NEWS

TIMELY SURGERY INCREASES BENEFIT OF SURGERY TO TREAT SYMPTOMATIC CAROTID STENOSIS

Endarterectomy to prevent major stroke is most beneficial if performed within 2 weeks of a transient ischaemic attack (TIA) or non-disabling stroke, investigators report. There may be no benefit at all if surgery is delayed much beyond this time.

'Ideally, the procedure should be done within 2 weeks of the patient's last symptoms,' Dr Peter M Rothwell, at Radcliffe Infirmary in Oxford, UK, and his colleagues advise in their report, published in the 20 March 2004 issue of the *Lancet*.

The authors pooled data from two large trials of carotid endarterectomy, which included nearly 5 900 patients recruited after a recent carotid distribution TIA, non-disabling ischaemic stroke or a retinal infarction. Subjects were randomly assigned to immediate endarterectomy or medical treatment.

For patients with at least 50% occlusion, time from the last symptomatic event to randomisation was significantly associated with effectiveness of surgery ($p < 0.0001$). The number of patients needed to undergo surgery to prevent one ipsilateral stroke within 5 years was five among those treated within 2 weeks versus 125 for those treated after more than 12 weeks.

In fact, for patients with 50 - 69% stenosis, only those treated within 2 weeks of the onset of symptoms exhibited clinically relevant benefit, the authors note.

Endarterectomy 'is often not done until several months after the event — even if the patient seeks medical attention immediately after their warning stroke,' Dr Rothwell notes in a *Lancet* press release. 'Benefit from surgery is very much reduced at this time, and many patients who would have benefited have their major stroke whilst waiting for surgery.'

The cost implication of this information is immediately apparent.

MAKING SMART DRUGS THAT DELIVER THE RIGHT KIND OF PUNCH

The irony of cancer therapy is that treatments powerful enough to kill tumour cells also harm healthy ones, causing side-effects that diminish the quality of the lives that are saved. Researchers at the University of Michigan Medical School's Center for Biologic Nanotechnology hope to prevent that problem by developing 'smart' drug delivery devices that will knock out cancer cells with lethal doses, leaving normal cells unharmed, and even reporting back on their success.

The U-M group is using lab-made molecules called dendrimers, or nanoparticles, as the backbones of their delivery system. Dendrimers are tiny spheres whose width is ten thousand times smaller than the thickness of a human hair. They have 'loose ends' where a targeting agent that can recognise a cancer cell and distinguish it from a healthy cell can be attached. The drug that kills the cancer cells can similarly be attached. A smart drug knows which cells to attack if both of these functions occur on the same molecule.

Part of the project focuses on finding out how to get dendrimers into cancer cells without disrupting healthy cells. Previous work had shown that high concentrations of dendrimers are toxic — even without their cancer drug cargo — but no one was sure why that was or what could be done about it. An atomic force microscope (a device so sensitive it can take pictures of single molecules) was used to spy on interactions between dendrimers and membranes similar to those that surround living cells. By taking a series of pictures and putting them together into a movie, researchers could watch dendrimers in action. What they saw was that 'certain kinds of dendrimers disrupt membranes by literally punching holes in them'.

The researchers wanted to deliver tinkering with the dendrimers to see if they could prevent the damage. What the group found is that if you modify the surface of the dendrimers chemically, they become 'uncharged' and no longer damage cell membranes. Other research showed that uncharged dendrimers don't invade cells at all unless they have cancer-detecting targeting agents attached.

Early results of studies with mice show that the nanoparticle drugs do treat cancer effectively with fewer side-effects than conventional chemotherapy drugs, just as the researchers had hoped.

Source: **http://www.med.umich.edu/**

PLAN TO BATTLE AIDS WORLDWIDE IS FALLING SHORT

Three years after the United Nations declared a worldwide offensive against AIDS and 14 months after President Bush promised $15 billion for AIDS treatment in poor countries, shortages of money and battles over patents have kept antiretroviral drugs from reaching more than 90% of the poor people who need them.

An article in the *New York Times* reports that 84% of the 0.25 million people in the Americas who need AIDS treatment are receiving it, but only 2% of the 4.4 million people in Africa who need AIDS treatment are receiving it. The World Health Organisation's '3 X 5' plan to have three million people in treatment by the end of 2005 is collapsing from a lack of money. Donations to the Global Fund, currently about $1.6 billion a year, are barely 20% of what Secretary General Kofi Annan said was needed when he created the fund in 2001.

While generic drugs have been approved by the World Health Organisation (WHO), endorsed by the World Bank and used in several African countries, the Bush administration has so far paid only for medicines that are still under patent and cost much more. Generic combinations of three antiretrovirals that cost $244 - $292 per patient per year are being used in Zimbabwe. The Centers for Disease Control in Atlanta, however, plans to pay for the treatment of 1 000 Zimbabweans, buying the same three patented drugs separately from the manufacturers at a cost of $562 a year, and a daily dose is six pills.

Prices for both branded and generic medicines have plunged in the last 2 years. Last year, a foundation organised by former President Bill Clinton announced an agreement with Indian and South African generic companies to sell the drugs for $140 per patient per year if large orders were guaranteed, payment was in cash and the drug maker did not have to pay the legal and lobbying costs of getting each drug licensed in each country.

Experts, advocacy groups and health officials agree that the delays, compounded by inadequate medical facilities and training in very poor countries, are likely to persist unless spending is stepped up sharply.

FLU SHOTS CAN REDUCE EAR INFECTIONS IN YOUNG CHILDREN

Recent research has shown that vaccination with the annual flu vaccine is a simple means to reduce the incidence of the condition.

Medinfo reports that more than 60% of children have had at least one attack of acute otitis media (AOM) by their first birthday while more than 80% have had an attack before turning three. Moreover, higher rates of illness are being recorded among 6 - 30-month-old children attending day-care centres, with the incidence of AOM among children under 1 year of age in day-care being three times higher than those in a home environment.

Dr Stephen Toovey, Medical Director of MedInfo, explains that the majority of AOM incidents occur during the winter months coincident with the annual influenza season. Although generally caused by bacterial infection, considerable accumulated evidence shows that, in most cases, AOM is preceded by a respiratory viral infection — such as type-A flu. In fact, a simultaneous viral infection is observed in up to 42% of patients with AOM, says Dr Toovey. Emphasis has been placed on influenza A virus infection because the vaccine is available and has been shown to be safe and effective, and because AOM is a common complication of type-A flu.

Studies conducted in Finland and the USA during the 1990s showed that influenza vaccination of children in day-care provides protection against AOM during the flu season, resulting in a measurable decline in incidence.

The cost of flu vaccination is considerably less than the cost of treating repeated middle ear infections. It is also far less distressing for young patients to have a single flu shot at the start of the season than to suffer repeated ear infections throughout the winter months.

WHO SEES SURGE IN PROGRESS AGAINST TUBERCULOSIS ON EVE OF GLOBAL SUMMIT

The number of TB patients diagnosed and treated under the directly observed therapy short course (DOTS), the internationally recommended strategy for TB control, is now rising much faster than at any time since DOTS expansion began in 1995, according to a new report by the World Health Organisation (WHO). Indeed, the past 2 years have witnessed accelerated growth in the implementation of DOTS programmes worldwide.

The 2004 Global Tuberculosis Control report confirms that DOTS programmes are now treating three million TB patients every year, an increase of more than one million patients compared with just 2 years ago. That increase is nearly double the average annual increment of 270 000 patients during the previous 6-year period, and the trajectory is still heading upward. India is leading the surge, followed by smaller but significant increases in five other key countries with high rates of TB: South Africa, Indonesia, Pakistan, Bangladesh and the Philippines.

'DOTS expansion is one of the major public health success stories of the past decade, one that is saving thousands more lives every day,' said Dr Lee Jong-wook, WHO Director-General. 'But to reach the 2005 targets for detection and treatment, the challenge now is to add another one million TB patients to DOTS programmes each year.'

The global 2005 targets for TB control are to detect 70% of all infectious TB cases and cure 85% of those cases detected.

According to the WHO report, the case detection rate has risen to 37% and cure rates to 82%. Meeting the 2005 targets will put the world's TB control programmes on the path to achieving the Millennium Development Goal (MDG) of halving the global TB burden by 2015.

'HIV/AIDS is driving the TB epidemic in southern and eastern Africa and will worsen the situation in Eastern Europe, India and China in the years ahead,' said Dr Jack Chow, the WHO Assistant Director-General for HIV/AIDS, Tuberculosis and Malaria. 'We cannot control one without controlling the other, and must begin rapidly scaling up TB/HIV collaborative activities to provide a synergy of prevention, treatment and care for co-infected patients.'

SPLIT BILLING IS ILLEGAL — BHF

One of the challenges facing government as it considers restructuring of drug prices and legislation affecting the operation of medical schemes, is tracking actual health care expenditure, a process hindered by practices such as split billing. Medical schemes are irate at the increasing numbers of practices that are indulging in split billing, outlawed by a ruling of the Health Professions Council and the Medical Schemes Act, 1998.

'Split billing occurs when a provider of service, such as a doctor, issues more than one account for the same service,' explained Heidi Kruger, Communications Manager of the Board of Healthcare Funders. 'For instance, the doctor submits an account to a medical scheme for the amount covered by a benefit, and a separate account to the member for the amount which the member has to pay.'

Kruger said service providers in the medical care industry are permitted to issue balanced bills, recording both the amount to be paid by the medical scheme and that owed by the member. 'Unfortunately', said Kruger, 'it would seem that many members of medical schemes are unaware that split billing is illegal. Should they receive such a bill, they would be advised to contact their medical aid and seek appropriate advice about what action to take.'

POLIO MOVES SOUTHWARDS IN AFRICA

A 7-year-old child in the Ngami district of northern Botswana has been diagnosed with paralytic poliomyelitis, becoming the first victim of the disease since the World Health Organisation (WHO) declared the country polio-free in 1991. This has raised concerns that the virus has been reintroduced to countries in Africa that have been polio-free for many years.

Specialists report that the virus responsible for the infection is very closely related to that endemic in Nigeria, where approximately 300 cases of polio were recorded in 2003 — making this country the worst in the world in terms of polio incidence. The same virus has already spread to neighbouring territories in West Africa — including Benin, Burkina Fasso, Cameroon, Central African Republic, Chad, Ivory Coast, Ghana and Togo — threatening the lives of 15 million infants and prompting the WHO to organise a large-scale vaccination campaign against the disease.

Neutralising the virus requires comprehensive vaccination of the at-risk population resident where cases are reported, and the Botswana health authorities have announced an emergency vaccination plan. Neighbouring countries have also stepped up their polio vigilance.

'The emergence of polio in Botswana highlights the risk to which travellers to the region may be exposed,' says Dr Andrew Jamieson, medical director: SAA-Netcare Travel Clinics, 'especially as immunisation against polio during one's childhood years does not guarantee protection against the disease as an adult. To the contrary, adults generally lose immunity to polio with time, such that re-immunisation is advisable prior to visiting a country where polio is endemic or which may have been infected with the virus.'

In 1989, the WHO launched the US$3 billion global vaccination campaign targeted at eradicating polio by the end of 2004. The last remaining countries where polio is endemic include Afghanistan, Egypt, India, Niger, Nigeria and Pakistan. Ten West African countries are participating in a final drive to vaccinate 10 million children against polio, which began in February 2004.

BREAKTHROUGH STUDIES SIGNAL A POSSIBLE NEW MEANS OF COMBATING MALARIA

Scientists at the European Molecular Biology Laboratory (EMBL) have identified 4 mosquito proteins that affect the ability of the malaria parasite (*Plasmodium*) to survive and develop in the *Anopheles* mosquito. This breakthrough could be used to block the transmission of malaria from mosquitoes to humans.

'Many researchers focus on the direct effects of *Plasmodium* on the human body but the mosquito is an equally important battleground,' notes Professor Fotis Kafatos, EMBL's Director-General and leader of the malaria research group.

Three weeks after a mosquito ingests infected blood, the *Plasmodium* organism moves from the mosquito's gut into the

salivary glands; at the next bloodmeal it is injected into the victim's bloodstream along with the mosquito's saliva, infecting the individual.

One fact that had continued to puzzle malaria researchers is why 'susceptible' mosquitoes transmit malaria whereas 'refractory' insects do not. It was suspected that protein factors of the mosquito's immune system might be responsible for this difference. EMBL scientists have now shown this to be the case. Two of these mosquito proteins, TEP1 and LRIM1, were shown to be true defenders of the mosquito, killing the parasite in the insect's gut.

The researchers showed that TEP1 specifically locks onto the *Plasmodium* '...and it is this binding that mediates the killing of the parasite,' they explain. 'Different forms of this protein are present in susceptible and refractory mosquitoes, potentially accounting for the fact that refractory mosquitoes do not sustain parasite development.'

Other work revealed a new twist: In addition to the mosquito defender protein LRIM1, they discovered two proteins, CTL4 and CTLMA2, which have the opposite effect, actually protecting the parasite as it develops in the mosquito gut. With elimination of these proteins, the parasites died. Novel chemicals to inhibit the ability of such proteins to protect the parasite is a promising option to decrease the prevalence of malaria.

MINISTRY OF HEALTH AND PFIZER CELEBRATE DIFLUCAN PARTNERSHIP PROGRAMME SUCCESS

Nearly 4 years after the launch of the first health-related public-private partnership in South Africa, the Ministry of Health and Pfizer met recently to review the significant success of the programme.

Diflucan, manufactured by Pfizer, is provided free of charge to patients in government health care facilities in South Africa. To date it is made available at over 427 sites in all 9 provinces. Diflucan is the most sought after treatment for the two most common fungal opportunistic infections associated with HIV/AIDS — cryptococcal meningitis and oesophageal candidiasis.

One of the key components of the donation programme is the training provided to pharmacists, doctors, nurses and other health care professionals by the International Association of Physicians in AIDS Care (IAPAC). Pfizer global chairman, Dr Henry A McKinnell, announced in 2002 that the programme was to be expanded to all developing countries with an HIV infection rate of over 1%, with no dollar or time limit.

The programme has now been expanded to Botswana, Cambodia, Congo, Ethiopia (imminent launch), Gambia, Honduras, Ivory Coast (imminent launch), Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, Senegal, South Africa, Swaziland, Tanzania, Uganda, Zambia, Zanzibar and Zimbabwe. In 2004, a further 23 countries around the world with an HIV prevalence of 1% or higher will join the programme, providing their citizens with life-enhancing treatment.

In South Africa, over 16 000 health care professionals have been trained; over 4 million tablets have been distributed; over 137 000 scripts have been written, 96 708 for cryptococcal meningitis and 41 118 for oesophageal candidiasis at 427 sites across all 9 provinces.

In the expansion countries, over 3 million tablets have been distributed, 51 832 scripts processed and 1 645 health professionals trained across 458 sites.

DRIED BLOOD-SPOT TEST MONITORS HIV TREATMENT

A relatively simple test to monitor the effects of HIV treatment is showing early promise for use in less-developed countries.

Preliminary findings published in the *Lancet* suggest that a simple enzyme-based procedure to measure CD4+ lymphocytes could be possible with the analysis of dried blood spots on filter paper. Such an assessment method could become particularly useful as antiretroviral drugs become available in less-developed countries, where monitoring by more complex methods involving laboratory-based CD4 cell count assessment is unlikely to be widely available.

For their research, Professor Alimuddin Zumla from University College London, and colleagues at the University Teaching Hospital, Lusaka, Zambia, obtained blood from 42 HIV-infected Zambian patients. Blood spots were dried on filter paper and CD4+ lymphocyte counts were measured with a commercial enzyme immunoassay. The investigators compared these measurements with those obtained with standard flow cytometry, the laboratory 'gold standard' for CD4+ assessment.

Results of the filter-paper method compared well with flow cytometry CD4+ counts greater than 200 cells/ml. The investigators conclude that dried whole blood stored on filter paper could be developed into a field-friendly alternative for CD4+ lymphocyte count measurements.

Professor Zumla said: 'Many African countries are now introducing antiretroviral therapy to their HIV-infected populations. The monitoring of this treatment requires CD4+ count measurement which unfortunately is currently not

available to the majority of poor people living away from cities where the health clinics and hospitals are based. Furthermore, the current method of testing is expensive. Our results are very encouraging, for they point the way towards making cheap CD4+ count testing easily available to people receiving antiretroviral therapy in rural areas. Such methods could be used in a similar way towards HIV viral-load measurements, another test required to assess the success of HIV treatment.'

FNS