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NEWS. . .NEWS. . .NEWS

French scientists on strike

Senior French scientists have stopped carrying out administrative duties in a protest against cuts in funding and jobs (*Lancet* 2004, **363**, 9413:909). They say that young French scientists will move abroad unless the situation improves.

The Centre National de la Recherche Scientifique (CNRS) is still owed half its funding for 2002. The Institut National de la Santé et de la Recherche Médicale had its budget cut by 10% last year. Around 550 permanent entry-level posts have been axed, to be replaced by a handful of temporary contracts, according to the Lancet article.

Prime Minister Jean-Pierre Raffarin had offered an extra Euro 3.7 billion and said that he would unblock credits worth Euro 300 million but this was not sufficient to stave off the industrial action.

The scientists' protest was part of more generalised action against the government, with other public service workers in education and the arts also demonstrating against cuts in funding.

The strike was timed to raise awareness of the situation ahead of French regional elections in March 2004. In the event, the centre-right party was humiliated and Mr Raffarin resigned—only to be immediately reinstated by President Jacques Chirac.

Mr Raffarin has insisted that the deeply unpopular public service reforms are necessary and must continue.

European approval for fulvestrant

Fulvestrant (Faslodex) has received European marketing approval for the treatment of postmenopausal women with receptor-positive locally advanced or metastatic breast cancer, for disease relapse or progression on or after therapy with an anti-oestrogen such as tamoxifen.

Fulvestrant binds, blocks and degrades the oestrogen receptor in breast cancer cells and has no agonist effects. It is the first endocrine treatment for oestrogen receptor positive breast cancer to be approved in the EU since 1995.

Manufacturer AstraZeneca has announced the drug's launch in Germany and Sweden, with Austria to follow.

. . .and gefitinib

Gefitinib (Iressa) has been granted approval in Switzerland as third line therapy in patients with locally advanced and metastatic non-small cell lung cancer (NSCLC). It is the first country in Europe to approve the drug.

Patients in Switzerland whose disease has progressed after receiving at least two different chemotherapies were able to receive gefitinib from March 2004. It had previously been approved in 22 other countries including Japan, the USA and Canada.

Gefitinib is the first in a new class of anti-cancer drugs, the Epidermal Growth Factor Receptor tyrosine kinase inhibitors.

The approval by Swissmedic is based on data from the IDEAL 1 and IDEAL 2 trials, which were dose-randomised phase II trials. The trials demonstrated tumour shrinkage and stabilised disease in approximately 40% of patients, for whom there were no other treatment options. Approximately one third of the patients in the IDEAL studies—most of whom had a poor prognosis—were alive one year after starting treatment.

Pancreatic cancer progress

Adjuvant chemotherapy has a 'significant survival benefit' on survival from pancreatic cancer, according to the European Study Group for Pancreatic Cancer (ESPAC-1). Researchers say that, following their results, all patients who have operable cancer should be considered for chemotherapy after surgery (*NEJM* 2004, **350**, 1200–1210).

A pan-European multicentre trial included 289 patients with resected ductal adenocarcinoma. In a 2×2 factorial design, patients received chemotherapy, chemoradiotherapy, both or neither. Chemoradiotherapy had a deleterious effect, probably due to treatment-related toxic effects. By contrast, 5-year survival was 21% among patients who received chemotherapy and 8% among those who did not.

An accompanying editorial (*NEJM* 2004, **350**, 1249–1251) notes that several other studies of adjuvant therapy are in progress, including newer agents. 'In the future, decisions about adjuvant therapy will probably be influenced by improved methods for the assessment of the risk of recurrence, by the availability of more accurate surgical staging methods, and by the application of molecular diagnostic techniques.'

Lead researcher, Professor John Neoptolemos (Cancer Research UK, University of Liverpool) said, 'The common belief among doctors is that the disease is untreatable and this has become a self-fulfilling prophecy. Now we can say unequivocally that treating patients with standard chemotherapy does offer precious extra months of life.'

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Survival gap widens in UK

The gap in cancer survival between the richest and poorest patients in the UK has widened since the mid-1980s, according to a study funded by Cancer Research UK and the UK Office for National Statistics (*BJC* 2004). Researchers say that the poor have 'increasingly been left behind' in survival gains.

Researchers from the London School of Hygiene and Tropical Medicine compared outcome in patients diagnosed with cancer during three successive 5-year periods between 1986 and 1999. They were followed to the end of 2001.

Cancer survival in England and Wales has improved for most cancers, but during the same period, the gap in cancer survival between the richest and poorest patients has widened.

The study included data on 2.2 million adults, diagnosed with one of the 20 most common cancers. This is equivalent to 90% of all malignancies.

Survival improved for 15 of the 16 cancers examined among men, and for 13 of the 17 cancers among women. However, analysis of survival according to patient's deprivation status gave are more complex picture. Comparing outcome for patients diagnosed with cancer in 1986–1990 and 1996–1999, the gap in survival between rich and poor had increased for 12 of 16 cancers in men and for 9 of 17 cancers in women over that period.

Professor Michel Coleman (London School of Hygiene and Tropical Medicine) says, 'Survival from cancer in this country is improving steadily, thanks to developments in early diagnosis and in treatment. But taking a closer look it becomes clear that the poor have increasingly been left behind when it comes to cancer survival.

'The statistics indicated that improvements in survival and the deprivation gap are closely linked: as survival has increased, the deprivation gap in survival has widened. Our analyses show that cancer survival is likely to continue improving for people being diagnosed with the disease now. But while this is great news, we need to take action to ensure everyone benefits equally from advances in the detection and treatment of the disease.'

For example, there was a significant overall improvement in survival for colorectal cancer during the course of the study. But survival from rectal cancer in 1996–1999 was 9.4% higher for the richest patients than the poorest patients in men, and 8.3% higher in women. Over the three successive 5-year periods—1986–1990, 1991–1995 and 1996–1999—the gap widened by an average of 2.4% every 5 years in men and 2.5% in women. The same trend was seen in colon cancer.

The average widening of the deprivation gap every 5-years was statistically significant for cancers of the oesophagus, colon, rectum, larynx and prostate in men, and for cancers of the colon, rectum and for myeloma in women. For other individual cancers, the 5-yearly increases did not reach statistical significance, but the overall pattern provides strong evidence of a widening deprivation gap in cancer survival.

The UK Government's Cancer Plan was published in September 2000 and included equality in cancer treatment as one of its central aims. Patients in this study were diagnosed before the Plan was published but Professor Alex Markham, Chief Executive of Cancer Research UK, says the results provide a good baseline for measuring the outcome of the plan.

'The reasons behind the widening deprivation gap are unclear. But it seems that where healthcare resources are limited, the more affluent members of society have benefited more from medical advances than those from deprived groups,' he says.

HRT 'poses unacceptable risk' after breast cancer

Breast cancer survivors taking hormone replacement therapy (HRT) for menopausal symptoms experienced 'an unacceptably high risk' of recurrence, Swedish researchers said. The HABITS (HRT after breast cancer—is it safe?) study was halted early after an interim analysis. The steering committee recommended that all patients on HRT should stop treatment (*Lancet* 2004, **363**, 453–455).

The HABITS study was a randomised clinical trial due to include 1300 women, followed for a median of 5 years. Women were eligible if they had previously completed treatment for up to stage II breast cancer, were free of recurrence, had no other cancer or serious disease, no contraindication for HRT, and had menopausal symptoms deemed to need treatment.

In the event, only 219 were randomised to receive HRT, and 215 to have other treatments. At a median follow up of 2.1 years, the data monitoring committee found that women taking HRT were more than 3 times more likely to have a breast cancer event than those treated otherwise (hazard ratio: 3.3). All women with events in the HRT group were exposed to HRT, and most had the new event while under treatment. The trial was stopped.

Data from the HABITS study was being pooled with that from a similar trial in Stockholm, Sweden, because of slow recruitment. At the interim analysis, women taking HRT in the Stockholm trial were less likely than those not taking HRT to have a breast cancer event (hazard ratio: 0.82). The researchers could not explain why the findings should be so different, and suggested it could be down to chance. The pooled analysis showed a significantly increased overall hazard for breast cancer with HRT, and the Stockholm trial was also stopped.

"ALL BREAST CANCER SURVIVORS SHOULD STOP HRT"

Women in the trial will be followed up for at least 5 years after randomisation and the steering committee of the HABITS trial will continue to collaborate with other similar studies. However, an accompanying editorial (*Lancet* 2004, **363**, 410–411) said, 'The HABITS investigators' conclusion that even short-term use of hormone therapy poses an unacceptably high risk of breast cancer can now reasonably guide clinical practice for women with breast cancer.'

4th European Breast Cancer Conference *Hamburg, 16–20 March, 2004*

Hamburg statement urges support for academic research

Excessively rigid legislation, unjustifiable administrative restrictions and government budget cuts are threatening the future of breast cancer research, conference delegates agreed. Furthermore, the new European Directive on Clinical Trials could contribute to breast cancer research being left almost entirely to the pharmaceutical industry.

The Hamburg Statement was issued at the close of the conference, after computerised voting by delegates in a plenary session. Participants called for more determined financial and structural support for academic research; free circulation of tissue samples within the European Union (EU) for research purposes; greater involvement of patients in research planning and monitoring; and allocation of funds from the EU central budget to translational research.

Other issues selected for special attention over the next 2 years were: improved individual risk assessment, greater attention to elderly breast cancer patients and a rethink on care after breast cancer.

Older women 'are retaining young breasts'

Many of today's generation of postmenopausal women have breast tissue more akin to that of younger women, which is causing potential screening problems, Dutch research concludes (*EJC Supplements* 2004, **2**(3), 57 #18).

Dr A. Verbeek (UMC St Radboud, Nijmegen, the Netherlands) examined 2000 screening mammograms, randomly selected from a screening programme in the Netherlands. Breast tissue was classified as 'dense' if more than a quarter of the breast was composed of dense tissue. If less than a quarter was composed of dense tissue, it was classified as 'lucent'.

The study found that, overall, 25% of women aged between 50 and 69 years had 'dense' breasts. Almost half (44%) of those aged between 50 and 54 were classed in this way, reducing to 17% among those aged between 65 and 69 years.

The density of the breast affected the accuracy of screening. Mammography detected existing cancer in 59% of women in the dense group, compared with 67% in the lucent group.

Radiologist Dr Fred van der Horst (Breast Cancer Screening Centre, Nijmegen, the Netherlands) said that the difference in sensitivity between the 2 groups indicated the size of the potential screening problem. Use of hormone replacement therapy among the study group was low and unlikely to have played a major part in changes to breast density.

'We know that women who have given birth have more lucent breasts than childless women. It's possible that demographic changes such as women having fewer children than 30 years ago and having them at a later age may play a role,' he said.

Self-examination 'is positively harmful'

Instruction in breast self-examination (BSE) increases women's anxiety but does not reduce mortality from the disease, researchers said. A Russian study found that the numbers of cancers diagnosed, and mortality rates, were similar, whether or not women had been trained in BSE (*EJC Supplements* 2004, **2**(3), 87 #109).

The Russian group, headed by Professor Vladimir Semiglazov (NN Petrov Research Institute, St Petersburg, Russian Federation) conducted a randomised controlled trial between 1985 and 2003. More than 96,292 women were taught BSE, while a further 101,000 were controls. Physicians provided weekly breast clinics and all women were able to seek consultation either by self-referral or on the advice of their doctor.

Women in the BSE group consulted more frequently for relatively harmless conditions, but were no less likely to die of breast cancer compared with controls.

Commenting on the results, Professor Lars Holmberg (Regional Oncologic Centre, Uppsala, Sweden) said, 'BSE has been widely advocated in the belief that it is beneficial. In fact we now know that it can be positively harmful. The women in the BSE group consulted more frequently for relatively harmless conditions, thus having more surgical biopsies, not to mention increased anxiety.

'It is worrying that BSE is still being touted as an alternative to mammographic screening. It is time that this ghost was laid to rest,' he said.

Exemestane and tamoxifen go head to head

Women with advanced breast cancer given the aromatase inhibitor (AI) exemestane had longer progression-free survival than those on tamoxifen, according to a pan-European study (*EJC Supplements* 2004, **2**(3), 126 #241).

The phase III study involved 382 patients from 81 centres in 25 countries. The primary objective was to identify whether exemestane would produce an increase of 3 months progression-free survival over tamoxifen (ie an increase from 7 to 10 months).

The incidence of serious toxicity was low and exemestane was well tolerated. No adverse effects on the lipid profile were seen.

Lead researcher Dr Robert Paridaens (Universitair Ziekenhuis Gasthuisberg, Leuven, Belgium) said many questions remain, such as whether steroidal and non-steroidal AIs can safely be combined with chemotherapy, the effect of exemestane on the bones, and whether resistance to treatment can be delayed by use of other drugs such as HER pathway blockers. 'A door that has been opened shows numerous other doors to be explored,' he said.

Pioneer in Targeted Therapy wins Award

Professor John Mendelsohn, president of the University of Texas MD Anderson Cancer Center (Houston, Texas) is to receive the 27th annual Bristol-Myers Squibb Freedom to Discover Award for Distinguished Achievement in Cancer Research. He was recognised for pivotal work on receptor-targeted cancer therapies and the development of clinically active monoclonal antibodies directed towards the epidermal growth factor receptor.

Professor Mendelsohn gained his BA from Harvard in 1958, was a Fulbright Scholar at the University of Glasgow in 1959 and graduated from Harvard Medical School in 1963. He was the founding director of a new Cancer Center at University of California (San Diego) in 1977, moved to Memorial Sloan-Kettering (New York) in 1985 as Chair of the Department of Medicine and co-Chair of Molecular Pharmacology and Therapeutics. He took over as president of MD Anderson in 1996, where he is also Professor of Cancer Medicine.

For the past 3 decades, he has studied mechanisms that control the abnormal proliferation of cancer cells. Specific growth factors and their receptors on the cell membrane are key in cancer cell proliferation;

Professor John Mendelsohn

Professor Mendelsohn, with his colleague Dr Gordon Sato, developed a series of monoclonal antibodies, including monoclonal antibody 225, that specifically bind to and inhibit the epidermal growth factor receptor (EGFR). In the mid 1980s, he demonstrated that an antibody targeting EGFR could inhibit the growth of a variety of cancer cells, in culture and in nude mouse xenografts. His laboratory has continued to work on monoclonal antibody 225.

This work led to the development of a modified, chimeric human-mouse monoclonal antibody (C225) cetuximab (Erbitux), recently licensed in Switzerland and the US for the treatment of patients with EGFR-expressing, metastatic colorectal cancer who are refractory to irinotecan-based chemotherapy. Its use in other cancers is being explored.

Dr Robert Kramer (Bristol-Myers Squibb) said Professor Mendelsohn's work 'led to a fundamental shift in thinking' about controlling cancer cell proliferation, and has opened up a number of therapeutic possibilities. 'This award is given in recognition of a lifelong career that has focused on taking brilliant research conducted in the laboratory and translating those efforts in the clinic and into therapies that can advance the fight against human cancer,' he said.

Professor Mendelsohn will be officially presented with US $50,000 cash and a silver commemorative medallion at an Award Dinner in New York in October, 2004.

Formulae predict shorter follow-up for early stage breast cancer

A set of simple mathematical formulae can be used to predict how long oncologists should follow up patients with early-stage breast cancer after treatment, according to a new study (*Phys Med Biol* 2004, **49**, 10790–10783).

For T1 and T2 cancers, the new model suggests a follow-up of just 4 years—rather than the usual practice of 10 years.

Richard Mould and colleagues used parametric modelling, based on log-normal distribution, to determine the formulae. In a typical set of patients with early-stage breast cancer, Mould says about 15% have a recurrence: "The basis of this methodology is that I found a formula that will describe the survival-time distribution of early breast-cancer patients who experience a first recurrence".

"The formulae are not rocket science", says Mould. "If you are at a large oncology clinic and you have a cancer registry, then you can repeat this study, which was based on real data from the Curie Institute in Paris, France, for early breast cancer."

"This paper shows for the first time, using real patient data, the [type of] methodology necessary for a physician to decide how long to follow patients after treatment", Mould says.

A lengthy period of follow-up results in many associated healthcare costs such as physicians' time and financial overheads for the clinic. Mould says these formulae allow a trade-off: "If money is saved, then you can theorise that this can be used for [other purposes], perhaps, chemotherapy, which costs lots of money".

Mould also comments that the formulae could potentially be applied to any type of cancer that can be cured if caught in its early stages and for which a large registry of data is available.

While cautioning that use of the formulae will depend on identifying what levels of risk people are willing to take, the method is "a potentially useful tool", comments Larry Norton, Memorial Sloan-Kettering Cancer Center, New York, NY, USA. Norton, who is in charge of the centre's breast cancer programmes, says he would like to see further research into the frequency of follow-up, which is not addressed by the current study, rather than just the length of follow-up. "I would expect this to be the beginning of a long scientific conversation", he concludes.

Ivan Oransky

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PODIUM

A new era in informatics

Dr Liam O'Toole is the first Director of the UK's National Cancer Research Institute (NCRI), which was established in April 2001. NCRI is a partnership of the major sources of funding—Government, charities and industry—and provides a strategic oversight for cancer research in the UK. Dr O'Toole has worked for the British Diabetic Association (now Diabetes UK) and the Medical Research Council and his experience covers management, peer-review, science policy and strategy.

Dr Liam O'Toole

What has NCRI achieved in its first 3 years?
Firstly, we set up a database to map out where UK resources go and this allowed us to identify gaps; for example, we found we spend only 2% of our resources in prevention. We're also developing the infrastructure for cancer research in the UK. We've set up the National Cancer Research Network, which has already doubled the numbers of UK patients entering clinical trials, and we're developing a National Cancer Tissue Resource. Now we're looking at cancer informatics.

What are you going to do?
We want to create an internationally compatible informatics platform that would facilitate access to, and analysis of, data generated from research funded by all NCRI partner organisations. It will include data from all disciplines, from genomics, to clinical trials and epidemiology.

Don't scientists and clinicians already share their data?
The research community does share its data but we want to make it much easier for them to do it routinely. With the advent of high-throughput technologies, the cancer research community is generating massive amounts of data, much more than 10 years ago. As funders, we want to make sure that we are making maximum use of it. It's generally acknowledged that only about 20% of the information from a typical research project is ever used. Researchers intend to write up the rest but they move on and it is lost.

Data is also stored in many different formats, making it difficult to use and to combine. The new informatics platform will require common standards of data storage and new ways of archiving, to enable straightforward access to, and cross-referencing of, data.

How is this going to be achieved?
NCRI's 19 partners have agreed to a common vision (*Nature* 2004, **428**, 6980: xii) and we've set up a Task Force (chaired by Professor Richard Begent, Royal Free & University College Medical School, London, UK) to work towards it. We're hoping that the publication of the vision will stimulate debate and help us identify existing standards. We'll arrive at a consensus over which of the existing standards to use, and plug the gaps in areas where there are none. Progress is being mapped online at *www.cancerinformatics.org.uk* and anyone who would like to be involved should contact us (*info@cancerinformatics.org.uk*). The Task Force will report back in March 2005.

What demands will the initiative create?
Over the next couple of years, researchers applying for UK funding will be asked to include a data sharing strategy and say how they plan to make their data accessible and available to other researchers. This is already happening at the National Institutes of Health in the States. In the first instance, this will apply only to the data required to support a publication but later we hope to bring in all data generated by a research project.

What obstacles do you foresee?
There are important ethical issues such as informed consent, but we'll be dealing primarily with fully anonymised data. Where there is identifiable patient data, we'll be working within the Department of Health's requirements for security and confidentiality.

How internationally relevant is the informatics platform?
For it to be at all effective it must be fully international. We're working in partnership with the US' National Cancer Institute (NCI) and the European Bioinformatics Institute (EBI).

How will it develop in the longer term?
We'd like to work with European partners on a number of issues including informatics and rare cancers. But one of the challenges is to identify the funding bodies. It would be wonderful if we could link together all sources of funding in Europe. Scientists and clinicians are good at working together; it's time the funding bodies did the same thing.

What are the overall benefits of the informatics platform?
For researchers, it could provide selected items of information on the genetic or proteomic pathway under investigation and could indicate further analyses. For clinicians, it will be integral to the development of individualised therapy. The platform will be linked with the National Cancer Tissue Resource, so that details of a tumour sample should be sufficient to point clinicians to key findings from clinical trials. Information on how individual patients with similar tumours responded to treatment in trials will help clinicians identify the most appropriate therapies.

This project is being driven by the science and there's a lot of excitement about it. We're pushing at an open door. We have to make sure we pool resources and co-ordinate our activities to make sure we're having maximum impact for the money we're spending.