiretroviral drugs to either the HIV infected mother or the HIV exposed infant "can significantly reduce the risk of postnatal transmission of HIV through breast feeding."

The revised guidelines recommend two key approaches: treatment, involving lifelong antiretrovirals for HIV positive women in need of treatment; and prophylaxis, involving short term provision of antiretrovirals to prevent transmission from mother to child.

Jimmy Kolker, the head of Unicef's HIV programme, told the *BMJ* that of 15.7 million women with HIV in 2008, 1.4 million gave birth. He said that in that year 430 000 new HIV infections were reported worldwide among children aged under 15 years. Over 90% of these were through vertical transmission, mostly in sub-Saharan Africa.

Mr Kolker said that hundreds of thousands of lives could be saved each year "because it was now possible to reduce transmission whilst allowing HIV positive mothers to continue breast feeding."

He explained that decisions on infant feeding had been a big problem for HIV positive mothers, because they were often given conflicting advice by health professionals and members of their communities. "Now we know it is safe for such women to continue breast feeding if they are receiving appropriate medication and there is clear guidance on what is appropriate."

He said that the worldwide elimination of such transmission in the next five years is an "ambitious goal" but that "we could achieve this if we get the finance and the systems in place and find ways to ensure that the most difficult to reach don't get left behind."

WHO Guidelines on Mother-to-Child Transmission of HIV is available at www.who.int/.

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