



International Cancer News

Compiled by Helen Saul, News Editor.

From the Globe

China Overtakes Europe and America in Number of Tobacco Deaths

A third of the young men in China will eventually be killed by tobacco if current smoking patterns persist, according to new research. Data presented at the 10th World Conference on Tobacco or Health in Beijing suggests that there are already three-quarters of a million deaths a year in China from smoking. This compares with half a million in Western Europe or in the U.S.A.

Professor Richard Peto from Oxford University in the U.K. presented results from the biggest ever study on smoking deaths. The study was led by Professor Liu Boqi from the Chinese Academy of Medical Sciences and included data on one million deaths in China between 1986 and 1988. Researchers interviewed family members on the smoking habits of the deceased, who came from 99 rural and urban areas across the country.

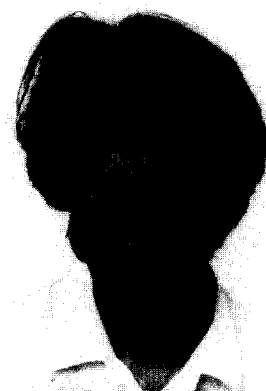
They found that tobacco kills far more people by chronic lung disease than by heart disease, which is the opposite of what happens in the West. Tobacco caused as many deaths from each of liver cancer, stomach cancer and oesophagus cancer as it did from heart disease. There was wide variation from one city to another in lung cancer mortality rates among non-smokers. In Xi'an, the old imperial capital, the non-smoker rates were as low as in Europe, while in North East China they were ten times higher. But the differential between smokers and non-smokers remained intact across the country with smokers three times as likely to develop lung cancer as non-smokers. Smoking carried particularly big lung cancer risks where the disease is already common among non-smokers.

Professor Peto said it had previously been assumed that smokers in developing

countries would be less likely to die as a result of their habit than smokers in the West, but this study quashed that hope. "This is the first nationwide evidence on smoking in the developing world. We thought that maybe a quarter or a third of smokers in developing countries would be eventually killed by tobacco. This evidence suggests that about half of them will be, which is the same 50% risk as in Britain or the U.S.A."

Findings from this study were largely confirmed by work from Professor Niu Shiru from the Chinese Academy of Preventive Medicine. He outlined results from the Chinese Prospective Study of Mortality which enrolled 250,000 men aged more than 40 in 1990 and 1991. Deaths were monitored up to 1995. Approximately three-quarters of the men were current smokers and their risks of lung cancer, respiratory disease and all-cause mortality were significantly higher than for non-smokers. Chronic obstructive pulmonary disease was, again, the main cause of tobacco-related death in this study.

Dr Yang Gonghuan, also from the Chinese Academy of Preventive Medicine, presented results from the 1996 National Survey of Smoking Prevalence in 120,000 people which showed that the average age at which men start smoking is 20, three years lower than was found in a survey conducted in 1984. A rare hopeful finding in her work was that young women are unlikely to start smoking. By age 25, only 1% are using tobacco. However, Dr Yang warned that this situation could easily be reversed. Knowledge about the health risks of smoking was sketchy and few of the people interviewed in Dr Yang's study even knew that smoking could cause lung cancer.



Professor Richard Peto

Professor Peto said that although there is now Chinese data on the dangers of continuing to smoke, we still have to use Western data on the effects of quitting. 'We can't do the studies locally because, so far, very few people have given up smoking in China,' he said.

'Tobacco already causes about 3.5 million deaths a year worldwide but the total is rising and it will kill about 100 million people over the next 20 years unless large numbers of people do give up the habit. Nearly all these deaths will be of people who are already adult smokers. So, just preventing children from starting to smoke would have almost no effect on the tobacco deaths of the next 20 years in China, Europe or anywhere else,' said Professor Peto.

10th World Conference on Tobacco or Health, Beijing, 24-28 August, 1997. 'Tobacco: The Growing Epidemic'

Resolutions of the 10th World Conference on Tobacco or Health

- The public health community should make strenuous efforts to help people stop using tobacco products
- Governments should provide meaningful support for the efforts of the World Health Organization to develop an International Framework Convention for Tobacco Control. Technical and financial resources at international and regional levels are needed
- The tobacco industry should pay the costs of the damage caused by tobacco. However, Governments should consider the international implications of tobacco control policies and settlements
- Governments should subject the contents of tobacco products and smoke, and all aspects of the tobacco business to strict and legally binding regulatory control
- All relevant bodies should increase the participation of women and representatives of developing and transition countries in the strategic planning and policy development, implementation and evaluation of tobacco control measures
- A worldwide monitoring system of the tobacco epidemic should be established. Research programmes should be set up to carry out a full economic analysis of

Menstrual Cycle Phase May Reduce Mammogram's Accuracy

Women who are screened for breast cancer in the last 2 weeks of their menstrual cycle have twice the usual risk of a false negative result, according to a Canadian study. Researchers from the Faculty of Medicine at the University of Toronto found that this effect was especially important in women who had ever used hormones.

Data was collected prospectively from the Canadian National Breast Screening Study. Women who were still menstruating and were aged between 40 and 44 years were eligible to be included in the study. The women were followed over five screen examinations conducted annually.

The study included 8,887 women, most of whom had used or were currently using hormones in the form of the oral contraceptive or replacement therapy. They compared mammogram results of women in the follicular phase of their menstrual cycle with those in the luteal phase.

tobacco growing, production and use, taking into account costs of damage to the environment, harm to workers, damage to smokers and passive smokers and all other tobacco-induced costs that fall on society

- All non-governmental organizations

Women who had ever used hormones were twice as likely to have a false negative result if they were screened in the luteal rather than the follicular phase.

The authors state that mammography is known to be less accurate in younger women but that many women in the 40s have a mammography without an accompanying clinical breast examination. They say that without the examination false negative mammograms may be missed.

They suggest that the accuracy of mammograms could be improved by arranging to carry them out during the first half of the menstrual cycle.

CJ Baines *et al.* 'Impact of menstrual phase on false negative mammograms in the Canadian National Breast Screening Study', *Cancer* 1997, Aug 15.

involved should support the International Non-Governmental Coalition Against Tobacco. International networking should be established in all sectors involved with tobacco control

Managed Care Hits Publication Rates at American Medical Schools

The introduction of managed care into American medical schools is having a dramatic effect on funding for research, according to a study by researchers in Washington D.C. They found that the higher the managed care penetration in an area, the slower the growth in medical schools' research awards from the National Institutes of Health (NIH).

Ernest Moy and colleagues at the Association of American Medical Colleges found that of the 115 medical schools which received NIH funding from 1986 to 1995, only 11% were in high managed care markets. By contrast, 40% were in low managed care markets. Moy said that policy makers should examine the reasons behind the trend. 'Additional research is needed to examine whether medical schools in high managed care markets are committing fewer resources to research, recruiting fewer clinical research faculty, increasing

clinical demands on existing faculty or losing faculty to other institutions.'

A second study backed Moy's findings. A team led by Eric Campbell from Massachusetts General Hospital in Boston looked at the life-science departments in the 50 universities that received most NIH funding in 1993. They found that among more than 2,000 clinical researchers, those in the least competitive markets published an average of 14.5 articles in peer-review journals over 3 year period. Researchers in the most competitive markets published 12. Young faculty members in the least competitive markets also had fewer patient care duties than those in the most competitive.

Campbell said that failing to protect clinical research from the effect of the market may lengthen the time it takes to put basic research into practice and may also turn young graduates away from

clinical research careers. He suggested that deans and department chairs might want to increase the sense of community and cooperation in the faculty.

- The provision of adequate funding for clinical research is also a problem in Europe. The first European Conference on the Economics of Cancer will take place on 19-21 November 1997 in Brussels, Belgium. Information from Mrs Van Der Hayden, EORTC Central Office, Ave E Mounier 83/11, B-1200 Brussels, Belgium. Fax: +32 2 772 67 01

On line registration is also available through internet: e-mail: mvh@eortc.be

Moy *et al.* *Journal of the American Medical Association* 1997, **278**, 217-221. Campbell *et al.* *Journal of the American Medical Association* 1997 **278**, 222-226.

Cochrane Recovers Missing Cancer Studies

At the end of January last year, some retired professional people in Oxford and other parts of the South East of England began an unenviable task. They started searching cancer journals painstakingly and systematically, paper by paper, for randomised controlled trials. These people are volunteers, members of the University of the Third Age in the UK and they are one of many groups working for the Cochrane Cancer Network to plug gaps in databases such as Medline and EM-base.

Mark Lodge, trial register co-ordinator, estimates that these databases may include as few as two-thirds of the randomised controlled trials published in mainstream, prestigious journals. The volunteers aim to find the neglected papers so that they can be included in the Cochrane library and gain the recognition they deserve.

Papers may be missed because they are ambiguous or badly written and do not include the phrase 'randomised controlled trial' in either title or abstract. Indexing errors may lead to the omission of a clearly-worded paper, or even the exclusion of an entire volume of a journal. These errors bias the information on which clinicians ultimately make decisions on patients' treatment.

The randomised controlled trial and systematic reviews of these trials are at the heart of modern research. But according to Chris Williams, co-ordinator of the Cochrane Cancer Network, reviewers are notoriously unscientific in the way they

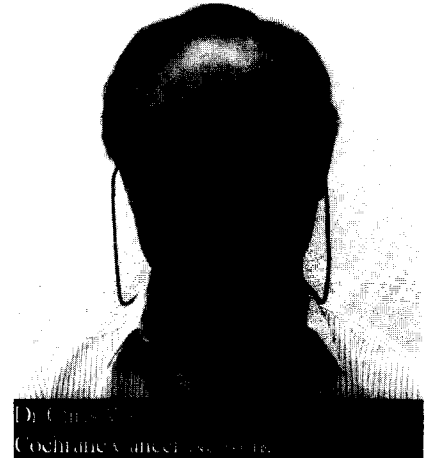
select trials for inclusion in the review. Less than one in ten gives any indication of why trials were included or excluded and the average Medline search picks up only half of the studies included on it.

Dr Williams says databases in turn are loaded with hidden biases: 'If someone is bilingual, they are more likely to publish positive findings in English in prestigious international journals. They will publish negative findings in their own language. When someone is searching a database, the easier it is to find a study, the more likely it is to be positive.'

For the future, the Cochrane Cancer Network aims to raise the standard of reporting and recently launched CONSORT (Consolidation Standards of Reporting Trials), a system designed to ensure that all essential information is contained within reports. *European Journal of Cancer* intends to adopt CONSORT and a statement will be published early next year.

Cochrane is also running a programme of electronic database searching which devises optimal search strategies for specific groups to help them recover as high a proportion of the reports in the database as possible. The programme helps unify the information from multiple databases which are each based on a different selection of journals.

Dr Williams believes that systematic reviews hold an increasingly important role in medicine and says clinicians should know



what has already been done before starting a new study. Reviews often give no clear answer because most cancer therapies produce only a modest benefit. But they may identify important therapeutic questions that need to be addressed by a new large clinical trial. 'People have got to learn how to use the literature to find out whether there is still a question to be asked,' he says.

For information on how to take part in the work of the Cochrane Cancer Network, contact Chris Williams, Institute of Health Sciences, PO Box 777, Headington, Oxford OX3 7LF, UK.

e-mail: cwilliams@cochrane.co.uk

Westernisation of Singaporean Chinese Women may be Behind Rise of Breast Cancer

More food and fewer births among women in Singapore may partly explain the rise in breast cancer, according to the results of a new survey. A prospective case-controlled study involving 1086 women found that an increase in central obesity as indicated by a larger waist to hip ratio increased risk for breast cancer. Height was also important and women taller than 159 cm had approximately twice the risk of women shorter than 150cm.

The report noted that the incidence

of breast cancer in Singapore has nearly doubled over the past 25 years. The authors said that increased calorie intake and declining fertility may have contributed to this increase. However, these findings should be restricted to postmenopausal and older premenopausal women because only those aged between 45 and 69 were included in the study.

The study concluded that the same mechanisms behind the rise in breast cancer among Western women may be responsible

for the increased incidence in Singapore. The authors warn that since similar changes in lifestyle and reproductive patterns are becoming common in other Asian countries with rapidly growing economies, breast cancer is likely to become a growing problem in Asia.

Eng-Hen Ng *et al.* Risk factors for breast carcinoma in Singaporean Chinese Women: The role of Central Obesity, *Cancer* 1997, 15 August.

From Europe:

MAGE-3 Tumour Vaccine Trial to Start

The first clinical trial of a tumour vaccine based on the whole MAGE-3 protein is due to start in October 1997. Patients with advanced melanoma will make up two thirds of the study group, but those with head and neck, oesophageal, bladder and lung cancer, especially non-small cell lung cancer, will also be eligible for entry. The trial is being conducted under the auspices of the EORTC and the Ludwig Institute for Cancer Research in partnership with SmithKline Beecham Biotherapeutics which provided the vaccine and adjuvant.

MAGE-3 is a gene which encodes for 3 peptides, derived from the MAGE-3 protein. These peptides, in combination with relevant HLA class I molecules, are recognised by cytolytic T lymphocytes (CTL) on some human cancers. Previous trials have entailed vaccinating patients with the peptides, but this study will use the whole protein for the first time. Results from earlier work suggest that vaccinating patients with MAGE-derived peptides can, in some cases, reduce the size of melanoma. Sample sizes of patients with other cancers have so far been too small to determine its effect.

The trial will include 39 patients, at least 24 of whom will have melanoma. In order to be eligible to join, patients will have to express one or more of the relevant HLA molecules and their tumour must express the MAGE-3 gene. This should be true of almost half the melanoma patients but fewer of those with other cancers.

Professor Gerrit Stoter from the Rotterdam Cancer Institute and Dr Marie Marchand from the Ludwig Institute for Cancer Research in Brussels are co-chairing the trial. The idea behind the vaccine is that it stimulates the immune system to destroy all the tumour's locations. Professor Stoter said that the MAGE-3 vaccine will be given in combination with an adjuvant, a substance which stimulates a non-specific immune response and which in turn promotes a more vigorous reaction from the specific CTL. Once activated, the CTL will find micrometastases not only at the injection site but even in remote locations of the body.

He said there were good reasons why this vaccine may be more effective than one based on peptides. 'A possible advantage of using the whole protein over peptides is that

the protein may contain other useful molecules which are recognised by CTL. We know about MAGE-3 peptides, but there is a very good chance that the whole protein may contain many more molecules which are also recognised by the immune system as non-self. This would reinforce the immune response.'

So far, the work with MAGE peptides has been remarkable in its lack of short-term toxicity. The antigens are not made in normal tissue and vaccination with these peptides does not destroy normal cells. Dr Marchand: 'In our experience with the peptides we have used so far, we have not observed any toxic effects associated with the vaccine, even in patients who have had partial or complete regression of their tumour. Now we have to see whether this is confirmed for the protein.'

Phase I/early II study of immunisation with a MAGE-3 protein based vaccine plus immunological adjuvant SB AS-2 in HLA class I selected patients with MAGE-3 positive tumours.

From the Countries:

ITALY

Sentinel Node Biopsy may Spare Breast Cancer Patients Axillary Dissection

Axillary dissection is probably unnecessary in patients with breast cancer who have a clear sentinel node, according to researchers at the European Institute of Oncology. A team led by Professor Umberto Veronesi found that a clear sentinel node reliably predicts a disease-free axilla. They concluded that women with a negative sentinel node biopsy could be spared axillary dissection.

The study included 163 women with operable breast cancer. Researchers used lymphoscintigraphy and gamma-probe guided surgery to locate the sentinel node. In almost half the women, the node was

negative and within this group, 95% of the women had no axillary node involvement. If patients with multifocal tumours and those with tumours more than 1.5cm were excluded, the status of the sentinel node was 100% accurate in predicting axillary node involvement.

The authors acknowledged that lymphoscintigraphy is slightly more expensive than the alternative technique of injecting blue dye just before surgery. However, it indicates exactly where the skin incision should be made and guides the dissection. By contrast, surgeons using blue dye have to dissect blindly until



PROFESSOR VERONESI

the blue node is located, which can be some distance from the incision. Savings from the reduction in elective axillary dissections would in any case render the difference in cost between the two procedures negligible.

The researchers wrote that further studies with longer follow-up were needed

to confirm these results. However they said that in patients with small carcinomas the procedure could be applied immediately in place of axillary dissection. They concluded: 'We believe that sentinel-node biopsy is an important step forward in the search for more conservative treatments for

patients with breast cancer.'

U Veronesi *et al.* Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes, *The Lancet* 1997, 349, 28 June, 864-1867.

U.K.

Call for Researchers to Find Infections Linked with Cancer

Oxford scientists have called for a co-ordinated effort to hunt down infections and their links with disease. They say that new, improved study methods are allowing researchers to find previously unrecognised infections and to study their possible links with various diseases.

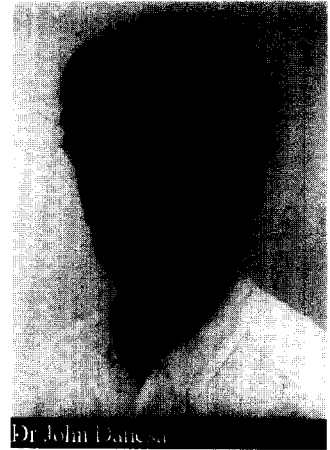
The researchers, from the Imperial Cancer Research Fund in Oxford, say that persistent infections cause about 15% of cancers worldwide. Research fellow Dr John Danesh said, 'This makes them second only to tobacco as the leading known cancer killers.'

Several of the common cancers linked with infection are most prevalent in developing countries. In China, hepatitis B infection is endemic and liver cancer is 100 times more common among those infected by the virus. Other infection-linked cancers occur frequently in the West and, for example, some types of the human papillomavirus are 30 times more common in women with cervical cancer. The

Epstein-Barr virus was seen in cells from Burkitt's lymphoma in 1964; more recently a variation of the polymerase chain reaction was used to identify human herpesvirus-8 in the lesions of patients with Kaposi's sarcoma.

Dr Danesh claims that drugs and vaccines are being developed which may prevent or cure the consequences of many persistent infections. This makes the discovery of infectious causes of serious diseases especially welcome. Trials of anti-infective agents have led to the use of antibiotics in some cases of B-cell gastric lymphomas. Vaccines and antibiotics are now being tested for prevention of cancers of the liver, stomach and cervix.

He calls for a joint effort including microbiologists, virologists, molecular biologists, clinicians and epidemiologists. 'Scientists interested in infections could learn from the successful collaboration of our genetics colleagues. A co-ordinated effort might help to hunt for unrecognised



Dr John Danesh

infections and for new links of infections with various diseases — perhaps a 'human germ project'.

A human germ project? *Nature* 4 September 1997.

Following an error made in the August Issue of the *European Journal of Cancer* (Volume 33 Issue 9) the photographs of Professor Robin Weiss and Professor Larry Norton were published with the wrong captions attached. The publisher apologises for this error and the corrected News stories appear below.

APPOINTMENTS

Royal Society Elects Cancer Fellows

Three cancer researchers were among the new fellows elected to the Royal Society this year. The Royal Society is the U.K. academy of science and election to the Fellowship is a sign of the highest regard in science.

The new fellows are Alan Rickinson, Professor and Head of Cancer Studies at the University of Birmingham; Robin Weiss, Professor of Viral Oncology at London's Institute of Cancer Research and Richard Wood, principal scientist at

ICRF. 'It's a wonderful honour,' said Dr Wood. 'Now we just have to keep doing good science to measure up to it.'

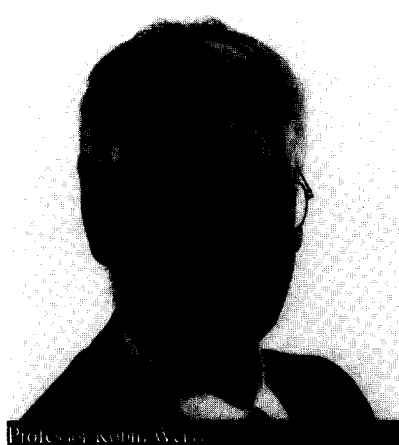
Professor Rickinson is renowned for his work on the Epstein-Barr virus and its relationship to certain human cancers. His findings have shed important light on the different mechanisms by which EBV can contribute to malignant change.

Professor Weiss' work on the virus genome paved the way for later research on oncogenes. More recently, his

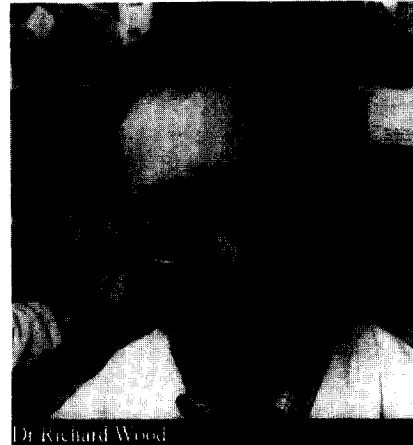
group has studied the human immunodeficiency virus and was the first to demonstrate neutralising antibodies against HIV. Dr Richard Wood is distinguished for his work on DNA repair and mutagenesis. He elicited the DNA sequence changes caused by ultraviolet light and found a way of achieving nucleotide excision repair (NER) of DNA with human proteins. Recently he has reconstituted the NER process using purified proteins.



Professor Alan Rickinson



Professor Robin Weiss



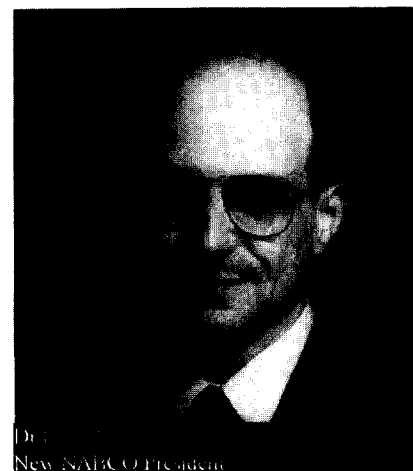
Dr Richard Wood

New President for NABCO

Dr Larry Norton has been elected president of the board of directors at the National Alliance of Breast Cancer Organisations, New York. He succeeds Valerie Salembier, who was president in both 1995 and 1996.

Dr Norton has worked in prevention, detection and treatment of breast cancer for the past 10 years. He is

chief of the Breast Cancer Medicine Service at the Memorial Sloan-Kettering Cancer Center and director of Medical Breast Oncology at Memorial's Evelyn H Lauder Breast Center. He has been a member of NABCO's board of directors since 1994 and he is also an Associate Editor of the *European Journal of Cancer*.



Dr Larry Norton
New NABCO President