Research suppressed for seven years by drug company

Jacqui Wise, *BMJ*

A drug company suppressed research which showed that generic thyroid drugs were as effective as its own branded product for almost seven years, says the *Journal of the American Medical Association*.

A randomised four way crossover trial concluded that two brand name and two generic forms of thyroxine sodium (levothyroxine) were bioequivalent and interchangeable without loss of therapeutic efficacy in most patients for the treatment of hypothyroidism (*JAMA* 1997;277:1205-18). The two brand name products were Synthroid—the most commonly used brand in the United States—and Levoxine (now renamed Levoxyl)—a newer, cheaper product similar in price to generic forms.

Thyroxine sodium is widely prescribed in the United States as the drug of choice for thyroid replacement treatment. The Food and Drug Administration (FDA) does not recognise thyroxine sodium products as bioequivalent, and generic substitution is not recommended. The authors of the study estimate that using generic or less expensive brand name products in the United States could save $356m (£223m) a year.

In an accompanying editorial Dr Drummond Rennie, deputy editor of *JAMA*, explains why these findings have only just been published despite being ready for publication in 1990. In 1987 Betty Dong and colleagues from the department of clinical pharmacy at the University of California Medical Center in San Francisco were asked by Flint Laboratories, the manufacturer of Synthroid, to carry out research comparing their drug with three others. Both sides apparently expected the study to show that Synthroid was superior. By the end of 1990, when the study was complete and it became clear that all four preparations were bioequivalent, the results were sent off to Boots Pharmaceuticals, which had taken over Flint Laboratories.

Dr Rennie says that over the next four years Boots "waged an energetic campaign to discredit the study and prevent its publication." The study was eventually submitted to *JAMA* in April 1994, and a publication date was set for 25 January 1995. On 13 January 1995 Dr Dong suddenly withdrew her manuscript from publication, citing impending legal action by Boots. Apparently, Dr Dong had signed a restrictive covenant at the beginning of the study stating that all information gathered in the study was confidential and could not be published or released without written consent from Flint Laboratories.

In March 1995 the pharmaceutical branch of Boots was taken over by Knoll Pharmaceuticals. Dr Rennie writes that Dr Gilbert Mayor from Boots/Knoll then published the study without reference to Dr Dong, but he had reanalysed the data to reach the opposite conclusion. The article was published in a new journal called the *American Journal of Therapeutics*, of which Dr Mayor was an associate editor. As a result, the FDA wrote to the company saying that its assertion that Synthroid was pharmokinetically superior to other preparations was misleading and that the information should not be disseminated.

Under pressure from the FDA Knoll agreed on 25 November 1996 to allow the research to be published, but it still insisted that the conclusions were not supported by the data. In a letter in *JAMA* it says that the study is flawed in design and execution. One criticism is that the residual thyroid function of the patients in the study was not measured and that there were only 22 patients in the study.

But Dr Rennie said: "We believe it is good work, not merely because it passed peer review by more than the usual number of experts but because it has passed careful and prolonged scrutiny by the university in response to widely disseminated allegations of scientific defects and ethical violations."

Dr Rennie says that there are many lessons to be learnt from this case. "Investigators should not assume that the sponsors will encourage publication of unfavourable results and should never allow sponsors veto power."

He says that academic research institutions should forbid such clauses in contracts. He also warns of the dangers of increasing reliance on industry sponsorship. "The research community is getting progressively more entangled with industry." □

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The research community is becoming more entangled with industry

The seven year delay to publication that occurred with the Synthroid research is rare but shorter delays are quite common. Around a fifth of research papers are delayed by at least six months, according to a survey of 2167 members of life science faculties (*JAMA* 1997;277:1224-8).

The most common reasons for delay were to allow time for patent application (46%), to protect the proprietary or financial value of the results (33%), and to protect the investigators' scientific lead (31%). However, 28% said that the delay was "to slow dissemination of undesired results." It is not clear whether such delay came from the scientists themselves or from industry sponsors.

The authors conclude that withholding research results is not widespread. But Dr Rennie, deputy editor of *JAMA*, said: "If 'undesired results' are withheld by only 5% of all researchers, the fears induced by the increased part industry is playing in the funding of research are not dispelled."

In brief

UK High Court will rule on rationing: A man who has multiple sclerosis has been given legal aid to challenge North Derbyshire Health Authority's refusal to fund his treatment with interferon beta.

House of Lords condemns tobacco subsidies: The House of Lords committee on the European Communities has condemned the subsidy of tobacco production in the European Union as a scandalous waste of taxpayers' money. The EU spends 1000m ecu (£800m) a year subsidising the production of low quality tobacco, which is dumped on developing countries.

Philippines introduces vitamin A fortified sugar: The Philippines government has announced the first production in Asia of vitamin A fortified sugar. Every day an estimated 17 Filipino children go blind because of vitamin A deficiency.

WHO advises on bovine sources in medicine: The WHO recommends that, whenever possible, cattle (bovine) sources should be avoided in the preparation of medicinal products and devices, although it reiterates that no link can definitely be established between bovine spongiform encephalopathy and the variant form of Creutzfeldt-Jacob disease.

Brazil presumes donors' consent: Brazil has passed a law allowing surgeons to presume that all individuals consent to the use of their organs after their death unless the family objects.

Lack of screening for cystic fibrosis wastes money: A British specialist in cystic fibrosis, James Littlewood, says that health authorities are wasting millions of pounds by refusing to screen newborn babies for the disease. The test costs £1.50 ($2.20).

Body parts used by UK artist: A former employee of the Royal College of Surgeons has been arrested and released on bail after allegations of theft and illegal burying of body parts used by a sculptor who is also on police bail.

Doctors fight US company patent on umbilical cord blood

Jacqui Wise, *BMJ*

Doctors in Europe are fighting against the granting of a patent to a United States company for the use of blood from umbilical cords and placentas. This cord blood, which is rich in stem cells, can be used as an alternative to bone marrow transplants.

Biocyte was granted a Europe-wide patent last year by the European Patent Office in Munich for the cryopreservation of cord blood. The blood itself cannot be patented but the patent means that doctors wanting to extract and store the blood will have to pay royalties to the Pennsylvania based company who claim they did much of the original research on the procedures. The company was refused a patent in the United States.

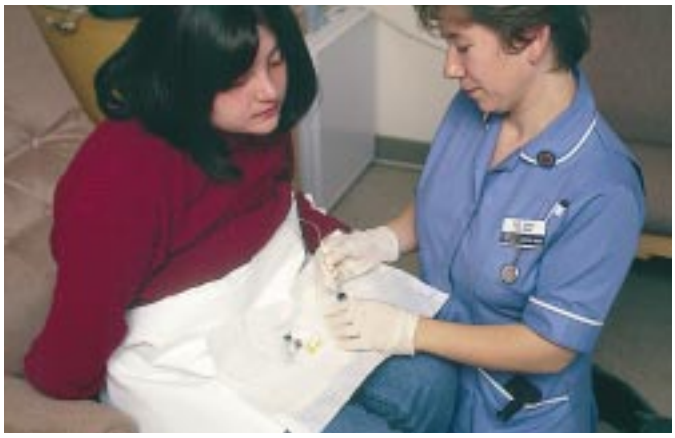
The news has sparked an ethical debate about the commercialisation of the human body. Peter Gibson, a spokesman from the National Blood Service, said: "Does this mean you can patent a heart transplant? Where does this stop?"

The European Patent Office allows nine months for any decisions to be opposed. Eurocord—an organisation representing transplant centres and cord blood banks—has just done so. Helene Jacobs, the project manager of Eurocord Netherlands Foundation, said: "We opposed the patent on the grounds that the process was not novel and the company did not invent it. Most of the information has been around since the 1970s and 1980s."

Eurocord are now waiting to see the response from Biocyte. Ms Jacobs said: "It may be a long process, perhaps up to two years, but we are confident we will win."

Transfusions of cord blood are a relatively new operation. The first one was carried out in Paris in 1988. Worldwide there have been around 300 transplants on children and 20 adults but the technique is likely to become more widely used as more cord blood banks are set up. If a woman consents to donate the blood it can be retrieved simply and painlessly from the umbilical cord and placenta. It is then frozen and stored in cord blood banks until a match can be found.

The London Cord Blood Bank in Edgware is the largest in the UK with 600 donations stored. Mr Gibson said: "At least four transplants have happened so far using the blood bank but the potential is huge. People who had no hope of getting a bone marrow transplant now have another option." □



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Cord blood is an alternative to bone marrow transplant

Sweden is healthiest place to live in world

Jacqui Wise, *BMJ*

Sweden and Israel are the world's healthiest countries, according to league tables drawn up by the Economist Intelligence Unit. Among the 27 developed and developing countries surveyed South Africa and India are the least healthy, while the United Kingdom is the least healthy in western Europe.

The league tables were drawn up using 12 different healthcare indicators rather than simply relying on life expectancy alone, as have other surveys. The indicators included maternal and infant death rates, deaths from cancer, infection, and heart and respiratory disease, HIV infection rate, and immunisation rates.

The new ranking system throws up some surprises, with Taiwan coming out above the UK and Mexico above the United States. Taiwan has a low death rate—less than 10% of the population is aged over 65. It also has a low incidence of maternal mortality—lower than the US—and a low incidence of AIDS.

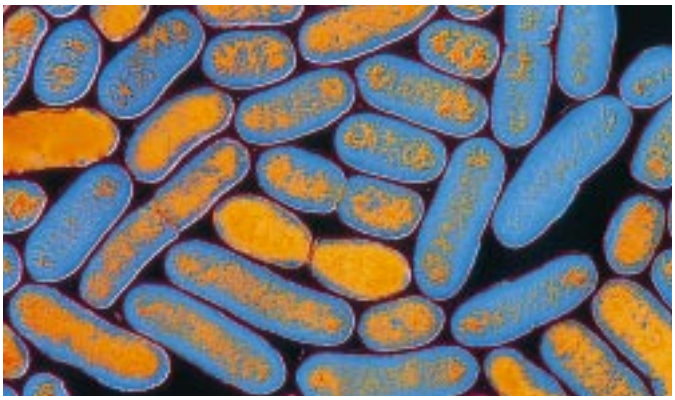
Mexico benefits from better immunisation coverage than the US and lower death rates from cancer and from respiratory and circulatory diseases. However, the report in Healthcare International acknowledges that, as the figures are mostly derived from government, politicians can be reluctant to divulge the true incidence of local disease in case this affects investment and tourism. Britain does badly mainly because of the high rate of cancer and circulatory diseases, which may be due to the country's poor diet.

South Africa came out as the unhealthiest of the 27 countries surveyed, below even India. Its totals for childhood and maternal mortality are nearly 13 times greater than those of Japan, Sweden, and Singapore, which have the lowest figures. South Africa also has the highest prevalence of HIV infection—15.7 out of every 1000 inhabitants.

The report also found no correlation between the numbers of doctors and quality of medical care. Italy has a large number of doctors—478 per 100 000 population—but is still middle of the table. Alexandra Wyke, editor of *Healthcare International*, said: "The conclusion must be that the amount spent on healthcare and the quality of doctors and hospitals have little to do with the quality of medicine." □

E coli report calls for better food safety

Bryan Christie, *Edinburgh*



E GRAY/SCIENCE PHOTO LIBRARY

More research is needed into the *E coli* organism

Food safety controls are to be tightened in Britain after an inquiry into the world's second worst outbreak of *Escherichia coli*, which killed 18 people and affected almost 500.

The government has accepted all the recommendations put forward by an expert group which examined the circumstances that led to the outbreak in the Scottish town of Wishaw late last year. The source of the infection was a local butcher's shop which supplied contaminated meat products to several retail outlets in the surrounding area.

The inquiry looked into every stage of food production from "the farm to the fork" and called for greater awareness among farmers of the nature of the *E coli* bacteria; higher standards in abattoirs to prevent meat becoming contaminated with faecal material; the introduction of a licensing system for butchers' shops to ensure that good hygiene practices are maintained; and improved education on food preparation in schools as well as training for food handlers. The report of the inquiry also recommended that a programme of clinical, microbiological, and epidemiological research should be funded to improve current understanding of the *E coli* organism.

The inquiry team, led by Hugh Pennington, professor of bacteriology at the University of Aberdeen, made a series of priority recommendations in January, and the full report builds on these. The only notable change relates to the licensing conditions for shops selling meat. The interim report recommended that raw and cooked meats should be kept apart, served from separate counters by separate staff (25 January, p 249). However, the final draft acknowledges that employing separate staff could be uneconomic, particularly for small butchers' shops. It says that provided certain conditions are met, including the provision of hand washing facilities in serving areas, licences can still be granted.

The report is critical of the government for adopting a slow approach in improving food hygiene standards. It says that these "have been pursued generally with a light touch, based on a 'graduated approach' " and that this approach can no longer be considered appropriate or acceptable.

The Royal Environmental Health Institute of Scotland said the recommendations would lead to a better trained and safer workforce. Dr Sandy Macara, chairman of the BMA Council, called for an independent body to advise the government, representing all the major interests and covering food safety, quality, and nutrition. □

Malnutrition grips North Korea

Richard Tomlinson, *Beijing*

North Korea has for the first time admitted that children have been dying as a result of malnutrition in the Stalinist state. According to a Unicef spokesperson last week, North Korean health ministry officials said that 134 children had died and nearly one child in seven was suffering from the country's severe food shortages.

The food shortage in North Korea has become so severe that official food rations have dropped to about 100g of rice a day per person, just 350 calories, according to the United Nations' world food programme. "They also live on whatever leaves, roots, or vegetables that they may have stored before the winter," said Catherine Bertini, the programme's executive director. The government has admitted that it has run out of the food that is distributed as state provided rations.

Children are among those worst affected by long term malnutrition. On a fact finding mission to North Korea last month, Ms Bertini and fellow representatives were taken to six schools. She estimated that about one quarter of the children were lethargic, and video footage showed malnourished children from one school sitting staring vacantly into space. Other recent UN visitors to North Korea reported that children had night blindness, scurvy, and rickets.

Last week the UN launched an appeal for a further $126m (£79m) of international food aid for North Korea. UN congressman Tony Hall spent three days visiting rural North Korea earlier this month and afterwards said that "evidence of slow starvation on a massive scale was plain wherever we made an effort to look." He described some of the children he had seen as "shockingly underweight."

The beleaguered country had severe flooding in 1995 and 1996, exacerbating existing weaknesses in its centrally planned system of agriculture. The central rations issued through the government's public distribution system in 1993 were 450 g of rice a day, which was reduced to 200 g in 1996 and halved to 100 g this year. "One of the problems that we see is a great lack of protein, and one of the reasons is that in the flood areas many of the animals which people had were washed away in the flood, and they have not been able to replace them," said Ms Bertini. □

On call rota system best for doctors' health

Martyn Halle, *London*

Junior doctors may have escaped 80-90 hour weeks, thanks to the New Deal reforms. However, some of the new work methods the reforms have spawned are not proving popular. A new study shows that the old fashioned, on call rota system still gets the thumbs up from juniors and is better for their mental wellbeing (*Journal of the Royal College of Physicians* 1997;31:162-7).

As part of the reduction in juniors' working hours, many hospitals have switched to full shift or partial shift systems. Doctors from the department of psychiatry at Leeds University compared two hospitals—one operates a one in six rota with on call and a partial shift system for its junior house officers, while the other operates a full shift system. Both hospitals are in the same city and are fed by the same medical school. The results showed that, although the hours worked were similar, half of the doctors working shifts showed signs of important psychiatric and psychological morbidity.

These levels were as high as 10 years ago, when juniors' hours were sometimes twice as long. There were no indications of major psychiatric problems, such as suicidal tendencies, but the problems were serious enough to justify seeking help.

Many doctors felt depressed because they found shift patterns disruptive to social and family life. They also found that working for a number of different consultants was difficult, and they felt that they were just dogsbodies.

"We were surprised to discover these problems among the shift workers because the shift system would appear to be less arduous than being on call," said Dr Navneet Kapur, one of the authors of the study. "They complained that they weren't getting sufficient breadth of training and did not feel part of a team because the shift system led to them working for several consultants rather than them being on one 'firm'." □

UN condemns female circumcision

Josh Hamilton, *New York*

The United Nations has called for an end to ritual female genital mutilation, a practice to which an estimated 130 million girls and women worldwide have been subjected.

The heads of the WHO, Unicef, and the United Nations Population Fund published a statement last week calling for an international effort to bring about a "major decline" within 10 years in what they termed an "unsafe and unjustifiable traditional practice." The aim is to eliminate female genital mutilation worldwide within three generations. The agencies announced plans to work with governments and political and religious organisations in countries where female genital mutilation is practised.

The practice, sometimes referred to as female circumcision, affects women and girls throughout the developing world, particularly among African countries, where the incidence may be over 90%. Female genital mutilation describes partial or total removal of the external female genitalia or other injury to the genital organs for non-therapeutic reasons—usually cultural or religious—with the aim of reducing sexual responsiveness or drive.

Female genital mutilation is traditionally performed by elderly women who have no medical training and commonly use unsterilised razor blades, kitchen implements, or even broken glass. In the short term mutilated girls and women may experience severe pain, shock, urine retention, ulceration of the genital region, or even fatal haemorrhage or infection. Long term adverse affects include cysts and abscesses, keloid scarring, urinary incontinence, dyspareunia, sexual dysfunction, urinary tract infections, infertility, and complications during childbirth.

The primary focus of the United Nations' efforts has been to educate women through workshops. "We are very respectful of the fact that these are long-standing traditions in these countries," said Marsha Zeesman, a spokeswoman for Unicef in New York. "That is why we work with women themselves."

In the past year Unicef campaigns have resulted in legislation against female genital mutilation in Cameroon, Côte d'Ivoire, Burkina Faso, and Egypt. □

Dutch GP in euthanasia case will not go to prison

Tony Sheldon, *Utrecht*

A Dutch court has rejected demands by the public prosecutor for a one year prison sentence for premeditated murder against a Frisian general practitioner, Dr Sippe Schat. Instead Dr Schat was found guilty of the lesser charge of euthanasia and of depriving his patient of life at her request and was given a six month suspended prison sentence.

Dr Schat was originally charged with murder and held on remand for 13 days (4 May 1996, p 1116) after failing to meet the guidelines laid down by the Royal Dutch Medical Association that allow doctors a legal defence in euthanasia cases.

Dr Schat claims to have acted at the explicit request of his patient, a 73 year old woman who was terminally ill with cancer and wanted secrecy. But he failed to consult with colleagues or report an "unnatural death," as required under Dutch law. Neither was there a written request for euthanasia.

Last week the court said that his actions were "reprehensible." It was convinced, however, that he intended to act in the best interests of his patient.

The court heard how his patient had breast cancer with complications affecting her lungs, liver, and stomach. She had told staff at her nursing home that she wanted to die.

Dr Schat told the court that on 17 April last year her pleading was so intense that he could no longer refuse. He gave her three injections of morphine, phenobarbitone, and insulin. Unsure of the dose, he returned a second time to give two further injections. He then left, and she was found dead in the morning.

Dr Schat said that his patient did not want him to tell anybody else. "I'm afraid that her interests prevailed over mine. I reacted to a patient in distress," he said.

Professor Johan Legemaate, legal counsel to the Dutch Medical Association, said that it was implicit in the association's requirements to report euthanasia and seek a second opinion. The regional health inspectorate has still to decide if Dr Schat will face disciplinary action. □

Health gap between Aboriginal and non-Aboriginal people is widening

Christopher Zinn, *Sidney*

A damning report has revealed a widening gap between the health of Aboriginal and non-Aboriginal people.

The most comprehensive survey ever on the subject shows that Aborigines are six to eight times more likely to die aged 25 to 55 years than white Australians. They have a life expectancy matched only by places like India and central Africa.

The report, *The Health and Welfare of Australia's Aboriginal and Torres Strait Islander Peoples*, states that there was "little improvement" in indigenous death rates in the decade to 1994 and that there was a "large increase" in deaths from diabetes.

The survey, carried out jointly by the Australian Bureau of Statistics and the Australian Institute of Health and Welfare, found that many Aborigines had "a lower life expectancy than any other indigenous minority within a first world country."

It confirmed that babies born to Aboriginal mothers were between two and four times more likely to die at birth than non-indigenous children. Nearly a fifth of 80 000 Aborigines in outback states could not rely on a water supply declared safe for human consumption.

Australia's governor general, Sir William Deane, who released the report in Darwin, said that he hoped the study's "unprejudiced statistical facts" would lead to action. "Any caring Australian who reads this report must recognise that nothing can justify any delay in our doing whatever we can to address the overwhelming health problems," he said.

But the federal government has warned against "quick fix" solutions and said that it could take 10 years to make substantial improvements. The minister for health, Dr Michael Wooldridge, said that no significant improvement in life expectancy was likely until moves were made to reduce smoking among Aborigines, which was twice the national average. Smoking is the most common cause of death among Aborigines, with 54% of men and 46% of women smoking regularly. □

PENNY TWEEDIE/PANOS PICTURES

Aboriginal people have a low life expectancy

Leading scientists call for action against malaria

Stephanie Swafford,
Clegg scholar, BMJ

NEIL COOPER/PANOS PICTURES

Nine out of ten deaths from malaria occur in Africa

World leaders in science and health have called for urgent collaborative action against malaria, warning that a disaster looms over Africa.

"The international community has a responsibility to recognise malaria, like the AIDS pandemic, as a major challenge and to commit itself to do more to prevent the disaster that looms over Africa," wrote the 18 scientists in a letter in *Nature* (1997;386:541). Signatories to the letter included Richard Feachem from the World Bank; Tore Godal, head of the Word Health Organisation's tropical disease research programme; Maxime Schwartz, director of France's Institute Pasteur; George Radda, chief executive of the British Medical Research Council; and Harold Varmus, director of the American National Institutes of Health.

The letter states that more than a million people die from malaria every year. Nine out of ten of these deaths occur in Africa, where resistance to chloroquine is spreading and resistance to Fansidar (pyrimethamine with sulfadoxine), the only other affordable drug, is also increasing.

Earlier this year scientists from around the world came together in Dakar, Senegal, for the first time to discuss possible solutions to the malaria problem. The WHO and the World Bank are now considering the conclusions reached at this meeting as part of the development of an African developed and led strategy to control malaria. The Dakar meeting proposed greater collaborative research efforts both among African scientists and between scientists in the north and the south. Some of the priorities for such collaborative long term research include sequencing the *Plasmodium falciparum* genome, developing a vaccine, using bed nets impregnated with pyrethrum, and developing case management strategies and new drug treatments.

Research could be facilitated by having common protocols and joint materials such as insects and reagents. An immediate need is internet and email access for African scientists so that they can tap into scientific information and communication around the world.

Priorities from the Dakar meeting can be obtained at: http://www.niaid.nih.gov/dmid/malafr/; anyone interested in collaborative research projects contact: http://www.naid.nih.gov/dmid/mal_Itr_en.htm

Gene therapy hope for motor neurone disease

Jacqui Wise, *BMJ*

A team of French and Danish scientists has shown that gene therapy can slow the gradual destruction of motor neurones in mice.

The delivery of neurotrophic factors by gene therapy produced a 50% increase in life span, reduced loss of motor axons, and improved neuromuscular function in mice with symptoms of motor neurone disease (*Nature Medicine* 1997;3:429-36).

The research, although preliminary, shows that gene therapy for motor neurone diseases is feasible and that neurotrophins are effective when given in a precisely targeted manner. These proteins had been thought to have potential as they allow neurones to survive in conditions in which they would otherwise die. Clinical trials in which these factors were injected directly into patients, however, have shown disappointing results because of poor bioavailability and toxicity. The continuous administration of small amounts of neurotrophic factors by gene therapy more closely resembles the physiological situation.

Untreated mice exhibiting the symptoms of human motor neuron disease die on average after 40 days. When scientists introduced the gene coding for neurotrophin-3 the average life span increased to nearly 62 days or by more than 50%. In addition, treated mice were more mobile, and the muscle fibres remained more numerous and conducted nerve impulses more efficiently than in untreated mice. Combined therapy with gene coding for two neurotrophic factors increased the average life span to 66 days, with some animals surviving for more than three months.

In an accompanying article Dr Michael Sendtner, a neurologist a the University of Würzburg in Germany, sounds a note of caution. "Injection of adenoviral vectors into newborn mice that lack a mature immune system is relatively straightforward. Adult patients who have already been in contact with adenoviral antigens are likely to mount a rapid and strong immune response to adenoviral vectors."

The authors acknowledge that the currently available vectors should be further improved before their use for gene therapy in humans. □

Chemokines show potential against HIV

Susan Mayor, *London*

Researchers are making progress in new approaches to protect cells against the AIDS virus, with the discovery of molecules that are able to prevent HIV-1 entering and infecting T cells.

A team from the Institute of Cancer Research in London report that a modified chemokine—AOP-RANTES—potently inhibits infection of several cell types by certain HIV-1 strains (*Science* 1997;276:276-9). Project leader Dr Paul Clapham said: "This is the first real evidence to show that chemokines can be modified to improve their inhibitory effects on HIV."

The finding follows the discovery 15 months ago that HIV infects cells by "hijacking" cell surface receptors that normally bind to chemokines—naturally occurring proteins which regulate the movement of white blood cells in the body. HIV's primary target is a subset of T cells with CD4 molecules on their surface. But CD4 is not sufficient for infection—chemokine receptors are needed as well.

Two types of receptor are implicated. Chemokine receptor 5 (CCR5) is the cofactor for HIV strains that occur early and throughout HIV infection (macrophage tropic HIV) and CXCR4 is associated with strains that emerge in late stage disease (T cell line tropic HIV).

Researchers have previously tried to prevent CCR5 from acting as an HIV cofactor by blocking it with the chemokine RANTES, but this achieved only poor inhibition in some cell types and could induce inflammatory side effects in vivo. However, the London researchers found that a modified form of the molecule, AOP-RANTES, developed by GlaxoWellcome, effectively prevented infection by macrophage tropic HIV strains in a range of cultured cells types, including T cells and macrophages, without causing an inflammatory response.

"While this is still a long way off use in patients, there is great potential for this approach," said Dr Clapham. □

Boycott threat forces French company to abandon RU486

Alexander Dorozynski, *Paris*

Pressure by American antiabortion activists has led the French pharmaceutical company Roussel-Uclaf, subsidiary of the German company Hoechst, to abandon production and distribution of mifepristone (RU486), the "abortion pill."

The company has transferred all patent rights, without charge, to Dr Edouard Sarkiz, one of the pill's developers, who hopes to develop its potential in other therapeutic areas.

Antiabortionists had long threatened to boycott Hoechst and Roussel-Uclaf's products in the United States if the pill was marketed there. A few months ago, Hoechst acquired all shares of Marion Pharmaceuticals and formed a new group, Hoechst-Marion-Roussel, so increasing its share of the US pharmaceutical market from 1% to about 4%. A Hoechst spokeswoman said that the threatened boycott is a risk that the new group cannot afford to take.

Mifepristone, discovered by Professor Etienne Baulieu, was introduced in France in 1987 as a pharmaceutical alternative to surgical abortion.

In 1988, Hoechst, already a majority shareholder of Roussel-Uclaf, asked the French firm to interrupt production, but Claude Evin, then the French minister of health and social affairs, ordered Roussel-Uclaf to continue, saying that the drug was "the moral property of women."

Currently, about a quarter of French women seeking abortion opt for mifepristone. It is also marketed in Britain and Sweden. It is produced in China, but users have to pay for it, whereas surgical abortion is free.

Roussel-Uclaf has tried to sell the drug to several American firms, but all refused. An offer was made to the World Health Organisation, which did not act on it. In 1993 the American Population Council obtained the right to use it. Now Dr Sarkiz has formed a small non-profit company, Exelgyn, to continue production and distribution of RU486 and to research its potential.

"It is a remarkable French scientific discovery, and it would have been unacceptable to bury it," said Dr Sarkiz. "We haven't been able to develop other potential therapeutic uses of this molecule. This is what I shall now do."

Professor Baulieu said: "In a way, the molecule has now been set free, and I hope Dr Sarkiz will be able to give it its chances."

Until now, it has only been used for voluntary abortion through its action on the uterine mucous membrane. There has also been limited research into its potential as an emergency contraceptive and for treating endometriosis, uterine fibroma, and breast cancer.

Professor Baulieu points out that RU486 also has antiglucocorticoid and immunosuppressive properties, which suggest possible use for treating wounds and burns.

Mifepristone acts on spermatozoa's membrane, and preliminary research by Dr Baulieu suggests that it could possibly be used as a reversible male contraceptive. □

Focus: Westminster

NHS on election back burner

John Warden,
parliamentary correspondent, BMJ

Public opinion polls in Britain consistently place the NHS high on the list of what people regard as "most important"—though so far in this general election the NHS has been conspicuous mainly by its absence as an issue. In fact, close examination would show more convergence than contrast between the parties' health policies. And while Labour is perceived by the public to have the best policies on health, the reality is that a Labour government will not radically change what is already in place.

Within sight of its 50th anniversary, the NHS is a durable survivor of Britain's postwar socialised services: state run, tax funded, and universally available—despite having been under Conservative rule for 35 of these years. Half that stewardship has been continuous since 1979 so this may be a timely moment to reflect on it, spanning the terms of seven secretaries of state—Jenkin, Fowler, Moore, Clarke, Waldegrave, Bottomley, and Dorrell.

Over that period central funding of the NHS rose by 75% in real terms and now eclipses defence spending (£43 billion against £22 billion). The number of hospital treatments has increased by four million. Infant mortality has halved; life expectancy is four years longer; one year waiting lists are down by 92%, doctors' pay up by 34% above inflation, and junior doctors' contracted hours down from an average 90 to 60 a week—figures which conceal much hard fought controversy, with resources ever balanced on a financial knife edge.

Initially, the NHS was not a target of Conservative ideology. Once or twice in the 1980s the leadership toyed with moving to private health insurance, but shied away. The stated objective was to manage a state run NHS more efficiently. Patrick Jenkin abolished the middle tier of area health authorities but it was still essentially a centrally administered service until Norman Fowler brought in a supermarket chief, Roy Griffiths, and introduced the concept of local general managers along with competitive tendering and generic prescribing.

Yet at three successive general elections, the Conservative platform was to keep the NHS much as it was. It was working well, they said. Then came the funding crisis of the "John Moore winter" of 1987, named after the luckless secretary of state, who lost his way in attempting root and branch reform. That was left to Kenneth Clarke, whose make or break reforms of 1991, built around an internal market of health purchasers and providers, brought the biggest upheaval since the inception of the NHS. Despite the blanket opposition to change, Clarke's reforms now merit the description of a new start, in the sense that this election clearly shows there is no going back.

William Waldegrave, who made the Health of the Nation strategy his main plank, and Virginia Bottomley, who pushed through the technical detail of the reforms, notably in London, spanned another general election to consolidate what was a golden era for the Department of Health, now separated from its social security twin.

When Stephen Dorrell arrived in 1995 he was able to declare that institutional change in the NHS was complete. As a result, Dorrell set out to depoliticise the managerial revolution and reduce tensions without relaxing the process of service change. For example, in contrast to the furore of the Clarke reforms, when Dorrell initiated a review of primary care he called it a "listening exercise." And although it extended the purchaser-provider split into primary care it was done by general consent, with the BMA on board.

The reforms have thus come full circle from confrontation to consent. If the NHS stays on the back burner for the remainder of the election campaign it will signal a tacit recognition of that situation. □