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Importance of obesity “underestimated”

The importance of obesity as a risk factor for cancer is underestimated even by cancer experts, according to Professor Paul Kleihues (International Agency for Research on Cancer, Lyons, France). He said that rates of colorectal, breast, prostate and endometrial cancers increase strongly in unison as countries start to become more affluent. Excess weight contributes to 30% of all cancers.

At a plenary session of the 3rd Global Conference for Cancer Organisations (hosted by UICC, Imperial Cancer Research Fund and Cancer Research Campaign, Brighton, UK, 24–27 June 2001), Professor Kleihues said that Sweden is one of the leanest countries in Europe and even there, half of all adults are overweight. By contrast, Greece and Spain, which became affluent later than other European countries, are the fattest countries in Europe. In Spain, 75% are overweight and 25% obese.

This epidemic of weight gain is leading to an increase in common

cancers. In rural India, for example, breast cancer is rare, but cities like Bombay are moving rapidly towards Western patterns. Spain, Greece and southern Italy, which were poor 30 to 40 years ago and had low rates of breast cancer, are now seeing



Professor Paul Kleihues

dramatic increases in incidence. Professor Kleihues said that obesity rates tend to increase as countries start to become affluent, and decline

later. “It moves like a wave across continents,” he said.

Breast cancer survival has increased dramatically across Europe, where average survival is 75%. In Sweden, France and Switzerland, survival is approaching 80%. But Professor Kleihues said that improvements had come from early detection

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and better treatments: “If breast cancer is associated with Western lifestyles, we can’t anticipate a drop in incidence. There is no indication that Europeans are prepared to change their lifestyle in respect to nutrition.”

Refraining from smoking remains the number one way to avoid cancer but maintaining a healthy weight is fast rising in importance, he said. It includes eating a balanced diet including fruit and vegetables and engaging in physical activity.

Mass media campaigns “should be welcomed”

Cancer organisations should be strong advocates of mass media campaigns to change cancer-related behaviours, according to Dr David Hill (Center for Behavioural Research on Cancer, Victoria, Australia). “Economic analysis shows that the up front costs associated with campaigns that change cancer behaviours are a sound investment. Cancer organisations, which may not be able to afford these campaigns themselves, should be strong advocates of them.”

Speaking at the 3rd Global Conference for Cancer Organisations, he said that a mass media campaign in

Victoria, Australia, led to a steep reduction in the number of people sunburnt over a number of weekends. A hard-hitting anti-smoking campaign in Australia over the past 4 years was similarly successful and led both to a reduction in smoking and an increase in numbers of people thinking about quitting. The campaign, which used graphic images from within the body to demonstrate the effects of smoking, has now been exported to 30 other countries.

A message based on fear, such as this, is appropriate in encouraging prevention, whereas reassuring mes-

sages may be needed to encourage people to come forward for screening, according to Dr Hill. He is cautious about the use of humour in anti-smoking campaigns. “Human laughter is a way in which we reduce anxiety. If what’s driving behaviour change is fear of the consequences, laughter may undermine this mechanism,” he said.

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Benefit of mammography “overestimated”

The addition of mammography to physical examination of the breast and self-examination does not reduce deaths from breast cancer, according to Professor Anthony Miller (Deutsches Krebsforschungszentrum, Heidelberg, Germany). Improvements in treatment are responsible for much of the improved outcome and they have reduced the benefits of screening, he said.

“If we could cure everybody no matter what stage they were detected, we would not need to screen. We initially hoped that good treatment added to screening in reducing the death rate,” he said. “In fact what is happening is that (good treatment is) effectively taking away some of the benefit of screening.”

The Canadian trial CNBSS-2 (*J Natl Clin Oncol* 2000, **92**, 1490–1499) was designed to compare physical examination of the breast along with breast self-examination, plus or minus mammography. It found that mammography “added lots of biop-

sies but made no impact on breast cancer mortality,” said Professor Miller at the 3rd Global Conference for Cancer Organisations. “This was unanticipated,” he said. He had expected that the benefit of screening was going to come from the detection of small impalpable breast cancers but says the results suggest that screening is maximal when it involves early detection of advanced stage II breast cancer. “Unless you have an effective treatment there is no benefit from screening,” he said.

The Swedish Two Counties study, which influenced the introduction of screening programmes worldwide, did show a beneficial effect of mammography. However, women in the control group were initially identified only from records and were less likely than women in the screened group to receive adjuvant chemotherapy and tamoxifen. According to Professor Miller: “Women identified as having cancer in the control group did not get good treatment at the time.” This

would have contributed to their higher mortality.

He concluded that countries which could afford mammography programmes would still benefit, but that breast examination was a “viable alternative”. However, Professor Paul Kleihues (International Agency for Research on Cancer, Lyons, France) said that mammography programmes should not be discouraged where the disease is highly prevalent and where the resources are available. They also enable scientists to learn about the natural history of early lesions. “Physical examination won’t make progress from a scientific point of view,” he said.

Professor Miller believes that research aimed at improving mammography using computer aided technology with digitalisation is “not the way to go”. Research needs to go in a different direction. “We have got to find cancers which are going to kill at a stage at which current treatment will cure them. That’s the research agenda,” he said.

First results from EPIC

Higher consumption of preserved meats such as ham, sausages and bacon are associated with a modestly increased risk of colorectal cancer, whereas consumption of red meats are not. This finding is one of the first to be presented from the European Prospective Investigation into Cancer and Nutrition (EPIC).

The EPIC study was set up in 1991 and is the largest ever conducted on the relationship between diet and cancer. It includes 500 000 subjects in 10 European countries and aims to elucidate cause–effect relationships between dietary balance, anthropometric measurements, physical activity, hormonal and genetic factors and cancer.

Previous studies have suggested that high consumption of red meat is associated with a 20–40% increase. However, EPIC was one of the first to consider the contribution of preserved meats separately from other red meats. Researchers cautioned that the results are preliminary and that analysis has not so far taken methods of cooking into account.

Public health community creates first legislation

A World Health Organization (WHO) initiative to control tobacco represents the first time the public health community has been responsible for leading a treaty-making process, said Dr Douglas Bettcher (WHO, Geneva, Switzerland). The Framework Convention on Tobacco Control (FCTC) will, when adopted in 2003, have the force of international law for those countries which ratify it.

The first rounds of negotiations included participation from 157 countries and according to Dr Bettcher, the process of negotiation itself is extre-

mely important. “As in climate change, the process of developing the treaty is a very important learning curve and can stimulate changes in public opinion.” Such a change is already occurring: “Ten or 15 years ago, the idea of a global treaty on tobacco would have sounded like something from outer space,” he said.

At the 3rd Global Conference for Cancer Organisations, he said the FCTC aims to reduce the cancer burden world wide and is intended to complement rather than replace national laws.

Other findings from EPIC, which were presented at the European Conference on Nutrition and Cancer (Lyons, France, 21–24 June 2001) include confirmation of the protective effect of fruit and vegetables on cancers of the colon, rectum and upper aerodigestive tract. Daily consumption of 500 g or more is sufficient to decrease the incidence of cancers of the upper aerodynamic tract by 50%. No clear protective effect has so far

been shown in cancers of the stomach or lung.

The “disastrous” combination of alcohol and tobacco was also highlighted. Smoking more than a pack of cigarettes a day increases the risk of cancer of the upper aerodigestive tract 8 times compared with a non-smoker. Drinking the equivalent of a bottle of wine increases the risk 9 times. Doing both together increases the risk 50 times, researchers said.

PSA test “changes incidence, not deaths”

PSA screening may increase the incidence of prostate cancer without reducing mortality, say Italian researchers. Preliminary results from a study comparing two areas of Tuscany hint that the reduction in deaths may be down to other factors, such as improved treatments for advanced disease (*J Natl Clin Oncol* 2001, **93**, 876–877).

The study compared two provinces in Tuscany: Florence and Prato. Figures from regional registries showed that between the mid-1980s and mid-1990s, prostate cancer deaths fell by a similar margin in both regions. However, in Florence, where opportunistic PSA screening was widespread, the incidence increased by 75% over the study period. In Prato, where there was no official screening programme, the incidence was almost stable. Further, in Florence, the decline in deaths was constant over the study period, but the incidence rose sharply only in the later years as screening became established.

The authors, from the Centro per lo Studio e la Prevenzione Oncologica, Florence, suggest that mortality reduction may be due, not to screening but to other reasons such as prolonged survival because of better treatment of advanced disease. “We warn about the risk of misinterpreting a reduction in prostate cancer mortality related to recent screening activity,” they write.

US cancer rates continue to fall

Cancer incidence and death rates continued to fall through the 1990s in the US, researchers say. A new report (*J Natl Clin Oncol* 2001, **93**, 824–842) found a continued reduction in the overall incidence and death from cancer between 1992 and 1998.

The ‘Annual report to the nation on the status of cancer’ is compiled by the American Cancer Society, the National Cancer Institute, the North American Association of Central Cancer Registries and the Centers for Disease Control and Prevention. It concluded, “Measures to sustain this progress must address the entire spectrum of prevention, early detection, and improved treatment and quality of life, and must be aimed at reducing mortality among all populations”.

The single most critical determinant of future rates will be the ability to reduce tobacco use in all segments

of the population, according to the report. However, preventive campaigns such as those to limit sun exposure or immunisation against hepatitis B, could substantially reduce the cancer burden.

An editorial in the *Lancet* (*Lancet* 2001, **357**, 1897) says the findings show that prevention and early detection remain the most effective weapons against cancer. “But perhaps not enough is being done to advance prevention,” it says. Diet and obesity may be major contributors to cancer risk, but they are so much part of our lifestyle that addressing them “is likely to prove even more difficult than addressing tobacco smoking”.

It concluded, “Programmes promoting prevention, even if they are only partly successful, can have substantial effects on the burden of disease”.

Avoidable deaths from testicular cancer

Hundreds of potentially avoidable deaths from testicular cancer are occurring every year in Eastern Europe, say researchers from Switzerland and Italy (*Lancet* 2001, **357**, 1853–1854). Analysis of national mortality data revealed that death rates in the US and Western Europe have fallen by about 70% since the 1970s. However, in Eastern Europe, the decline started later and is of only about 20%. Between 1995 and 1997, for example, testicular cancer deaths in the Czech Republic were 4 times

more common than in the European Union.

“Trends in testicular cancer should be monitored especially carefully in Eastern Europe”, said Professor Peter Boyle (European Institute of Oncology, Milan) “We must find out why testicular cancer death rates are so different in Central and Eastern Europe, otherwise there will continue to be several hundred preventable deaths occurring every year. If the reason for this is merely financial, then we must take rapid steps to correct this situation.”

HRT “may improve survival from breast cancer”

Taking hormone replacement therapy (HRT) after a diagnosis of breast cancer was apparently beneficial in a case-control study (*J Natl Clin Oncol* 2001, **93**, 754–762). Researchers found that women on HRT had half the recurrence rate and only a third of the risk of death, compared to controls.

The researchers followed 2755 women diagnosed with invasive cancer while enrolled in a health maintenance organisation. Of the group, 174 used HRT after diagnosis, and these women were matched to four non-users of similar age, disease stage and year of diagnosis. The HRT users had a rate of recurrence of 17 per 1000 person-years compared with 30 per

1000 among non-users. Breast cancer deaths were 5 per 1000 person-years among users, compared with 15 per 1000 in non-users. The researchers concluded, “The results suggest that HRT after breast cancer has no adverse impact on recurrence and mortality.”

Commenting on the results in an editorial, Professor Jack Cuzick (Imperial Cancer Research Fund, London, UK), said the results must be considered preliminary. HRT has been found to increase the risk of developing breast cancer, but the cancers that develop in HRT users tend to have a better prognosis than those in postmenopausal non-users. “Any sugges-

tion that use of HRT might improve survival remains unproven,” he said (*J Natl Clin Oncol* 2001, **93**, 733–734).

Women with breast cancer are particularly in need of relief from menopausal symptoms as treatments tend to exacerbate symptoms and these results underline the importance of ongoing randomised trials of HRT use in women with breast cancer. Professor Cuzick concludes, “One hardly dares speculate on the possibility that HRT might be beneficial; however, should this beneficial effect be confirmed in randomised studies, the hormonal treatment of breast cancer will require very major re-evaluation”.

AWARDS AND APPOINTMENTS

The first Emmanuel van der Schueren Fellowship

The Emmanuel van der Schueren Fellowship Programme was created in 1999 in memory of Professor van der Schueren, a former EORTC President (1991–1994) who died in 1998. He was Head of Radiotherapy at the University of Leuven. The aim of the fellowship is to promote research on quality assurance (QA) in radiotherapy. The first year, the cost of the Fellowship will be covered by the Vlaamse Liga tegen Kanker and the EORTC and, for the second year, the Vlaamse Liga tegen Kanker, FECS, ESTRO and the EORTC will provide financial and logistical support.

Dr Vassilis Kouloulis, radiation oncologist from Greece took up the first Emmanuel van der Schueren Fellowship in January 2001. Dr Kouloulis has a first degree in physics from the University of Athens, where he also took his MD. He holds one Ph.D. on use of image-processing techniques in the evaluation of recalcification of bone lytic metastases after radiation therapy and IV bisphosphonates, and another Ph.D. on biomedical engineering from the National Technical University of Athens.

He previously worked for several years monitoring data and biostatics at the Hellenic Heart Foundation. He was in charge of large epidemiological trials into the rate of hyper-lipidemia in young recruits. He was a medical advisor at the Institute of Communication and Computer Systems of National Technical University of Athens. He also worked at the research centre, Infoproject, in Athens, where he developed software and databases dedicated to surgical and gynecologic oncology.

He has co-authored several scientific publications on QA, quality of life, radiotherapy, hyperthermia, epidemiology-biostatics and image processing.

During his fellowship Dr Kouloulis is supporting the EORTC Radiotherapy Group and the QA committee in developing and evaluating procedures to check the con-

formity of transferred data relating to treatment techniques. He monitors the data and registers the broad spectrum of techniques used in EU countries. "It is like being in the virtual radiotherapy department as I nearly have all the material at the EORTC Data Center to do my work," he says. He has also reviewed the methods used by the EORTC Radiotherapy group QA programme since the early 1980s.

The QA programme ensures the QA of data and of protocol compliance. Dr Kouloulis works with each study co-ordinator to define, document and monitor clinical criteria and endpoints for disease outcome, such as tumour control or morbidity. In this way, the clinical impact of learning curves within each trial are quantified.

Dr Kouloulis' primary concern is QA in radiotherapy: "I believe that although we have some guidelines for radiotherapy practices—such as for equipment and data transfer accuracy—what is clearly needed is a common platform. I hope to see the



Dr Vassilis Kouloulis

implementation of radiotherapy-guidelines for all EU countries one day."

The idea of a common platform in terms of International Commission on Radiation Units (ICRU) recommendations was discussed at the EORTC Radiotherapy Group meeting in Ber-

lin this year. The European Society of Therapeutic Radiology and Oncology (ESTRO) also aims to develop both minimum requirements and higher standards for the QA of radiation oncology, radiophysics, radiation technology and radiobiology in Europe and is trying to promote their implementation.

QA in radiotherapy matters throughout routine clinical practice but especially in stereotactic and conformal radiotherapy. "During my specialisation in radiotherapy in Areteion University Hospital of Athens, I was facing the real challenge of QA mainly in 3-D conformal radiotherapy. Applying new radiotherapy techniques without QA is like driving a car without passing your driving licence," he says.

The EORTC QA programme in radiotherapy was initiated in the early 1980s to improve the quality of cancer management in radiotherapy centres conducting clinical research. What Dr Kouloulis hopes for are international guidelines to ensure that common radiotherapy clinical data criteria are applied similarly in community hospitals in all EU countries.

His work at the EORTC Data Center is extremely stimulating as he feels that treatment management, improvement of quality of life and QA in radiotherapy are undoubtedly progressing. "The work here at the EORTC Data Center is a fantastic experience which I hope to apply in Greece one day," he adds.

Dr Kouloulis is conducting his project in close collaboration with the EORTC Radiotherapy Group and mainly with Dr Philip Poortmans who is in charge of the Group's QA.

When he is not analysing data, he plays piano partitions from Mozart and Chopin, his favourite composers. If he had chosen a career other than medicine, it would have been in classical music or jazz.

*Samantha Christey
EORTC Communications Officer*

INTERVIEW

Professor Nicholas Pavlidis is head of oncology at University of Ioannina, Greece. He is Chairman of ESO's office for the Balkans and the Middle East; a member of the ESMO Education Committee and Task Force for Guidelines and of the EORTC's ECSG (secretary), IDBBC, BDTG and Continuing Medical Education groups. He is on the editorial board of prominent European and American journals, including EJC.



Professor Nicholas Pavlidis

Where did you train?

I completed my medical training at the University of Athens, studied medical oncology at the Royal Marsden Hospital, London, and undertook research work at the National Cancer Institute (NCI), Bethesda, USA.

Who inspired you?

M. Peckham, E. Wiltshaw and I. Smith in London impressed me with their peculiarly British way of thinking in medical oncology. M. Chirigos at the NCI introduced me to the techniques and ideas needed to explore tumour immunology in the laboratory.

Why did you choose to work in the field of cancer?

As a medical student, I worked in the oncology department of the cancer hospital in Athens and was astonished by the diversity of cancer medicine. It had everything from basic to clinical research and beyond. My first publication—on the co-existence of solid tumours and leukaemia—appeared when I was a 5th year medical student.

Did any other branch of medicine appeal?

Psychoneuroimmunology has always been my parallel hobby. Macrophages

play an essential role in carcinogenesis and I have studied the effect of stress on their tumoricidal activity. It is a fascinating and promising field in cancer research with important psychosocial implications.

Might you have done something else altogether?

My third love in life, after my family and medicine, is marine biology. I have loved medicine since I was at high-school, long before I knew anything about it, and I could never have done anything else, but I would have enjoyed studying marine biology at the same time.

What is your greatest regret?

I don't really have any regrets in my scientific life or in my life, in general.

What has been the highlight of your career to date?

In the late 1970s, a new medical school was being established at the University of Ioannina. I knew Professor H. Moutsopoulos, Head of Medicine, from the States, and he asked me to set up the Department of Oncology. Ioannina had previously had no cancer medicine at all and this was a unique opportunity, it felt like giving birth and raising a child. Since then, our links with EORTC, ESMO and ESO have put the department on the European map.

If you could complete only one more task before you retire what would it be?

To be able to keep patients' care, education and research going in the best possible way and to allow capable followers to continue and further improve what has already been achieved.

What is your greatest fear?

Following on from this, I fear the loss of continuity and tradition in a system that is not fully reliable.

What impact has the Internet had on your working life?

It is like your breakfast and your dinner. You start with it early in the morning and you end up with it before you go to bed. It is fast, cheap, and allows easy communication with colleagues wherever they are. In addition, you have immediate access to information about cancer. It is a revolution and a gift from modern technology to medicine.

How do you relax?

By diving, collecting, exhibiting and reading about sea shells. I spend 3–4 h a week reading about shells and have collected them for the last 20 years. I donated my collection of approximately 2000 shells to the Metsovo Conference Centre. The shell is unique among living things in being beautiful and valuable as a gift long after its death.

“Air he is, you can not touch.

Yet, wherefrom is he grasped? Is it by the sea's edge of sheet lifting it so high that

for a moment you can see the sky's naked

back so full of spume and shells?”

Odysseas Elytis

The Garden with Illusions.

Who is your favorite author?

In medicine it is Hippocrates, in life, the Ancient Greek Philosophers: Socrates, Plato, Aristotle, etc. Just part of the inheritance of Greek civilisation.

What do you wish you had known before you embarked on your career?

That cancer is a more complicated phenomenon than we initially thought. That cancer is rarely a one-cause disease. That cancer needs a more holistic approach both as a carcinogenic process and as therapeutic management. That responses do not necessarily mean survival benefit. That a 1-year survival difference of 10% for 3 months is not a scientific breakthrough. That quality of life and proper management of terminally ill patients are more important than a partial response or a statistical survival difference of 0.05.

What piece of advice would you give someone starting out now?

First, medical oncology requires good training in Internal Medicine. Second, don't be just a 'chemotherapist' or don't work only in an outpatient clinic. Third, don't forget the beauty of differential diagnosis and think first as a capable internist. Fourth, medical oncology without research is like summer without sun. And fifth, see cancer research and clinical oncology in a holistic manner and not as a local epiphenomenon.

What is your greatest vice?

It is not heredity. It is not smoking. It is not excessive drinking. But sometimes a fatty diet and inadequate exercise.