

NEWS

Annan calls for action on AIDS at UN meeting

The United Nations Secretary-General Kofi Annan opened the UN General Assembly Special Session on HIV/AIDS on June 25 in New York and declared that “the world has started to wake up” to the biggest epidemic since bubonic plague swept through Europe in the 14th century.

The 3-day conference, the first-ever UN meeting devoted to a public-health issue, was aimed at drafting a political Declaration of Commitment, and increasing support for a global AIDS fund, the total need for which has been conservatively estimated at US\$7–10 billion. Other highlights of the meeting were the tension between prevention and treatment strategies, cultural controversies over categories of high-risk behaviour, and the debate on appropriate responses of individual countries to the crisis.

Some 3000 delegates participated in the conference—with presidents and prime ministers of western nations conspicuously absent. 26 presidents and prime ministers who did attend were mainly from African or Caribbean nations. Ministers of state and health often represented their countries; the USA, for example, was represented by Secretary of State Colin Powell, and the UK by Clare Short, Secretary of State for International Development.

Commitments to the global fund have been modest so far, with the USA pledging \$200 million, France \$125 million, the UK \$100 million, and the Bill and Melinda Gates Foundation \$100 million. Carlos Lage Dávila, Vice-President of the Republic of Cuba, noted that 100 times more money than the proposed fund is spent on commercial advertising worldwide, and that 22 individuals around the world each have more money than the fund’s goal, with their combined wealth 43 times greater than its total. He called for the placing of “all the world’s infinite resources in the service of humanity”.

In a press conference after his address to the Assembly, Secretary Powell downplayed criticism of the USA’s commitment to the global fund by calling it “seed money”. He said it

was always clear that the USA would be adding to its \$200 million pledge, which came from the budget for the current fiscal year. Powell said the amount would be increased in years to come. He characterised the timetable, which calls for the fund to be operational by next year, as “quite doable”. Powell affirmed the US government’s

Rights were not granted to include this image in electronic media. Please refer to the printed journal.

Press Association

Annan (centre) displays the AIDS quilt

commitment to combating the AIDS crisis, noting that President Bush has appointed him and Health and Human Services Secretary Tommy Thompson as co-chairs of a special task force to ensure a “comprehensive and coordinated effort” by the USA.

“According to Carol Bellamy, Executive Director of UNICEF, a child is orphaned by AIDS every 14 seconds”

In the days leading up to the special session, the delegates argued over a number of issues, including the language of the draft declaration, the empowerment of women, and the inclusion of gay and lesbian groups as participants in the debates. Some member states opposed language that would explicitly describe vulnerable groups, those persons in high-risk categories—homosexuals, prostitutes, and injecting drug users. Islamic nations, in particular, argued that these behaviours are offensive to them on religious, moral, and cultural grounds.

Debates on the opening day, led by a group of Islamic states, quickly became mired in procedural

wrangling, focusing on the inclusion of non-governmental organisations in the conference. A vote was taken on whether to allow a representative of the International Gay and Lesbian Human Rights Commission to participate in the roundtable discussion. With more member states voting yes than abstaining, Scott Long, a spokesman for the gay rights organisation, declared victory.

As *The Lancet* was going to press it was still possible that the meeting would end without an agreed declaration, but Penny Wensley, Australia’s ambassador to the UN, called this possibility “unlikely”. The draft declaration contains compromises, she said, but is strong in many areas, with significant targets and strategies creating “a valuable blueprint for future action”. She said the three areas of greatest controversy had been questions of HIV/AIDS and human rights, the rights of women, and descriptions of vulnerable groups. The negotiations were concluded by the opening day of the conference, and it is now up to the member states to decide whether to accept the declaration. The Organisation of Islamic States, which had profound concerns about language that conflicts with their religious and cultural values, was still considering its position, Wensley said. Other groups, including faith-based organisations that have already provided many services to people with HIV/AIDS, were also struggling with their response to the document.

In the 20 years since the disease was first reported (see p 2073), HIV/AIDS has affected more than 58 million people, killing 22 million, with 14 000 new cases occurring daily. 10 million children have lost their parents to the disease. According to Carol Bellamy, the Executive Director of UNICEF, a child is orphaned by AIDS every 14 seconds. Harri Holkeri of Finland, President of this Special Session, said that this number could be expected to increase to 40 million within 10 years.

Faith McLellan

Brain plasticity allows recognition of transplanted hands

Loss of a limb is known to result in changes in cortical organisation, but the impact of limb transplantation on the cortical map has only just been described. "We were very excited to find that amputation-induced cortical reorganisation in a patient who suffered traumatic loss of both hands was reversed following bilateral hand transplantation", says Angela Sirigu (Institute for Cognitive Science, CNRS, Lyon, France).

Sirigu and colleagues studied one patient, who lost both hands in 1996 and who had a successful bilateral hand transplantation in January, 2000. "We performed four identical fMRI [functional magnetic resonance imaging] examinations, the first 6 months before the grafts, and the others 2, 4, and 6 months afterwards", explains Sirigu. During fMRI, the patient was asked to flex and extend each finger in each hand while brain activity patterns were recorded. These patterns were compared with those recorded before the graft. "Although flexion and extension of the missing fingers could not be done during this exam, it was possible to monitor the

corresponding extrinsic muscles at the forearm level, which were active", explains Sirigu. Prior to surgery, movements in the phantom hands activated only the most lateral part of the motor cortex, which is spatially close to the face area. But 6 months after the graft, hand representation expanded back to occupy the whole hand region. Similarly, activity created by elbow movement shifted from the hand region back into the area normally associated with representation of the upper limb. The shift appeared to occur during the first 4 months after surgery (*Nat Neurosci* 2001; 4: 691-92).

"These observations suggest that new peripheral inputs from the transplanted hands allowed a global remodelling of the limb cortical map", comments Sirigu. Regrowth of peripheral sensory nerves probably plays an important, but not an exclusive, role. "Novel information arising from joint, muscle, and skin receptors may induce a reactivation of the sensorimotor loops, but nerve regrowth happens slowly and is unpredictable", adds Sirigu. "We

believe that if central pathways survive de-efferentation and de-afferentation, the sensorimotor circuit may be functionally ready after the graft, and this could explain why activity shifts are observed as early as 2 months post-surgery", she explains.

Peter Schwenkreis (Ruhr-University Bochum, Germany) notes that "the results emphasise the role of the peripheral input in the formation and maintenance of the cortical sensorimotor map, and the life-long ability of the brain to adapt to an increase or decrease of this peripheral input". However, he cautions that although this is an important fundamental study, it may not lead to any clinical applications for amputees. Sirigu agrees, pointing out the study does not explore the issue of phantom pain, for example. However, she suggests that "a better understanding of brain reorganisation mechanisms may help in areas such as the rehabilitation of stroke patients, and in building artificial limbs".

Kathryn Senior

Diabetes: thinking beyond sugar

In his address to the Annual Meeting of the American Diabetes Association (ADA) in Philadelphia on June 24, the president, Robert S Sherwin, urged delegates "to think beyond glucose, even beyond diabetes itself".

The theme of his address centred on the epidemic of type 2 diabetes and associated macrovascular disease. Estimates of a worldwide prevalence of 300 million by 2025 are projected, and the disease is affecting a younger, as well as an ageing, population. The explosion in cardiac, cerebrovascular, and peripheral vascular disease is set to become both a health and an economic disaster, and Sherwin went on to elaborate on two main themes—which are relevant throughout the developed world.

The first was that although scientific advances are leading to some improvement in the treatment options available for established disease, the real way forward is prevention. Medical bodies should take the lead, he said, but this is primarily a case for massive public investment to start to reverse the

damage done in recent decades. It requires recognition of the need for action on our increasingly unhealthy dietary habits, Sherwin said, as well as on the dwindling opportunities available for physical exercise. Urgent action is required, and should be targeted primarily at the young, he added.

The second theme related to the desperate need for a continuing expansion in the number of physician scientists. He identified two problems: the first is the tendency to reduce the scientific and research aspects of a physician's training and practice, while the second is the relative lack of attractiveness of the diabetes specialty to newly qualified doctors. Steps must be taken to remove the physician scientist in diabetes from the endangered species list, he said. With this in mind, the ADA, in collaboration with the European Association for the Study of Diabetes (EASD), is initiating a number of new research fellowships.

William Jeffcoate

News in brief

DASH diet reduces cholesterol

The DASH (Dietary Approaches to Stop Hypertension) diet, which has previously been shown to decrease blood pressure, also reduces cholesterol concentrations. 459 patients were randomised to a control diet enriched with fruit and vegetables or to the DASH diet, also high in fruit and vegetables but low in saturated and total fat, and cholesterol. The DASH diet reduced total cholesterol concentrations by 7.3% and LDL cholesterol concentrations by 9%. The findings are published in July's *American Journal of Clinical Nutrition*.

Whiplash and future disability

A neck-movement test in people with whiplash can predict those who will still be disabled 1 year later. The test of how far the neck can move predicts 1-year disability with 91% accuracy, and inclusion of estimates of pain intensity and the number of problems associated with whiplash increases the predictability to 94% (*Neurology* 2001; 56: 1637-43).

Breast self examination does more harm than good, says task force

Breast self examination should not be taught routinely to women aged 40 to 69 years and there is little evidence to suggest it is a useful screening tool at other ages, reports the Canadian Task Force on Preventive Health Care. “Despite all the promotion that breast self examination has had over the past 30 years, less than 50% of women do it and the vast majority don’t do it properly”, asserts lead author Nancy Baxter, formerly of the University of Toronto. “People who are strong advocates of breast self examination have to start proving their case because it certainly hasn’t been proven, and what we do have is proof that breast self examination is harmful.”

Canadian Task Force conclusions

- Women aged 40 to 49: fair evidence of no benefit; good evidence of harm; routine teaching of breast self examination should be excluded from periodic health examination
- Women aged 50 to 69: fair evidence of no benefit; good evidence of harm; routine teaching of breast self examination should be excluded from periodic health examination
- Women less than age 40: insufficient evidence to evaluate breast self examination effectiveness; risk of net harm likely
- Women more than age 70: insufficient evidence to evaluate breast self examination effectiveness

Baxter and colleagues reviewed studies published since 1966 that evaluated the effectiveness of breast self examination in reducing breast cancer mortality. Assessment of the evidence—particularly from randomised controlled trials in China and Russia—“failed to show a benefit for regular performance of breast self examination or education” compared with no breast self examination, and showed “good evidence of harm from breast self examination instruction”, including significantly increased physician visits for benign breast problems and significantly increased rates of benign breast biopsy (*Can Med Assoc J* 2001; **164**: 1837–46).

Robert Smith, director of cancer screening for the American Cancer Society, disagrees. “I’m not sure that I would judge the evidence of no benefit as ‘fair’ [see panel], and I am sure that ‘fair’ evidence isn’t

sufficient to discount the value of breast self examination. It’s really the only way that most women younger than 40 can determine that they have cancer. After this age, breast self examination detects the tumours that mammography did not pick up. In these cases, physical examination is a safety net”, he says. “A significant number of women find masses when they’re bathing or dressing, and breast self examination once a month may contribute to a woman’s heightened awareness of what’s normal for her on other days. Not teaching breast self examination may result in women not being alert to significant lesions.”

“We don’t have any early detection methods for women under age 40”, concedes Baxter, “but we don’t seem to be able to teach them to do breast self examination better. We’re concerned that women will stop being aware of their breasts, and that’s not the message we want to come out of this.”

Marilynn Larkin

Rights were not granted to include this image in electronic media. Please refer to the printed journal.

Is education harmful?

Potential specific breast cancer treatment uncovered in mouse experiments

Researchers at Harvard Medical School (Boston, MA, USA) believe that cyclin D1 inhibitors might provide a specific way to treat some breast cancers. Qunyan Yu, Yan Geng, and Piotr Sicinski base their prediction on experiments involving genetically engineered mice in which the gene for cyclin D1 has been removed. “Our results indicate that cyclin D1 might be a good target for therapeutic intervention in human breast tumours that overexpress *c-erb-B2*—about 30% of all tumours”, says Sicinski.

Several lines of evidence suggest that cyclin D1, a component of the core cell-cycle machinery, is important in breast cancer development. “The gene for cyclin D1 is amplified in about 15% of breast tumours and the protein is overexpressed in more than 50% of all breast cancers”, explains Sicinski. “Overexpression is seen throughout tumour development”, he continues, “and mice that overexpress

cyclin D1 in the mammary glands are prone to tumour development.”

Most of the cells in the body express cyclin D1. Nevertheless, apart from some minor developmental abnormalities and incomplete mammary gland development during pregnancy, cyclin D1 knockout mice seem normal. Sicinski and co-workers have now crossed these mice with breast tumour-prone mice overexpressing the *neu* (*c-erb-B2* or *HER-2*), *ras*, *c-myc*, or *Wnt-1* oncogene in their mammary glands (*Nature* 2001; **411**: 1017–21). “Cyclin D1 knockout mice were resistant to breast cancers induced by *ras* or *neu*”, explains Sicinski, “but cyclin D1 ablation had no effect on breast cancer induction by *c-myc* and *Wnt-1* or on transformation of other cell types by *neu* and *ras*.”

“Our results indicate that *ras* and *neu* are wired to the cell-cycle machinery in breast cells uniquely through cyclin D1”, says Sicinski.

“If cyclin D1 inhibitors could be developed, they might provide a specific way to tackle human breast cancers that overexpress *c-erb-B2*. And combining the use of such an inhibitor with treatment with herceptin (an antibody against *c-erb-B2*) might be a very effective treatment for many breast cancers.”

“These results are new and exceptional”, comments William Muller (McMaster University, Hamilton, Canada), “and provide substantial evidence for cyclin D1 being a direct target of *c-erb-B2*. However, mammary gland development is defective in cyclin D1 knockout mice, so another explanation for the observations is that the cell type targeted for transformation by *c-erb-B2* and *ras* is missing and the lack of tumours is an indirect result of cyclin D1’s absence.”

Jane Bradbury

New perspectives on the management of intersex

New parents are always asked: “Is it a boy or a girl?” In some circumstances, however, there is no ready answer. As many as 1 in 3000 babies are born intersexed—where it is difficult to tell from the outward appearance whether the child is a boy or a girl. Established management of these children has been to use surgery to “normalise” the ambiguous genitalia as early as possible. But an increasingly vocal group of patient advocates are questioning this practice, claiming that many of the surgical techniques used to correct anomalous genitals can be mutilating and harmful. As a result, the clinical management of intersex conditions is under scrutiny, and the medical community has begun to question the need for early intervention.

“I think what surgeons are a bit guilty of is taking the simplistic view that there was something obviously wrong and therefore needed surgical correction, and the sooner you did it the better. That’s where we start backpedalling furiously”, says Laurence Rangelcroft, a paediatric surgeon at the Royal Victoria Infirmary in Newcastle, UK. Rangelcroft is currently leading a working party set up by the British Association of Paediatric Surgeons, which is drawing up guidelines on the management of gender-ambiguous children.

Intersex conditions include a vast array of genital anomalies, often an enlarged clitoris or very small penis, with an inadequate vagina or underdeveloped testes. The most frequent disorder leading to newborn genital ambiguity is congenital adrenal hyperplasia (CAH) owing to 21-hydroxylase deficiency. Girls with this deficiency are genetically female but androgen excess causes genital masculinisation, beginning in fetal life. Although most women with CAH are decidedly female, the virilisation can result in an unusually large clitoris.

30 years ago, it was common practice to remove the clitoris completely in an attempt to feminise the appearance of the genitals. Today, clitorrectomy is thankfully rare, with surgeons preferring to trim down the enlarged tissue to retain the nerve-rich glans area and so preserve sensation. But gynaecologists Catherine Minto and Sarah Creighton at University College Hospitals, London, UK have found that the more recent technique of clitoral reduction is not entirely successful. A follow-up study of 37 adult intersex women born with ambiguous

genitalia, including individuals who did not have surgery, highlighted the difficulties. “Both groups had sexual dysfunction, but those who did have surgery had worse problems. The main difference is that of those whose clitoris was operated on, one in four

Rights were not granted to include this image in electronic media. Please refer to the printed journal.

Robert Harding

Is it a boy or a girl?

would not be able to reach orgasm at all”, explains Creighton. She also questions early vaginoplasty—where a vagina is constructed with a portion of the patient’s gut or with skin flaps. Intervention in the first 12 months of life, it is thought, guarantees a better outcome, and avoids further surgery. But, Creighton notes, after examining a group of 45 adolescent girls who underwent vaginal surgery as babies, she and Minto found that most still needed further major surgery. “If they need major vaginal surgery to have sex, then they don’t need a vagina as a baby”, asserts Creighton. “Why don’t we leave that until they are old enough to be involved in the decision?”

But is it ethical to wait that long? Children left to grow up in gender limbo will encounter many of obstacles in our highly sexually dimorphic society. For example, what toilet should a girl with a small phallus use at school? They will be teased and bullied and may grow into adolescence feeling frustrated and sexually inadequate. And, as endocrinologist, Nathalie Josso (École Normale Supérieure, Montrouge, France), points out: “Many parents have strong opinions themselves, and this can influence clinical decisions.” Thus, anguished parents may find it hard to accept an intersexed child and so will opt for early surgery.

The debate grows especially fierce about the management of a child with a micropenis—a rare disorder that occurs in 1 in 50 000 births. These XY boys are born with a penis that is less than 2.5 standard deviations below mean for age and race, but is otherwise normal. Because penile reconstruction is technically more difficult than creating a vagina,

management of severe cases has been to surgically reassign the child as a girl, often in the first week of life.

But sexual reassignment of XY boys has its critics, such as psychiatrist and urologist William Reiner at the Johns Hopkins Children’s Center (Baltimore, MD, USA). Reiner has studied children with the severe and extremely rare disorder, cloacal exstrophy. Male babies born with this multisystem anomaly have normal testicles but no penis, or one that is highly malformed. But despite early surgery to feminise their genitals and being reared as girls, most XY individuals affected by this condition elect to live as boys by adolescence or even earlier, says Reiner. “In general, if there is a Y chromosome, you have to be very worried about raising the child as female”, he warns.

Other long-term studies are less condemning. “Many patients are quite traditional and are content with their own early surgery”, concludes clinical psychologist Heino Meyer-Bahlburg (Program of Developmental Psychoendocrinology, Columbia University, New York, USA) from a survey of XY intersex people who had genital surgery in early childhood. For some, it is the secrecy that commonly surrounds these conditions that has the most devastating psychological consequences, notes Meyer-Bahlburg.

What is best for an intersexed baby remains a contentious issue in need of good long-term follow-up data. As Eric Vilain (Department of Human Genetics, UCLA School of Medicine, California, USA) pointed out during a Novartis Foundation Symposium in May: “Medical practice is now very cautious and does not use surgery without at least a specialist team of people from various disciplines, including endocrinologists and geneticists, to make the most precise diagnosis and help gender assignment if this is the parents’ choice. The problem is isolated surgeons making decisions on their own without understanding what is going on.”

Ever-increasing knowledge of the genetic and endocrine bases of intersex and data from follow-up studies are shedding light on the controversy. To Melvin Grumbach (Department of Paediatrics, School of Medicine, UCSF, California, USA), one consideration is paramount: “Cosmetic appearance is not the big thing—it’s how they will function as an adult.”

Lisa Melton

TOKYO **Alleged biotech espionage rocks Japan**

The media on both sides of the Pacific have been abuzz in recent months with a most unusual spy story: the alleged theft by Japanese scientists of potentially lucrative genetic research material. After an investigation by the Federal Bureau of Investigation, law authorities in the USA filed charges in May against two Japanese scientists for stealing DNA samples from an Alzheimer's disease research project.

The case, which will come to court in November, has drawn attention, since it is the first time that the USA has attempted to apply the Economic Espionage Act against a member of a foreign research institute. It has also highlighted the intense international competition to exploit advances in DNA research to develop new treatments to delay or cure disease—an industry expected to be worth billions of dollars by the end of the decade.

At the centre of the "DNA spy" controversy is Takashi Okamoto, a 40-year-old neuroscience researcher at the Japan Institute of Physical and Chemical Research (known in Tokyo as Riken). This unlikely looking James Bond—a graduate of Tokyo University and a scholar at Harvard—worked at the Cleveland Clinic in the USA from January, 1997, to July, 1999.

He is alleged to have secretly sent DNA samples and cell-line reagents to Riken, a quasi-governmental Japanese body, shortly before returning to his home country. According to an indictment filed by Ohio State prosecutors, Okamoto attempted to cover his tracks by destroying research material and by switching the stolen samples with test tubes filled with tap water. The change was noticed by junior researchers at the Cleveland laboratory, who reported their suspicions to the US authorities.

An FBI investigation found that the espionage carried out by Okamoto and his alleged accomplice, Hiroaki Serizawa, a 39-year-old clinical researcher at the Kansas University Medical College, had caused US\$2 million worth of damage to the Cleveland Clinic. If convicted, Okamoto faces a prison term of up to 15 years and a fine of US\$500 000 for violating the Economic Espionage Act, transporting stolen property, and making false statements to the FBI. The Act was established in 1996 to stop other countries from stealing US technology developed with federally funds.

US authorities have reportedly begun preliminary moves to request Okamoto's extradition from Japan, where his exact whereabouts are unknown. The Japanese government has said it would "consider" a formal

Rights were not granted to include this image in electronic media. Please refer to the printed journal.

Riken—under scrutiny

request, which would need the approval of the justice minister and the high court before it could be carried out.

Serizawa, who is believed to have sent four boxes containing the samples to Japan, has been arrested in the USA on a charge of conspiracy that carries a prison term of up to 5 years. He is currently free on bail of \$20 000 until the first hearing of the case begins on Nov 5.

“Okamoto made clear that he did not bring back the DNA sample to Japan. We are puzzled. We even feel as if we were tricked”

Both Japanese scientists have pleaded not guilty. Okamoto has claimed through his lawyer that he developed the research material before he joined the Cleveland Clinic and that, therefore, he is the lawful owner of the research. "The US government has a fundamental misunderstanding of the facts in this case", his lawyer, Brent Gurney, told reporters. "The evidence would not establish that Dr Okamoto has in any way committed any crime."

While the full facts of the case are still to emerge, it has raised public awareness about the cut-throat competition in the field of genetic research, where Japan is attempting to close the gap with the USA. Research into Alzheimer's disease—the most common cause of dementia—is of particular interest to Japan, which has the fastest ageing population in the world. According to government forecasts, up to 1.5 million people in Japan could be

living with the disease by the year 2025. Domestic pharmaceutical companies have built a profitable and fast-expanding business around drugs that are intended to delay the onset of the disease. Sales of such products are already worth \$0.56 billion a year for domestic pharmaceutical giant, Eisai Co.

The case has also been embarrassing for Japan, which places a priority on its relations with the USA. According to the indictment, the materials were sent to Japan "with the intent to benefit a foreign government and instrumentality of the foreign government". It noted that Riken is 94% funded by the state. Education, Science, and Technology Minister Atsuko Toyama has set up a team to look into the allegations, acknowledging that they have attracted global attention. Riken has also launched an internal inquiry and ordered Okamoto, who has been on leave since the scandal broke, to remain close to the institute, located in Wako, Saitama Prefecture.

The initial findings of their investigation have already forced them on the defensive. After initially asserting that no samples had been sent to Japan, they acknowledged earlier this month that genetic materials from Cleveland were stored inside a laboratory fridge. "Okamoto made clear that he did not bring back the DNA sample to Japan", Riken spokesman, Minrou Yanokura, told reporters. "We are puzzled. We even feel as if we were tricked."

Yanokura insisted that Okamoto's work at the institute, where he heads the neurogenerational research unit, did not involve the samples in question. But proving this fact may not be enough to avoid blame. According to the daily *Mainichi Shimbun*, the Education, Science, and Technology Ministry is considering whether to punish Riken officials for hiring Okamoto in September, 1999, despite the fact that he was already facing a civil court action by the Cleveland Clinic at that time.

At the court hearing in November, Okamoto and Riken will hope to clear their names, but whatever the outcome, the real concern raised by this case is that commercial competition between nations is taking precedence over scientific collaboration for the greater good of mankind.

Jonathan Watts

Israeli Parliament set to debate euthanasia bill

A Knesset debate about Israeli patients' right to die was put into perspective last week when one of Israel's leading clinicians committed suicide after battling a long illness. The death shook the nation, but did not move the Knesset to speed progress on a euthanasia bill before it goes into recess at the end of July.

Baruch Padeh, aged 94 years, committed suicide with an overdose of prescription drugs at home with his wife on June 18. Padeh was a pioneer of the Israeli health system in the 1950s during the infancy of the state. A few years ago, he was awarded the Israel prize for lifetime achievement in the field of medicine.

12 days earlier, on June 6, the Tel Aviv District Court, decided to allow doctors from Meir Hospital (Kfar Sava, Israel) to disconnect a patient from the life support systems in accordance with the patient's wishes. The 58-year-old patient with advanced muscular dystrophy expressed gratitude and relief for the decision. The judge stated that the action should be regarded as passive

euthanasia (despite the fact that the act of disconnecting the machinery is active), in part, because the patient had been connected to the machinery despite her own strong objections.

A bill that would give a terminally ill patient the right to choose not to accept life-prolonging treatments is making its way through the Knesset under the sponsorship of MK Anat Maor who said this is a "natural amendment to the patients' rights law", and also cited the precedent in the Netherlands (see *Lancet* 2001; 357: 1188).

Mordechai Halperin the Health Minister's advisor on ethics, which includes Halacha (Jewish law), said "from experience we know that this law if passed would give only a very few terminally ill patients greater autonomy" adding that "the attempt to make the law more progressive and humane does not go against the Halacha".

Lilach, a patients' rights organisation, proposed a compromise for the bill, which has to go before the Knesset for three readings and simul-

taneous examination by a national health committee including 50 legal, medical, and religious experts. The group is also lobbying to move the bill faster in light of "the acute and pressing need", said Rita Gur, head of Lilach. "When the patient is dying and . . . there is no medical solution", an evolution of changes that reflects the maturation of medicine and ethics is consistent with Halacha, she adds.

Halperin continued, "there is widespread agreement that 'active euthanasia' is strictly prohibited. But, nothing in Halacha prohibits withholding aggressive treatment from suffering terminally ill patients [or passive euthanasia], nor would it force a suffering and dying patient to accept aggressive treatment against his will. The essential question is what specific treatments and under which conditions of terminal illness [should passive euthanasia be allowed], or, how not to slide onto a bottomless slippery slope".

Rachelle HB Fishman

UK prion clinic launched

The UK National Prion Clinic, based at St Mary's Hospital, London, was launched at the World Congress of Neurology on June 20 in London. The clinic (www.st-marys.org.uk/prion), which will work in parallel with the Medical Research Council's prion unit, has been established "to assist with the investigation and ongoing management of patients with, or suspected to have, any form of prion disease".

The clinic's staff include three consultant neurologists, a specialist registrar, a prion disease counsellor, and a clinical nurse specialist. "As patients may be travelling a considerable distance, reserved access to MRI and other neuroimaging, neuropsychometry, and neurophysiology is available so that most investigations can be performed on the day of appointment", explained John Collinge, the clinic's director. "Clinicians are encouraged whenever possible to refer patients at an early stage, when the diagnosis may be unclear. Research into early diagnosis is underway and therapeutic trials for prion diseases are being planned but will require a high level of patient referral in order to be feasible."

James Butcher

USA and Brazil end dispute over essential drugs

The US government has retracted a complaint filed with the World Trade Organization over a law that enabled Brazil to produce cheap generic versions of antiretroviral drugs manufactured by multinational drug firms. The US government made the announcement at the 3-day UNAIDS meeting in New York (see p 2107).

"Brazil and the US consider that this agreement is an important step towards greater cooperation between the two countries regarding our shared goal of fighting AIDS and protecting intellectual property rights", said the joint statement.

The US government had protested to the WTO last year that Brazil's patent law broke the Trade-Related Intellectual Property Rights (TRIPS) agreement. Brazil had broken the law by deciding to produce generic versions of drugs if a foreign firm had not started production in Brazil within 3 years. The US government argued that this was discriminatory behaviour. The Brazilian president, Fernando Henrique Cardoso, had defended his country's right to produce generic drugs, noting the success of Brazil's HIV/AIDS programme.

The South American country has managed to halve the number of AIDS-related deaths since 1995, mainly because it has been able to manufacture and distribute free generic drugs. The programme has been able to help 90 000 patients and might have been under threat if an agreement had not been reached.

Ellen 't Hoen from Médecins Sans Frontières access to essential medicines campaign welcomed the agreement. "Local production of pharmaceuticals is at the core of Brazil's successful AIDS programme. Through local production they've managed to lower the prices of retrovirals by 78%."

The Brazilian government expressed "great satisfaction" at the outcome and said that its law was "an important instrument available to the government, in particular in its efforts to increase access of the population to medicines and to combat diseases such as AIDS". Brazil has agreed that from now on it will give the USA 10 days' notice before starting compulsory licensing procedures.

Haroon Ashraf

United Nations agency launches new appeal for Palestinian refugees

On June 22 the UN Relief and Works Agency (UNRWA) appealed for US\$77 million for Palestinian refugees to provide basic food and medical aid and to help rebuild accommodation shattered by 9 months of unrest in the West Bank and Gaza.

At the launch of the appeal, Peter Hansen, the commissioner-general of UNRWA accused Israel of worsening an already fragile supply situation with security restrictions. He said that medical aid donated by Saudi Arabia worth US\$200 000 and other important supplies were stuck in a Jerusalem warehouse because of Israel's refusal to let trucks move.

As a result there are looming shortages of medicines against various diseases including tuberculosis, polio, and diphtheria. Vaccination rates, which had decreased by 10% during the early months of the conflict, have recovered somewhat thanks to emergency mobile UN clinics, he said.

There are no cold storage facilities in Gaza and medicines with a short shelf life have to be brought in from Israel. "We cannot all of a sudden begin to invest in cold storage facilities in Gaza when we do not have money to pay our nurses and teachers

and other necessities", said Hansen.

The International Committee of the Red Cross (ICRC) has also criticised the security measures, which vary on an almost daily basis, making it difficult to plan, according to spokesman Vincent Lusser. He said the ICRC has protested to Israel and the Palestinians about the targeting of ambulances by both sides.

Israeli authorities say the restrictions are necessary for security reasons given the Palestinian violence against Jewish settlers and their infants, and the wave of suicide bombings on buses, shopping malls, and even in a crowded discotheque.

In May the WHA passed a resolution voicing concern at the high human toll of the hostilities and the strain of the high demand for emergency medical and surgical treatment on Palestinian health institutions. The hostilities have left nearly 500 people dead on the Palestinian side and at least 115 on the Israeli side. Hundreds of people have been

permanently physically and mentally disabled.

Palestinians are banned from entering Israel to work and so unemployment has soared and an about half of the three million Palestinians in the West Bank and Gaza now live below the poverty line. Hardest hit are the 145 000 refugees in the West Bank and the 450 000 refugees in the Gaza, all of whom are cared for by UNRWA.

Hansen said the US\$77 million, meant to last until the end of the year, would help supply 217 000 refugee families with basic food aid, and create 700 000 emergency job opportunities to support the unemployed, buy two ambulances, supply 51 health centres with medical supplies, create extra school days to replace those lost because of closure and siege, and create summer activities for children traumatised by the fighting. It is UNRWA's third appeal since the fighting started.

Clare Kapp

Rights were not granted to include this image in electronic media. Please refer to the printed journal.

Press Association

Refugees hit by conflict

Ireland tackles antimicrobial resistance in hospitals

Irish authorities launched a national programme to tackle the country's high incidence of antimicrobial-resistant bacteria in hospitals and community clinics on June 19.

The strategy, prepared by the scientific advisory committee of the National Disease Surveillance Centre (NDSC), will try to control the use of antibiotics and implement better hygiene practices to minimise the spread of multidrug-resistant bacteria. The Strategy for the Control of Antimicrobial Resistance in Ireland (SARI) also calls for an aggressive publicity campaign to increase awareness about the proper use of antibiotics among the general public.

Unless the problem is tackled, Ireland could see "a return to the pre-antibiotic era of untreatable infections", said the Minister for Health and Children, Micheál Martin. In a study of 14 European countries, Ireland ranked third for penicillin resistance, with 19% of infections resistant to penicillin. This compares with 0.3% for Norway, 2% for Germany, the Netherlands, and

Iceland, and 3% for Finland and Sweden.

The Irish agency says equal blame for the country's overuse of antibiotics is shared by general practitioners (GPs), hospitals, and veterinary practitioners. The NDSC report says 80% of antibiotics used by human beings are prescribed by GPs, who often have inappropriate prescribing patterns. But the report points out that family doctors are often given insufficient information about antibiotic prescribing. It says all doctors should have expert advice available to them at all times on the treatment of infections. A system must be developed to monitor the use and supply of antimicrobial drugs, it says, and the "tight legislative controls" on the prescribing of the drugs must be maintained and enforced.

Ireland also has a high rate of methicillin resistant *Staphylococcus aureus* (MRSA) in hospitals and nursing homes compared with other north European countries. The report says only 41% of hospitals have an antibiotic policy and only 65% of hospitals

have an infection-control committee. The report notes that Ireland has only seven public health specialists with responsibility for infectious diseases. In addition, some health boards do not employ any consultant microbiologists. Less than a third of the recommended number of consultant microbiologists or virologists are currently employed by the health service.

10% of hospital patients develop infections partly because poor facilities mean that hospital staff do not wash their hands often enough. "The current level of infection-control support both in hospitals and in the community is inadequate", the report says. Preventive measures must be put in place in hospitals, and hand washing or "equivalent methods of hand decontamination" must be reinforced "and compliance improved".

The strategy will involve a public awareness campaign on antibiotic use including the overuse of detergents, cleaners, and toiletries that contain antimicrobial agents.

Karen Birchard

France cautiously proposes research on embryos

On June 20, the French government proposed to allow medical research on frozen surplus embryos, but refused to lift the ban on therapeutic cloning. The government's draft was designed to renew bioethics laws that were introduced in 1994, but will have to be discussed by parliament before being passed early next year.

Prime Minister Lionel Jospin and Health Minister Bernard Kouchner have said that they would like to allow therapeutic cloning. But the French government's bioethics committee has been extremely divided on this issue. Furthermore, the French committee for human rights and the Conseil d'Etat, France's higher administrative court, have expressed their opposition to therapeutic cloning.

French President Jacques Chirac has also clearly rejected any form of cloning, and described the ban as a "ground principle which should in no case be trespassed". Chirac said that, although stem cell research should be regarded as a priority, alternative methods to therapeutic cloning can be developed.

This strong opposition has forced the government to produce a draft that has already been regarded by many medical experts as a "compromise". Although the draft could be subject to important changes by the time it is definitively adopted by parliament.

Rights were not granted to include this image in electronic media. Please refer to the printed journal.

Press Association

Chirac stands firm on cloning research

According to the current version of the draft, research will be allowed only on surplus embryos, for stem cell research. Any research on embryos will require the informed consent of the parents. Any attempt to clone embryos will remain forbidden and scientists who try to develop reproductive cloning techniques will face up to 20 years in jail. The draft

also proposes the creation of a "national agency for procreation, embryology, and human genetics" to supervise and provide guidance on the ethical and scientific issues raised by such research.

According to Claude Huriet, the rapporteur of the 1994 bioethics laws, the draft must now enable rapid development of research on embryos to avoid isolating French scientists from their colleagues in other countries. But Jean-François Mattei, a geneticist strongly opposed to cloning, criticised the "hypocrisy" of allowing research on embryos and at the same time banning therapeutic cloning.

Other sections of the draft focused on organ transplantation and organ donation. Since 1994, organs from living donors can only be transplanted to a patient if he or she is a close family relative of the donor—such as, a parent or sibling. The draft now intends to extend this option to other relatives, under the condition that the donor and the patient have a "close and stable relationship".

Denis Durand de Bousingen

Healthy volunteer dies in US physiology study

US government officials are investigating the death of a healthy volunteer who died while participating in a lung physiology study at Johns Hopkins University (Baltimore, MD, USA). Citing the family's wishes as a reason, the university has refused to confirm the volunteer's name, but according to press reports she was Ellen M Roche, a 24-year-old laboratory technician who worked at the university's Asthma and Allergy Centre where the study was done.

The death comes at a time when US medical researchers have come under intense scrutiny after several patients have died in clinical trials in which there appear to have been protocol violations. Subsequent investigations have led to the suspension of a number of programmes and the termination of others.

According to officials at Johns Hopkins, the volunteer became ill 3 days after she had inhaled hexamethonium as part of a study looking at how healthy lungs avoid asthmatic responses when exposed to irritating chemicals. Hexamethonium is a ganglionic blocking agent

that has been used intravenously to treat hypertension and induce controlled hypotension during surgery to reduce bleeding.

The goal of this study was to determine how deep inspiration can prevent bronchospasm or reverse bronchospasm once it has begun. The researchers had hypothesised that deep inspiration stimulated stretch receptors in the lung, triggering a reflex that causes relaxation of bronchial smooth muscle. If this is the case, they had reasoned, then inhaled hexamethonium should block this protective reflex. The compound has been used in other inhalation studies. The lead investigator of the study was Alkis Togias, an asthma researcher and associate professor of medicine at the university.

Roche was diagnosed with pulmonary inflammation and was admitted to Johns Hopkins Bayview Medical Center. Her condition worsened, however, and although she was transferred to the hospital's intensive care unit, she died on June 2. The cause of her respiratory failure remains unknown.

In a statement, the university (www.hopkinsmedicine.org) said that the experimental protocol had been approved by the Johns Hopkins' Institutional Review Board for Human Subjects Research but that a preliminary investigation of the death has raised questions as to whether the study was done as described in its original protocol (see editorial p 2067).

The US Office for Human Research Protections, which oversees all federally funded human research, and the US National Heart, Lung, and Blood Institute, which funded the study, are investigating the death. NHLBI director Claude Lefant has also issued a letter to lung-disease investigators requesting that they assess all protocols in which human lungs are exposed to chemical challenge, especially those involving the inhalation of hexamethonium, and asks them to "Please consider suspending research with hexamethonium in light of this event until more information is available".

Michael McCarthy