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Keyhole surgery 'effective' in colon cancer

Laparoscopy-assisted colectomy (LAC) was more effective than open surgery in a study by Spanish researchers (*Lancet* 2002, **359**, 2224–2229). Morbidity, hospital stay, tumour recurrence and cancer-related survival were all superior in the LAC group. If the results are confirmed elsewhere, ''LAC could become the standard surgical approach in patients with colon cancer,'' they conclude.

''LAC SHOULD BE PREFERRED TO OPEN COLECTOMY''

The traditional view has been that open surgery is the treatment of choice, and the researchers acknowledge that LAC is "a technically difficult procedure that requires intensive training." However, they say the traditional view has not been substantiated.

Patients were assessed at a University of Barcelona clinic from November 1993 to July 1998. Randomisation was carried out the day before surgery, and the study included 219 patients with adenocarcinoma of the colon, 15 cm above the anal verge.

Postoperative recovery was faster and complications fewer among the patients treated with LAC. Further "unexpected positive findings" suggested that LAC also seemed to improve the long-term outcome in patients with colon cancer. Yet this superiority was due only to results among patients with advanced non-metastatic cancer. In patients with stage I and stage II cancer, rates of tumour recurrence, overall and cancer-related survival were almost identical in both groups.

The researchers speculate that LAC may give rise to less surgical stress than open surgery, and consequently reduced impairment of immunity. "Immunity has a critical role in tumour progression and metastatic spread," they say. A further possibility may be that manipulation of the tumour in open surgery leads to exfoliation of malignant cells into the peritoneal cavity and portal vein upstream. "Preliminary reports have shown that cell spillage is not made worse by the laparoscopic technique," they say.

"Our results show that LAC should be preferred to OC in patients with colon cancer because it reduces perioperative morbidity, shortens hospital stay, and prolongs cancer-related survival," the researchers conclude.

Physical activity and breast cancer

The importance of physical activity on breast cancer risk may depend on birth cohort, say Swedish researchers (*International Journal of Cancer*, 2002, **100**, 76–81). They found that regular leisure-time activity reduced breast cancer risk by 40% among women born between 1901 and 1917, but the association was only seen among women who were either normal-weight postmenopausally or overweight when premenopausal.

The study included 9539 same-sex twin women, identified from the Swedish Twin Registry, who answered a questionnaire about their work and leisure-time activity between 1967 and 1970, when they were aged between 25 and 50 years. In follow-up to 1997, 506 cases of breast cancer occurred. There was no overall association between physical activity and risk of breast cancer.

The data suggests that the inverse relation between physical activity and breast cancer is not mediated by a lower BMI nor confounded by other established breast cancer risk factors. If activity has an effect through reduction of fat tissue, it would be expected that the strongest protective effect would be seen among postmenopausal with high BMIs. This was not the case. Physical activity is known to reduce levels of circulating oestrogen regardless of BMI but its strongest effect was seen among lean postmenopausal women whose oestrogen levels were already low. "It appears that the change in hormone levels, be it due to physical activity or hormone replacement therapy, may be relatively more important among lean than among overweight postmenopausal women," they say.

PET in malignant melanoma

Use of positron emission tomography (PET) may alter the clinical management of stage III malignant melanoma, according to a Dublin group. In a review (*British Journal of Surgery* 2002, **89**, 392–396), they note that PET can uncover previously unsuspected widespread metastatic disease and thus identify people whose melanoma is unsuitable for resection. Its role in stage I or II melanoma, however, is uncertain. ''Further trials will be needed if PET is to be shown to be of benefit in the earlier stages of malignant melanoma,'' they write.

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Leonardo da Vinci: an update

The Federation of European Cancer Societies (FECS) received a mandate from the European Commission to perform a 3-year study (December 2000–November 2003) into continuing medical education (CME) in oncology in Europe (see *EJC* News 2002, **38**, 13).

The project, which involves 12 partners, aims to raise the standards of educational programmes on oncology in Europe and includes to main components: the accreditation of CME events and its mutual recognition in EU member states, and the development of new educational programmes and tools.

In the first wave of the study, FECS collected information about CME events organised between June 1999 and June 2001. More than 150 CME organisers sent information that led to the creation of a database listing events according to their title/subject, date, and location. FECS is now recontacting these CME organisers for their views on topics that are not sufficiently addressed in European CME programmes, and on the audiences who are not targeted energetically enough. This will sharpen up the survey on CME needs in Europe. Another survey asked health professionals for their views on CME and CME credits, and about their needs and preferences: whether they prefer international or national events, their opinion of other CME materials like CD-Roms and videos, and so on. More than 500 questionnaires were received and are currently being analysed.

On accreditation, a key aim is to streamline the process of mutual recognition of educational credits between EU member States. FECS, in close collaboration with its Accreditation Council (ACOE), is enhancing its relationship with the Accreditation body of the European Union of Medical Specialists (UEMS). The UEMS Accreditation body 'EACCME' has created a working group composed of representatives from two national authorities, two UEMS Sections and two European Professional Societies including FECS. This working group is analysing European accreditation of well-recognised accreditation bodies (rather than European endorsements of accredited events), European accreditation of enduring material/distance learning, and continuing professional development.

Furthermore, the 2-year pilot study aimed at setting-up a mutual recognition system between US and credits authorised by EACCME has been successfully renewed for 4 years.

FECS is also analysing new CME tools, and the Leonardo da Vinci partners have suggested the development of:

- a FECS educational website linked to the educational websites of different member societies and partners
- publication of an ECCO 12 education book as a supplement to *EJC*;
- audio and video capture of some ECCO 12 educational sessions, to be incorporated on CD-Rom and/or made available on the Internet. These techniques offer a user-friendly learning environment and interactive processes between the CME providers and the recipients. For each of the selected chapters, a case study would be incorporated together with a questionnaire allowing evaluation of the learning outcome. With a dynamic database, the results of the questionnaire could be collected, analysed and reported back to interested parties.

On evaluation, the Leonardo da Vinci partners concluded that the only practical way to assess the impact of a CME event is to set one test before the event, another immediately afterwards and a third 3 months later. Unfortunately, this is not feasible for events that gather more than 100 participants. In this case, the partners recommended that CME organisers should define in more detail the learning outcome of the activity on the application sent to ACOE for accreditation, and draft accordingly a detailed questionnaire to be filled in by participants at the end of the event.

An interim report of the Leonardo da Vinci project will be sent to the European Commission in October 2002. The final report for the Commission, due in November 2003, will be accompanied by a database and clear recommendations on: CME needs in oncology; The development of new CME tools, The assessment of CME activities; The state of mutual recognition of CME credits across Europe and with the USA.

Once the Commission has approved the final report, with its agreement, the database, recommendations and conclusions will be made public.

Kathleen Vandendael
Executive Director, FECS

Androgen suppression 'improves survival' in prostate cancer

LHRH analogues given during and for 3 years after external irradiation improve the survival of patients with locally advanced prostate cancer, according to an update of an EORTC study (*Lancet* 2002, **360**, 103–108). The phase III randomised trial has now followed 412 patients for a median of 66 months, and found significant gains in both disease-free and overall survival.

Patients were recruited from a number of European and Canadian centres between 1987 and 1995. They had histologically proven T1-2 prostate tumours of WHO grade 3, or T3-4 tumours of any grade. They received either radiotherapy alone or radiotherapy plus immediate androgen suppression. At 5 years, disease free-survival was 40% among those receiving radiotherapy-alone and 74% among those on combined treatment. Rates for 5-year overall survival were 62 and 78%, respectively.

The researchers suggested that androgen suppression may eliminate occult systemic disease. However, it is not known how long androgen suppressors need to be given; a shorter period of use would reduce costs and side-effects. This question is being addressed by another EORTC trail.

EUROFILE

A drive for drugs for children

Europe is dangerously short of medicines developed for, or even adapted to, children, said Enterprise Commissioner Erkki Liikanen recently. More than half the drugs prescribed for Europe's 75 million children have not been properly tested for them, and he found this "very troubling".

Liikanen was speaking at the launch of a Commission initiative to ensure that children get the medicines they need, and in the right doses. The consultation paper 'Better medicines for children' sets out the objectives that any new rules aiming to remedy the shortage of child-specific medicines should fulfil, and suggests ways to attain them.

"To get the best and safest treatments for children across Europe," said Liikanen, "society must strike the right balance between incentives and regulatory obligations. We need to ensure that both existing and new medicines are adapted to paediatric needs in the most resource-efficient manner for society as a whole."

"MEDICINES SHOULD BE ADAPTED FOR CHILDREN"

Pharmaceutical companies are often reluctant to invest in child-specific medicines, as the market is relatively small. The Commission recognises that they are unlikely to fund new research into medicines already on the market, and the paper explores the idea of creating an independent public fund to do this.

Encouraging companies to study, test and adapt new and old medicines for children is a cornerstone of the new proposals. One possible incentive is a long period of intellectual property protection to reward work on innovative medicines. Another is a new type of marketing authorisation giving intellectual property rights to new paediatric uses of older products. Companies could also be obliged to conduct paediatric studies as a requirement of marketing authorisation, unless the medicine was unlikely to be used in children.

A central European database on the use of adult medicines in children is proposed, together with a new expert working party at the EMEA, responsible for the development, availability, and follow-up of paediatric treatments. The Commission believes that such pan-European networks would help to pool expertise and avoid duplication.

It is unusual for DG Enterprise to launch such a transparent consultation process on pharmaceutical issues and the response was enthusiastic. Almost all those who commented felt that the matter is urgent, and that adequate resources and funding are essential for it to be successful. However, many respondents were concerned that the proposed incentives might lead to medicines being developed for financial gain, rather than for the benefit of children.

Professor Michael Stevens, President of SIOP (the International Society of Paediatric Oncology) Europe, said: "We are very well aware of the inconsistencies in current legislation relating to drugs used in paediatric practice. Many of us have experienced the frustration of being unable to evaluate new cancer chemotherapy drugs in the absence of willingness of pharmaceutical companies to support such studies."

The lack of resources in newer EU member states has prevented many of them from participating in clinical trials of new cancer treatments at the same level as Germany, France and the UK, says Stevens. "The development of trials across Europe to the levels required by the Clinical Trials Directive will require considerable additional resource. The most cost effective way of achieving this objective will be to support the development of the clinical trial network within clinical specialties across the EU. If achieved, such networks would have the structure, stability and professional credibility to work with the Commission and with pharmaceutical companies to agree and implement prioritised work plans directed at the improvement of treatment of children throughout Europe," he said.

The Commission is to study the responses before drafting formal regulatory proposals. A similar US initiative, enacted in the Federal Food, Drug and Cosmetic Act in 1997 and recently revisited as the 'Best Pharmaceuticals for Children Act', was signed by President Bush in January 2002. It has already led to more than 400 studies, changes to more than 20 medicines, and revised dose guidance, reflecting better information on specific use in children.

"IT IS INCREASINGLY DIFFICULT TO FUND STUDIES"

Whatever their final form, the new proposals will reopen an issue already discussed at length in the USA: the ethical acceptability of increasing the numbers of children in clinical trials. However, in Europe, guidelines on relevant consent requirements are contained in the 1997 European Convention on Human Rights and Biomedicine, and also included in the Clinical Trials Directive.

"Despite the expertise available and the generally excellent collaboration that exists within the paediatric oncology community," says Michael Stevens, "it is proving increasingly difficult to identity the resources necessary to undertake collaborative international studies across Europe at the level required under the Clinical Trials Directive. We are pleased to see this initiative from the Commission contains proposals to encourage high quality clinical trials in children, and particularly in children with cancer."

Mary Rice
Brussels

INTERVIEW

Dr Aron Goldhirsch is Director of Medicine at European Institute of Oncology, Milan; Chief of Medical Oncology at the Oncology Institute of Southern Switzerland and (titular) Professor of Medical Oncology at the University of Bern. He is Chairman both of the Scientific Committee of the International Breast Cancer Study Group, and of the Swiss Group Clinical Cancer Research. He has won several international awards.

Where did you train?
In internal medicine and infectious diseases, in Milan and in Southern Switzerland. Then in medical oncology in Bern, and at the Dana-Farber Cancer Institute, Boston.

Who inspired you?
First, my mentor in internal medicine, Dr Michael Reiner; and then Dr Franco Cavalli, with whom I have worked for almost 30 years. Both inspired me with their methodology, medical skills and humanity. Your approach to your profession and your patients is partly a question of temperament but largely reflects the verbal communication style you learn early on.

Why did you choose to work in the field of cancer?
Dr Cavalli wanted to establish a department for cancer medicine in the southern, Italian-speaking part of Switzerland, where no specific facility existed. While he was still in Bern, a nurse and I worked at the new department, now the Oncology Institute of Southern Switzerland which employs about 100 people. Oncology appealed but it was also the opportunity to create something new that attracted me.

Did any other branch of medicine appeal?
Endocrinology and gastro-enterology.

Might you have done something else altogether?
As a kid, I spent all my holidays with my late uncle, who was a vet. I considered veterinary medicine but he thought I should avoid the hard work in the open, so he influenced my choice for medicine. His only son, who was 7 years my junior, followed me into medicine and is now an oncologist in Jerusalem.

What has been the highlight of your career to date?
My work with the Ludwig Breast Cancer Study Group, now the International Breast Cancer Study Group. Also, my long-standing collaboration with its members, especially with my friend, biostatistician Dr Richard D. Gelber, with whom I continue to search for useful information for care of individual patients. Together, we developed descriptive methods for comparisons of quality of life (Q-TWiST) and for evaluating patterns of response to treatments (STEPP).

... and your greatest regret?
That I was so involved in my work I was late in putting down roots. I have three small children, they're 9, 5 and 3 years old, and I would have loved to have had children earlier.

If you could complete only one more task before you retire, what would it be?
To globalise clinical research, at least within breast cancer. True understanding of each other in a specific area means that the most relevant questions are asked more efficiently, with a much better chance of getting significant answers earlier. It is something we are moving towards.

What is your greatest fear?
None relating to my career, but exclusively to the life and security of my family. I am sure this sentiment is shared by many, and I assume that it is due to the history of my family during the 20th Century.

What impact has the Internet had on your working life?
On a scale of 1 to 10, it's 15. Research groups are linked by email, which is far cheaper than the telephone, and easier since colleagues in Australia or the US may be in bed during European office hours. I use the Internet for the literature and often also instead of reference books. It is remarkable to receive about one-tenth of the paper I used to, 5 years ago.

How do you relax?
By swimming and listening to music while I drive to work, which can mean 2 hours entirely dedicated to news and music. I prefer pop and surprise my friends by being able to chat with their children on new hits; I appreciate several recent singers like Kylie Minogue or Natalie Imbruglia, I also enjoy listening to Ella Fitzgerald, Grover Washington or Sting, who is always renewing himself.

Who is your favourite author?
Isaac Asimov, whom I read in Italian. His short stories continue to amaze me and tickle my curiosity. About 70% of my leisure reading is Italian, 20% in English and 10% in Hebrew.

What do you wish you had known before you embarked on your career?
Nothing. I need to maintain my curiosity and knowing things in advance is not much fun.

What piece of advice would you give someone starting out now?
Get some experience in medicine and then spend a year or two in the lab on basic science, following your curiosity even on some unrelated research programme. It will improve your knowledge of scientific language, influence the way you approach the literature and broaden your horizons when you return to the clinic. Always try to derive satisfaction from your work, especially in severe or dramatic situations.

What is your greatest vice?
I am involved in a lot of things that take me away from my family. I enjoy work, but the amount of time I devote to it feels like a vice.