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NEWS...NEWS...NEWS

Tobacco Industry's dirty tricks continue

The tobacco industry is still striving to challenge the science linking smoking to adverse health effects, say US researchers. Despite its claims to be working with the public health community, ''the industry has not changed its practice'', they say (*Lancet 2005, online http://image.thelancet.com/extras/03art3495web.pdf.*)

The researchers, from University of California, San Francisco, USA, call on authors, editors, and users of scientific literature ''to be vigilant in demanding and maintaining rigorous standards for disclosing and evaluating potential conflicts of interest''.

They examined the tobacco industry's response to research published in 1996, which demonstrated that benzo[a]pyrene, a carcinogen present in tobacco smoke produced patterned in-vitro mutagenic effects on the tumour suppressor gene *p53* (*Denissenko et al., Science* 1996, **274**, 430–32). The authors concluded that the study ''provides a direct link between a defined cigarette smoke carcinogen and human cancer mutations''.

Documents made public as a result of litigation in the States revealed that executives and scientists at the highest levels of the tobacco industry anticipated and carefully monitored *p53* research, according to the *Lancet* article. Tobacco companies supported scientific studies which appeared to cast doubt on the link between *p53* damage and BDPE, a metabolite of benzo[a]pyrene. Authors of the research did not clearly disclose their links with the tobacco industry. It was published in a peer-reviewed journal whose editor had longstanding, undisclosed ties to the tobacco industry.

Later research from International Agency for Research on Cancer (IARC) used human lung tumours and confirmed Denissenko's findings (*Environ Health Perspect* 1998, **106**, 385–91). It was subject to similar challenges from the industry.

''Tobacco industry responses to research linking smoking to carcinogenic *p53* mutations mirror prior industry efforts to challenge the science linking smoking and lung cancer'', say the authors of the *Lancet* report.

''THE INDUSTRY MUST DEMONSTRATE TRUE SOCIAL RESPONSIBILITY''

The Uniform Requirements issued by the International Committee of Medical Journal Editors (ICMJE) specify that authors of all submitted manuscripts ''are responsible for recognising and disclosing financial and other conflicts of interest that might bias their work''. Editors who make final decisions about manuscripts ''should have no personal financial involvement in any of the issues they might judge''. However, the Requirements are guidelines and journals are not obliged to comply with them.

Tobacco companies now claim to be working with the public health community ''to support a single, consistent public health message on the role played by cigarette smoking in the development of disease in smokers''. The authors of the *Lancet* report conclude, ''Their multifaceted response to p53 research as recently as 2001, suggests that the industry has not changed its practice''.

Commenting on the report, Dr. Peter Boyle, director of IARC, said, ''The use of consultants, to publish purchased critiques of scientific research appears to remain one of the key strategic approaches of the tobacco industry''.

''Their strategy of infiltrating the scientific community to undermine the normal process of peer review and publication is distressing for the scientists whose work is targeted. It is also damaging for outstanding journals and academic institutions whose record with respect to tobacco research might appear to be blurred by the actions of a few individuals who maintained undisclosed tobacco industry ties.

''This industry needs to demonstrate true corporate social responsibility. Until then, the public health community can have no confidence in the actions of the tobacco industry, and academic institutions should refuse any involvement with them, no matter how loudly the industry claims that they will not interfere in the research''.

Bevacizumab approved in Europe

Roche has announced that its anti-angiogenesis agent, bevacizumab (Avastin) has been approved in the EU for use in patients with previously untreated metastatic colorectal cancer. The company says the drug will be accessible to physicians early this year.

The drug is now approved for the first-line treatment of patients with metastatic carcinoma of the colon or rectum in combination with intravenous 5-fluorouracil/folinic acid or intravenous 5-fluorouracil/folinic acid/irinotecan.

The European Commission's approval was based on a Phase III study (*New Eng Jnl Med* 2004, **350**(23), 2335–342) which found that the addition of bevacizumab to chemotherapy increased survival and time to disease progression.

Roche and Genentech are exploring the use of the drug in the adjuvant setting and in other cancers, including non-small cell lung cancer, pancreatic cancer, breast cancer and renal cell carcinoma.

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Surgery 'may kick-start the growth of metastases'

A radical new model to explain the natural history of breast cancer suggests that the act of surgery could accelerate the clinical appearance of metastatic disease. The model, explained at length in this issue of *EJC*, (2005, **41**, 508–515) is proposed by a group led by Professor Michael Baum (Portland Hospital, London, UK).

Development of the model was prompted by the observation that the rate of relapse following surgery is non-linear, and peaks sharply 18 months after treatment. ''Some signal, perhaps the act of surgery or other adverse life-event stimulates [micrometastases] into fast growth'', they write.

The authors suggest that micrometastases may lie dormant while factors inhibiting angiogenesis dominate locally. If stimulating factors are increased or inhibiting factors reduced, the dormant condition will not be maintained. The first peak in the hazard for relapse is too sharp to be the result of steady transitions from single cells to avascular micrometastases. ''Some breaking of dormancy had to occur at surgery to explain the first peak'', they write.

Anti-angiogenic therapies, given pre-operatively, could be a therapeutic consequence of the model, so that at the time of surgery the system is primed to protect against sudden flooding with angiogenic signals. ''Indeed, some of the success attributed to adjuvant tamoxifen or chemotherapy might be a result of their anti-angiogenic potential rather than cytostatic/cytocidal effects'', the authors suggest.

''ANTI-ANGIOGENIC DRUGS COULD BE GIVEN PRE-OPERATIVELY''

In an accompanying editorial, Professor Samuel Hellman (University of Chicago, USA), says that the paper ''serves well to make us reconsider accepted paradigms''. The suggestion that the increased hazard of relapse 2 years after surgery could be due to the release from inhibitors produced by the primary, or because of some stimulation, is ''an interesting notion. This needs much more study'', he writes.

Randomised trials and meta-analyses of adjuvant breast cancer treatment could inform and enrich this observation, Professor Hellman said: ''These should be used to verify the observation and, if it is confirmed, to shed light on its cause with particular attention to the hypothesis that it is surgery that is the cause of the transient increase in the recurrences seen''.

Value of 'Excellence' Designation

Cancer surgery performed at a medical centre designated by the US' National Cancer Institute (NCI) as a ''Center of Excellence'' is associated with less perioperative mortality than if performed at a high-volume surgical centre. However, 5 year survival rates were similar.

Researchers from University of Michigan Medical School reviewed data on 63,860 patients undergoing cancer surgery. Results from the 51 NCI cancer centres were compared to those from 51 control cancer centres with the highest volumes for each procedure (*CANCER 2005 102*).

Perioperative mortality was significantly lower at the NCI centres for 4 of 6 procedures: colectomy; pulmonary resection; gastrectomy; and oesophagectomy. No significant difference in mortality was observed for cystectomy or pancreatic resection. Among the patients who survived surgery, there was no significant difference in 5 year survival.

In 1971, the NCI started awarding ''Center of Excellence'' status where excellence in research, cancer prevention and clinical services could be demonstrated. The NCI centres are well staffed with specialists, tend to have high procedure volumes and better access to multidisciplinary consultation and the latest therapies. However, the study's authors say that their relative performance has not been examined to date.

Lead author, Dr. Nancy J O Birkmeyer, concluded: ''Our study suggests that NCI cancer center designation should be weighted less heavily than other factors in deciding where to undergo major cancer surgery''. Patients who do not live near an NCI cancer centre will be able to find a high-volume surgeon with subspecialty training at a high volume cancer centres close to home.

Childhood cancers and prenatal pollution

Most childhood cancers and leukaemias are ''probably initiated'' by prenatal exposure to airborne pollutants, according to a UK professor (*J Epidemiol Community Health* 2005, **59**, 101–05). He suggests a redirection of research efforts relating to childhood cancer.

The study was based on maps of emissions of various chemicals, published by the UK's National Atmospheric Emissions Inventory. Hotspots were identified for 1,3-butadiene, carbon monoxide, PM10, dioxins, benzpyrene, benzene, NMVOC (non-methane volatile organic compounds) and nitrogen oxides.

All children who died before their 16th birthday in the UK between 1966 and 1980 were included in the study. Their home addresses at birth and at death were translated to map references. The analysis focussed on children who had moved more than 1.0 km between birth and death, and who had moved into, or out of, an emissions hotspot. An excess of those who had moved away from a hotspot, versus those who had moved towards one, would suggest an increased risk of cancer prenatally or in early infancy.

''1,3-BUTADIENE AND CARBON MONOXIDE CARRIED THE HIGHEST RISK''

The study found that children born within 1.0 km radium of emissions hotspots were between 2 and 4 times as likely to die of cancer before reaching the age of 16, compared with other children. Proximity to emissions of 1,3-butadiene and carbon monoxide carried the highest risk.

Professor George Knox, Emeritus Professor (University of Birmingham, UK) conducted the study, and said, ''Most childhood cancers are probably initiated by close prenatal encounters with one or more of these high emissions sources. The low atmospheric levels of these substances suggests that the mother may breathe them in, with carcinogens passing across the placenta. But he adds, ''Effective direct exposures in early infancy, through breast milk or even pre-conceptually, cannot be excluded''.

''The main policy implications are a need to regulate carcinogenic atmospheric emissions, especially 1,3-butadiene; and for a redirection of research efforts relating to childhood cancer. This research should now try to determine the exact timings of chemically-determined air-mediated cancer initiations … and to seek engineering and social solutions''.

World Hospice and Palliative Care Day

The first World Hospice and Palliative Care Day will take place on Saturday October 8th, 2005. The event is backed by Archbishop Desmond Tutu, who urged people to get involved, saying, ''This day is an important global event''.

Mick Thorpe, Chairman of Help the Hospices' UK Forum for Hospice and Palliative Care Worldwide, spoke on behalf of the group. ''Every year, millions of people around the world living with a terminal illness suffer unnecessary pain and distress, either unaware of or unable to access the care they need. Good quality hospice and palliative care which aims to meet the needs of the whole person can and does provide an answer'', he said.

An integral part of the day will be Voices for Hospices: a singing event which in 2003 involved 500 performances in 24 h world-wide. It has raised more than £4.5 million since it stated in 1991 and provides a simple way for people to raise both funds and awareness for local services.

The Day is intended to raise awareness on key issues:

Meru Hospice, Kenya.

- The need for all countries to include palliative care in their national health care programmes.
- The urgent need for greater and more secure funding to support hospice and palliative care services world-wide.
- The need for essential low cost opioid analgesics for pain and symptom control, particularly in resource-poor countries.
- The need to extend and develop the lessons learned in hospice and palliative care into wider disease groups.
- To improve availability of palliative care for people in resource-poor countries – particularly in rural areas. Also to reach marginalised groups throughout the world such as prisoners, the homeless and those with special needs such as learning difficulties.
- The need to integrate hospice and palliative care into all health care professionals' education programmes.
- That palliative care should not be a last resort but should be provided concurrently with disease treatment.

For more information, see www.worldday.org.uk and www.voicesforhospices.org.uk or email worldday@helpthehospices.org.uk

Androgen deprivation 'increases risk of fracture'

Androgen-deprivation therapy (ADT) for prostate cancer increases the risk of fracture, say US researchers (*N Eng J Med* 2005, **352**, 154–64). Their finding ''underscores the need for caution in the use of these therapies in settings without clear evidence of a benefit'', they say.

The researchers, from University of Texas Medical Branch (USA) studied the records of 50,613 men listed in the linked database of the Surveillance, Epidemiology, and End Results program and Medicare. They were diagnosed with prostate cancer between 1992 and 1997.

Of those who survived at least 5 years after diagnosis, 19.4% of those who received ADT had a fracture, compared with 12.6% of those who did not receive this treatment. After adjustment for characteristics of patient and tumour, there was a statistically significant relation between the number of doses of gonadotropin-releasing hormone received during the 12 months after diagnosis and the subsequent risk of fracture.

The hazard ratios may have been moderate but could be clinically important, the researchers say, ''given the substantial underlying rate of fracture among the elderly men in the study''. Use of ADT increased dramatically during the 1990s and their findings stress that such treatment ''is not benign''.

Most patients receiving this therapy have localised prostate cancer, and it is commonly given to those with a rising PSA level after radical prostatectomy. ''Yet there is no evidence from clinical trials of a survival benefit for ADT in either of these settings.

''Trials of therapies such as bisphosphonates to lower the risk of fracture are needed in patients for whom gonadotropin-releasing hormone agonists are clearly indicated'', they conclude.

Another study (*CANCER* 2005, **102**) found that few men receiving hormonal therapies for prostate cancer are tested for osteoporosis. Even those with other risk factors, such as advanced age, low body mass index, smoking or prolonged hormone treatment were unlikely to receive osteoporosis prevention or treatment.

Dr. Tawee Tanvetyanon (Loyola University Chicago, Illinois, USA) reviewed retrospective data on 184 patients who had received ADT with goserelin injection for a year or more. Most were elderly with multiple risk factors for osteoporosis.

Overall, less than 15% patients received any intervention. Dual-energy X-ray absorptiometry (DXA) scans had been performed on 8.7% at least once in the past three years; and bisphosphonates prescribed for 5% patients. The only factor that predicted clinical management of osteoporosis was the presence of bony metastases. Primary care physicians provided the greatest number of interventions; cancer-related specialists the least.

The report suggests that a lack of established guidelines for osteoporosis prevention among men undergoing ADT may be partially to blame. ''A great opportunity to improve osteoporosis prevention among men receiving ADT exists. Their frequent visits, especially nursing visits for goserelin injection…. can be used for future interventions'', Dr. Tanvetyanon concluded.

Bank on it: Umbilical-cord blood for transplantation

Two studies from Europe and the USA (*N Engl J Med* 2004, **351,** 2265–75 and 2276–85) support the use of stem cells from umbilical-cord blood as an alternative to bone marrow for transplantation in adults with leukaemia. Both studies conclude that cord blood is a reasonable graft source for adults who cannot find an HLA match in a bone-marrow registry or who need transplantation sooner than the 3–4 months needed to obtain unrelated adult-donor bone marrow.

Because sibling-matched bone marrow is available for only a third of patients with leukaemia, the findings ''open a door for the remaining patients who don't have any other chance for a cure'', says Miguel Sanz (Hospital Universitario La Fe, Valencia, Spain), author of an accompanying editorial (*N Engl J Med* 2004, **351,** 2228–30).

Cord-blood transplantations are done routinely in children, but the low number of stem cells per unit of cord blood has hindered use in adults. However, the advantages of cord blood over unrelated donor marrow – cells can be obtained within weeks from a bank and partial HLA mismatches are tolerated – has increased the number of adults who receive cord blood, usually as treatment for advanced leukaemia.

The studies compare cord blood with standard therapy of HLA-matched unrelated donor bone marrow in adults. Analysis of 1034 bone-marrow and 248 cord-blood procedures registered in Europe or the USA showed that cordblood recipients were younger, weighed less, and had more advanced disease than did bone-marrow recipients. Cordblood recipients received about ten times fewer nucleated cells per graft, had a delay in neutrophil recovery, and had lower engraftment rates than did recipients of HLA-matched bone marrow.

However, transplant-related deaths, relapse rate, and leukaemia-free survival were the same between the two groups in the European study. ''Cord blood is feasible in adults with acute leukaemia, and the results we get are quite similar to HLA-matched bone marrow from an unrelated donor'', says lead author Vanderson Rocha (Hospital Saint-Louis, Paris, France).

By contrast, the US group reported worse outcomes for patients who received cord blood compared with recipients of HLA-matched bone marrow for acute and chronic leukaemia. However, cord blood led to similar results as those seen with use of mismatched bone marrow (the alternative when fully matched bone marrow is not available). ''If one can't identify and mobilise a matched adult donor in time, physicians can proceed to the use of cord blood with confidence'', says lead author Mary Laughlin (Case Comprehensive Cancer Centre, OH, USA).

Although several differences in the studies could account for the disparate results, cord-blood outcomes have improved over the past 10 years. The first cord-blood transplantation in an adult was done in 1994, and the US study includes transplantations done since 1996. The European study looked only at cases after 1998, when cordblood transplantation techniques improved. A smaller comparison of cord blood with bone marrow also reported favourable results with cord blood (*Blood* 2004, **104**, 3813–20).

Poorer outcomes in the US study might be the result of the higher number of patients who received cord blood with two HLA mismatches compared with the European group. Although patients receiving cord blood can tolerate the immune consequences of two of six mismatched histocompatibility antigens, they are less likely to have effective engraftment.

Improvement of engraftment by increasing cell dose while optimising the HLA match is key to use of cord blood in adults. Rocha says that cordblood banks now store larger units with more stem cells. ''In the French cord blood bank, 50% of the units are now available for adults, [whereas] a few years ago only 10–20% had sufficient cell numbers'', he says. Trials on the transplantation of several pooled units of blood are under way, and several labs are investigating ex-vivo expansion of cord-blood stem cells. Direct injection of stem cells into bone marrow, or use of chemokines to increase homing to marrow, could also improve the effectiveness of transplantation.

Increasing the probability of finding an HLA match means boosting the numbers of stored cord-blood units. In the USA, increasing inventories from the current 45 000–55 000 units to 150 000 units would ensure a match of five of six HLA antigens. The US congress has promised US$50 million dollars over 5 years to promote cordblood banking. Europe has an established public banking system, but limited funds prevent expansion.

''It is extremely important to increase the number of cord-blood units available'', says Eliane Gluckman (Hospital Saint-Louis, Paris, France), a senior scientist in the European study, who predicts increasing demand for cord blood. Cord blood probably has several types of stem cells besides haemopoietic precursors, making it a ''very attractive'' stem-cell source, she says.

Pat McCaffrey

This story originally appeared in Lancet Oncol 2005 ***6****:5*

Non-medical needs 'are unmet'

Nearly half of those living with cancer feel that their non-medical cancer needs are unmet by the healthcare system, according to a poll of 1000 US cancer survivors. The poll, conducted by the Lance Armstrong Foundation, found that 49% had unmet needs, including depression, fear of recurrence, chronic pain, ongoing health challenges, infertility, sexual dysfunction, difficulty with relationships and financial or job insecurity.

Of those who felt these needs were unmet, 70% said their oncologists did not offer support in dealing with non-medical aspects of cancer. The other 30% said their oncologist was willing to talk about these issues but did not have enough information to really help them in these areas.

''These findings reaffirm the serious need for all of us in the cancer community to take a deeper look at how we can further support people living with cancer, with the research, information and tools to help them deal with the emotional, practical and physical effects of the disease'', said Doug Ullman (Lance Armstrong Foundation). ''The increase in survival rates creates a unique set of challenges for these people to deal with throughout their diagnosis, treatment and the rest of their lives''.

An encouraging 47% of those polled felt that having cancer had a positive effect on their lives, and they reported leading a better life after dealing with the diagnosis.

PODIUM

New directions in nursing

Jan Foubert, senior lecturer in nursing and midwifery (Erasmushogeschool Brussels) and fatigue consultant (Jules Bordet Institut, Brussels), is President of the European Oncology Nursing Society (EONS). His interests include cancer fatigue and nutrition, and he is involved in several European nursing education projects. He is Chair of the Nursing Programme at ECCO 13.

Dr. Jan Foubert

Did you have specific aims when you took over as President of EONS?

Too often education and research, while both extremely important, do not change reality for the nurse at the bedside. These nurses deserve to be our top priority and EONS' new mission is ''to add value to the work of its individual members and societies in delivering care to patients with cancer''.

How has this been reflected in practice?

At ECCO 13, we're aiming to attract nurse managers who tend not to come to congresses which focus on disease management. A specific programme will look for example at ways of keeping staff motivated and how to integrate new colleagues: very important when there is a shortage of nurses.

EONS needs to raise its profile among managers, because if managers don't see the importance of the society they won't distribute information, and the nurses on the ground will not find out about us.

How will the nursing programme be arranged at ECCO?

Every day there will be topics for each group: nurses, researchers, educators and managers. We've introduced sessions for critical reflection on pain management, fatigue management, etc. Experts (good speakers chosen in part for their ability to stimulate the audience to participate) will present case studies to show how nursing is changing.

You have encouraged links with the Pharmaceutical industry. What reaction have you received?

The older generation of nurses is more anti-industry, and concerned that they are being ''bought''. But EONS can only develop with industry's support. Realistically, it has the money, and if companies are interested in carrying out a project with us, it's up to us to determine whether it serves nurses.

What problems have you encountered?

In the past a lot of projects were done without proper planning: a company would produce training materials and ask if we could use them. The first step must be to find out whether there is a need for the materials. Similarly in education: there was little follow up to determine whether and how a course was useful. Both have changed.

So what happens now?

All projects are based on analysis and planning of the needs of EONS' membership. It is not straightforward. There are 18 000 oncology nurses in Europe, and a big variety in the organisation of nursing, and in education.

Can you give an example of a project which could act as a model?

TITAN (Training Initiative in Thrombocytopenia, Anaemia and Neutropenia), in collaboration with Amgen, started with a learning needs assessment, then pilot courses were run in several different countries. The course was adapted following the pilots, and the Europe-wide implementation will be in 2005. The TITAN programme is made up of a pre-course revision pack to ensure that all participants have basic knowledge; an attended course (most nurses prefer face-to-face learning rather than Internet-based packages); and then a dissemination project to be undertaken in the 6 months following the course.

It sounds extremely rigorous

It is, and it has been difficult to get the dissemination projects accepted. Some nurses see this as a PhD! But these simple projects allow us to see what happens to new knowledge. Some participants organise a lunchtime presentation for colleagues; others will reflect on patient education leaflets. It extends the reach of the programme, and in 3 of 4 pilots, the projects were excellent.

How interested is Big Pharma in supporting nursing projects?

Increasingly. Several companies are now sustained partners of EONS, and have stated their reasons for wanting to support nursing. I'm keen for us to approach companies, asking them to participate in our projects. Production of the EORTC guidelines on the erythropoietins was supported by all companies producing the drugs. This is ideal because it avoids publicising one product, but, unfortunately, companies are often reluctant to work together.

What are the barriers to advancing oncology nursing?

Language is a problem because training materials are often produced in English and need to be translated. The money is not always available for this, so I've set up a small fund at EONS, specifically to cover the costs of translating educational material. Having interpreters at ECCO 13 is the only way of attracting nurses whose English is poor.

How do you see the future for oncology nursing?

Patients are becoming more informed and autonomous and nurses are having to answer difficult questions. They are dealing with changes in the management and treatment of cancer.

Education is evolving and is no longer reproduction of knowledge. Younger nurses are using the Internet and conducting project-based research. They expect to be part of cancer care teams, using strategic clinical pathways and protocols. But they're still being confronted by older colleagues not educated in this way.

We must influence the political agenda. Oncology nursing is not recognised as a specialty in most European countries and we do not have common standards of training and education. National societies need to work with their own politicians because we won't be able to influence Europe if we have no political voice in our own countries.