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Fatima Cardoso

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A European report card

→ Kathy Redmond ■ EDITOR

Disparities in the speed at which patients in different European countries get access to the latest cancer drugs were highlighted last month in a report published by Stockholm's Karolinska Institute. The Roche-sponsored study, launched at a press conference at the European Parliament, shows that patients in Austria, Spain and Switzerland tend to get quickest access, with patients in the UK, Czech Republic, Hungary, Norway and Poland lagging behind. The authors of the report conclude with a call for governments to take "a broader perspective on the benefits these drugs bring to patients and society, and introduce a more rational system of allocation of resources to the healthcare system." The point is well made. But there is a danger that focussing narrowly on drugs will divert attention from inequalities in other aspects of cancer care that are at least as important.

The majority of cures are achieved through a combination of therapies, not just drugs. Surgery plays a key role, yet patients in many countries – particularly in rural areas – still have complex cancer surgery carried out in centres with insufficient case volume and skill, often outside of a multidisciplinary setting.

Few European countries have enough radiotherapy machines. Available knowledge and techniques are often not being

used to best effect; health professionals responsible for delivering cancer care are too often inexperienced and poorly trained.

Patients are suffering needlessly because symptom control is still not seen as a routine part of cancer care, and outdated regulations undermine pain relief. Europe's growing elderly population is let down by doctors who withhold intensive cancer treatment on grounds of age alone, and by a failure to train cancer specialists in geriatric medicine. Cancer rehabilitation services are often underfunded, and in some countries they are non-existent.

The Karolinska report was clearly intended to put pressure on governments to allow their citizens faster access to the drugs they need. A similar report, deserving equal attention, has recently been published on disparities in radiotherapy provision (see p. 32). But if, as the authors of the Karolinska report say, we are really looking for "a more rational system of allocation of resources", perhaps the time has come for this name-and-shame tactic to be used across all aspects of cancer care. An annual 'report card', for instance, could be just what is needed to promote such a rational approach. Providing solid comparative statistics on key quality indicators, it could show governments how their countries rate against others, and offer them an incentive to focus on the aspects of cancer care that need most attention.

Fatima Cardoso: the next generation

→ Marc Beishon

Fatima Cardoso's determination to put her considerable abilities to best use landed her the scientific directorship of a groundbreaking translational research trial at the tender age of 37. A founder of the Flims Alumni Club, she's now calling on other budding young researchers not to wait until they become the big shots, but to make their voices heard now.

Most people entering a medical career want to make a difference – and the choice of oncology is often made because of the potential to contribute to this most problematic disease management area. While it is possible to make a steady contribution in day to day treatment work, the ideal, perhaps, is to be part of an exciting research group as well as a good clinical physician – which is exactly what Fatima Cardoso, assistant professor at the Jules Bordet Institute's medical oncology clinic in Brussels, has achieved.

But in doing so she's encountered nearly all the major issues affecting oncology work in the European Union, such as mobility, career paths and research funding – obstacles that some other colleagues in her home country, Portugal, have found too tough to crack.

As a relatively young medical oncologist, still working on her PhD, Cardoso is already the scientific director of TRANSBIG, the translational research network spun out of the Breast International Group (BIG). TRANSBIG's first

project – MINDACT (Microarray for Node Negative Disease may Avoid Chemotherapy) – involves a major trial with 6,000 patients that promises to make a significant difference in determining which women with early breast cancer will benefit from chemotherapy. "It's almost like science fiction," she says of its potential.

Running a project of this size is certainly giving Cardoso her cutting edge research ideal, but as she points out, this sort of translational work requires expertise and oversight in both clinic and the laboratory, and she welcomes the chance to keep a foot in both camps. "I have learnt that for me to be fulfilled as a doctor I need to have enough time to see patients," she says. Cardoso loves the opportunities working at Jules Bordet offers to immerse herself in bringing together the worlds of lab and clinic, seeing patients every day, working on many of the 100 trials currently running, participating in the projects of the institute's translational research unit, and pressing on with MINDACT and her own research into Herceptin (trastuzumab) resistance.



“It’s also about making our voice heard now
and not waiting until we’re the big shots”

Cardoso hopes younger oncologists will help speed up recognition of medical oncology as a speciality

She's climbed very high for someone of her years, but Cardoso is not one to pull the ladder up behind her. She cofounded and enthusiastically promotes the Flims Alumni Club (FAC), which brings together young graduates of the highly respected Flims Methods in Clinical Cancer Research Workshop. At the Jules Bordet, she has also taken on the role of coordinator of the community of international fellows, which until recently she herself was a part of. Such networking, says Cardoso, is not just about learning how to run trials, for example. "It's also about making our voice heard now and not waiting until we're the big shots. We need to say now what we want for our careers."

There can certainly be frustration for younger cancer doctors in pursuing their goals, especially when, like Cardoso, they determine their interests fairly early on. The situation is particularly acute in Portugal, she says, because while standards of clinical care are high, the medical training is very long and there is simply very little research infrastructure. "I had my medical training at the University of Oporto, which is considered to have one of the highest standards of theoretical learning in Europe. But what is missing is the research infrastructure – you have to do everything yourself and you simply don't have the time with clinics so full." There is an excellent private research institute (IPATIMUP) in Oporto, she adds – known particularly for work on thyroid cancer – "But working there takes you away from patient care."

Cardoso's aim to be a doctor stems from her early years. She was born in Mozambique. Her parents – mother a teacher, father an insurance business manager – had moved to the Portuguese colony, but had to return when Fatima was eight after the political upheavals. "I never wanted to be anything other than a doctor – my mother says that ever since I was little

I was always playing doctors and my family had to pretend to be sick all the time."

When she became aware of medical specialities, her first choice when she arrived at medical school was to go into paediatrics, but a bit later she decided against, feeling it would be too hard in emotional terms. "I'm a very sensitive person – it especially hurts to see a child suffer. I believe that to be a good doctor you need to keep your humanity. People say that you have to keep your distance otherwise you'll get hurt all the time. But if you do that you lose your quality as a doctor. I felt it was easier for me to be able to keep my humanity, without being overwhelmed with pain, with adults than with children."

She chose internal medicine over an option to become a surgeon. "I realised I wouldn't be happy as a surgeon – no disrespect, but I'd be doing the same things over again and I would be bored. That may be a misconception but it was the way I saw it.

"And I'd discovered oncology, first through theory – cancer biology became a passion as soon as I encountered it – and then medical oncology became a speciality the year before I had to decide." To its credit, Portugal has moved faster than some other countries to recognise medical oncology, and it is certainly Cardoso's hope that younger oncologists will help accelerate the process of breaking open other national internal medicine systems to this core speciality.

She also benefited from excellent and inspirational teaching, and found added impetus in her personal life, especially from her sister, who had been through many operations after a childhood accident. "She's my role model in terms of courage and not letting things stand in your way – she's a robotics engineer now and I'm very proud of her." Then her best friend was diagnosed with breast cancer. "When you are young you have all these dreams. I thought if I worked hard and in the right team I could do something

to make a difference in cancer management, and eventually help my friend. It's why I went into medical oncology and one of the reasons I left Portugal to come to Brussels."

Despite Portugal having three regional cancer centres, Cardoso had found research opportunities, at Oporto at least, very limited. Such research as she was able to do was done in the evenings and weekends, and she was encouraged by her director to seek opportunities abroad. After 12 years in training – Portugal is said to have the longest medical qualifying time in Europe – she actually put in only three months as a fully-fledged medical oncologist in Oporto.

"We had a speaker from the Jules Bordet breast unit come to a meeting, and in the coffee break my director asked him if I could do a research project in Brussels, and I thought, 'Well, you could have asked me first!'" That was in 2000, and Cardoso duly took up an offer to become a fellow at Jules Bordet. She is now a staff member, and very grateful to her former director for his 'push'. As she points out, being single with no ties has made the move easier, and she already spoke French and English.

As for leaving Portugal, she admits that she's contributing to the 'brain drain' – a hotly debated issue in Portugal as in other countries. However, she debunks the idea that she is somehow in debt for the cost of her training. "The money spent on my training I've paid back in the long hours I worked as a resident. You can consider that it was cheap labour. I always gave my best and a lot of my time." While proud to be Portuguese, she says that its society needs to tackle some tough issues. People tend to look out just for themselves, she says, adding that this may well be a reaction to the long years of dictatorship. Those such as doctors who stay within public positions have continually to 'fight the system' to get professional fulfilment.

At Jules Bordet, Cardoso first completed a two-year clinical and translational research fel-



With her guide and mentor
Martine Piccart

lowship, where her focus on breast cancer was cemented. This was a crucial stage of her career, which she saw as a natural progression from her interest in targeted therapies. It also presented a wonderful opportunity to work with one of Europe's leading breast cancer groups, under the direction of Martine Piccart, who founded BIG in 1996, and who has been her guiding force over the last few years. And in a profession still heavily dominated by men, Cardoso feels that working for such a successful woman has helped pave the way for her own career.

More generally, with its heavy emphasis on multidisciplinary working across the clinical-laboratory divide, and given the many breast cancer patients referred to the Institute,

“We should be able to publish negative results
so others don't waste time on the same dead ends”



In the lab

Cardoso saw Jules Bordet as an ideal place for her to pursue her key research interest – the fundamental puzzle of why targeted therapies fail in such a high percentage of cases.

“There are people who prefer to go into areas that are not as well studied as breast cancer, so if they discover something it becomes their breakthrough,” she says. “Others go into areas where there are many groups studying variations on a theme, and where there is much more collaboration – although honestly I didn’t think of one or the other.” Nevertheless, it has since become abundantly apparent to Cardoso that there are tremendous advantages in the power of large-scale collaboration, such as that fostered by BIG. Typically modest, her wish is to play a part and not to see her name in lights.

While her PhD is on trastuzumab resistance, she adds that it is the overall problem of treatment resistance that is her major topic – the mechanisms and predictive markers. To develop her translational research capability, on completing her two-year fellowship she went to the MD Anderson Center in the US on a one-year basic research fellowship under Mien-Chie

Hung, head of breast cancer research and a pioneer in HER-2 science. This, she says, was for the very specific aim of finding out more about basic research, and she feels a year was sufficient. “I could also have gone to the UK and the University of Oxford, but I would have had to put in three years instead.”

Several ‘lessons’ emerged from this spell at MD Anderson. “It reinforced my understanding that I had to also work with patients, which you don’t do in basic research,” she says. “But the main lesson was finding out exactly how people in the lab think – it is different from those on the clinical side, where we need to know why we are doing something. In the lab they are usually doing science for science’s sake.”

Another lesson came the hard way – you can go into the lab with a hypothesis and test it out, but if it doesn’t work then some six months or so of the experience can be wasted, at least as far as getting a usable result is concerned. That’s clearly a potential risk of spending only a short spell in the lab environment, but as Cardoso adds, it brings home the importance of knowing what has already been tried and failed.

“I believe it’s unfortunate that we are much more likely to publish – and have accepted for publication – work with positive results. That’s perhaps even more striking in clinical research than lab work. It’s a bias that should change – we should be able to publish negative results so other people don’t waste time investigating the same dead ends.”

What’s more, she feels that without more publication of negative results, the oncology community is getting a biased view of research. “I guarantee that if you do a search on MEDLINE more than 90% of papers will have positive results.” It’s a situation that is changing though – Cardoso mentions one drug study she’s recently reviewed, in the breast cancer area, which has a negative result and will be

“The legal, ethical and financial aspects of the trial have been a roller coaster of a learning curve”

“We set an example: yes, we want our own societies, but we can also work in multidisciplinary groups”

published. “It’s a well-written paper and it should be known that that specific drug given this way doesn’t work.”

It’s another item to add to her change agenda for the oncology community, though she notes that all are to blame in the natural desire to be associated with positive outcomes. “In breast cancer, though, we are talking about this. I’ve found sessions where we discuss how to get manuscripts accepted very interesting, and editors and opinion leaders are aware of the issue.” In addition, she feels that the breast cancer research community is more organised and open to collaboration, so enhancing protocol power and the chances of positive outcomes.

From MD Anderson, Cardoso was taken onto the staff at Jules Bordet, but she had to complete a year of internal medicine and sit an exam before being accepted as a practising medical oncologist. This was a disappointment. “It is duplication of effort and not really fair, as if you look at my CV it’s exactly the same as a qualified Belgian medical oncologist,” she says. “I can understand it if you come from a country where your training is a few years less – you must demand that a person is competent. But we need to make procedures much more homogeneous throughout the EU, otherwise the free movement of people is not a practical reality, just a dream.”

At Jules Bordet, there has been an improvement – extra accreditation for some colleagues has reduced from a maximum of three years down to immediate acceptance in one case. But as Cardoso says, the situation is likely to be inconsistent across other cancer centres in the EU.

Cardoso was in at the beginning of the TRANSBIG project in 2002. It builds on the collaborative power of the structure developed in BIG and moves the agenda from the clinical to the translational arena. As she notes, “Most people working, for instance, on predictive

markers have been doing small studies, which despite being important, do not have enough power to provide definite conclusions. However, to do such a large trial as MINDACT requires a huge amount of money.”

MINDACT, she explains, is the first of a new generation of large-scale trials, and is using the new microarray technology to classify node-negative early breast cancer patients into high and low risk of relapse, and compare them with traditional clinical assessment. The project uses the 70-gene prognostic signature developed at the Netherlands Cancer Institute, and the clinical side of the trial is being coordinated by the European Organisation for the Research and Treatment of Cancer (EORTC).

As scientific director, Cardoso manages the network of 39 partners – clinicians, lab technicians, statisticians, and bioinformatics specialists among them. “This is why my training at MD Anderson is so important. I feel like a translator between one world and another.” It’s a big logistical challenge, particularly as the microarray technique requires fresh tumour samples to be sent to Amsterdam. “Patients are operated on, the sample is sent the same week, and within a maximum of 15 days we must have the full pathology report and the results from Amsterdam,” she says.

For this first TRANSBIG project, Cardoso has been Martine Piccart’s ‘right-hand person’. Her involvement has gone way beyond the fieldwork, to writing grant applications for the estimated 35mn euro funding that’s needed. She also plays a leading role in helping to publicise the trial. She was surprised to find that despite BIG’s success at now running some 20 worldwide clinical trials, it has been a struggle to obtain national or European Union funding. The EU is partially funding MINDACT, but has only given 7.5mn euros, and thanks to arcane rules, would only finance a new organisational



With her mother and sister Xana (right). Xana's courage in facing down obstacles after a serious childhood accident has been an inspiration to Fatima

structure and not the trial itself – necessitating the creation of TRANSBIG out of BIG. Two other TRANSBIG projects submitted to the European Commission, a microarray radiotherapy trial and a project aimed at older patients, had their funding requests rejected on the grounds they were “too ambitious” and have consequently had to take a back seat. The priority now is to court other funders for MINDACT.

In addition to all the discussions to do with funding applications, Cardoso has also had to tackle the thorny issues of intellectual property rights, the involvement of commercial interests (as part of EU rules), and ethical issues. “It’s been interesting to see the other side of clinical trials,” she says. “I imagined myself as just an investigator putting patients through trials, which is already a lot of work, but all these other legal, ethical and financial aspects have been a roller coaster of a learning curve.”

One requirement of EU funding that Cardoso has welcomed is the obligation to provide information about such trials that can be understood by a lay audience. The MINDACT/TRANSBIG descriptions are almost a

model in science communication, and Cardoso says they will be producing a patient package, perhaps with a video. She feels there is an acute need to promote wider understanding of clinical trials in general, to address the lamentably low participation rate even in the best centres, and she comments that media coverage on the ‘controversy’ of mammography, in particular, upsets her greatly.

It’s all experience that she can feed back to other young researchers via the Flims Alumni Club, where she has already served two terms as vice-president, and the Flims clinical cancer research workshops, where she is now part of the faculty. “You go on the course with an idea for a protocol and learn how to write it in a week – it would normally take months.” About 60–70 young oncologists a year now attend the workshop in Europe, with similar initiatives running in the US and Australia. “It was an important experience for me and for 99% of people who do it – it touches your career from then on.”

The Alumni Club came about, she says, because “a group of us decided we didn’t want to lose touch – young people who learn the basics of research should be kept together. So we thought about creating a society that would set up a network of young researchers across the board – not just clinicians, but scientists from other disciplines. It’s evolved nicely and we are now a member of FECS [Federation of European Cancer Societies], which has given us great support.”

The multidisciplinary nature of the Alumni Club, says Cardoso, is a feature members see as a key message for others “We want the societies to talk more to each other instead of infighting because our goal is the same. We wanted to set an example – yes, we are young and yes we still want our own societies, but we can also work in multidisciplinary groups. Perhaps our generation

“It’s put into your head that if you want to continue on top, you don’t open your game to everybody”

can be the one that really works together.” She’s happy to report that alumni members are already appearing on journal boards and various steering committees.

She adds that her own grouping, the powerful ESMO (European Society of Medical Oncologists), “must admit they can’t fight cancer alone.” But while the friction between professionals is perhaps most apparent at the society level, Cardoso feels that much of the problem stems from the very start of medical training. “The way you move up your career doesn’t facilitate communication. Medicine is an extremely competitive world and it starts in medical school.

You’re taught even before then that you have to be the best to get in and it’s put into your head that if you want to continue on top you don’t open your game to everybody. I know whenever I was second best in training I was extremely sad and disappointed.”

Second best Cardoso certainly isn’t – her medical oncology residency at Oporto was marked at 19.3/20 and in Belgium she earned a high distinction from the Free University in internal medicine and also an oncology masters (the highest distinction). “Only the best get the grants and go on getting funding – it’s the way the system works. But living and working in such a highly competitive world, you lose a bit of your idealism.”

While competitiveness for scarce resources is hardly unique to medicine, there is also an element of working the system and luck with opportunities. As she says, “I’ve known very good people who’ve been overwhelmed with clinical work and given up research. If I’d stayed in Oporto I would probably have done the same – you run out of steam at some point.”

When we interviewed Cardoso, it was at the end of a particularly difficult week that tested her idealism to the full. “I lost four patients this



week – it’s not a good time to ask me why I chose oncology. It’s so hard to tell a young girl her mother is going to die in a few days. I don’t want to lose my desire to put myself in the patient’s shoes, but it’s not easy. But when I see someone I know is going to die I know I’m doing something to avoid such deaths in the future.”

Since coming to Belgium, Cardoso has been pretty much immersed in oncology. “My family say I’m married to medicine, but I do have other interests. I love music, and also computers – I teach myself about them and have a laptop with me wherever I go. I’m a bit of a geek I guess.” She also writes poetry – as this is in Portuguese, we won’t attempt a translation here. Apart from family and friends, she misses being by the ocean – “The North Sea is not the Atlantic” – and her dream country to live and work in is Australia.

While such thoughts suggest a future move, TRANSBIG, her research and the Brussels clinic are the priority. Expect to see her name on a seminal paper on the MINDACT protocol fairly soon – and the longer the list of co-authors, the happier she’ll be.

Thanks for your help! Cardoso with her fellow vice-president of the Flims Alumni Club Vanesa Gregorc (left) present the veteran French oncologist Jean-Pierre Armand with the first FAC Award for Exceptional Support, 2003. Behind them stand the current president Razvan Popescu and past president Jean-Charles Soria

“If I’d stayed in Oporto I would probably have given up research – you run out of steam at some point”

‘We will help you live until you die’

→ Joanna Lyall

Cicely Saunders touched the lives of millions of terminally ill patients through her promotion of hospices and palliative care. Though she died this summer at the London hospice she founded in 1967, her fight for all patients to have the right to live well and die pain free and in dignity goes on.

Shortly before her death in St Christopher's Hospice this summer, Cicely Saunders took part in a television programme that called for better access to good palliative care in the UK. Few who knew her would be surprised that at 87, and only weeks away from her own death from cancer, she still accepted the opportunity to speak out on the issue to which she had dedicated her life.

Born in 1918, months before the end of the First World War, Saunders is widely recognised as a pioneer of the modern hospice movement, founding the trail-blazing St Christopher's hospice in south London in 1967. Though the concept of offering a place of support and comfort for the dying was not new, such hospices as existed at that time were mainly run by nuns. Saunders' unique contribution was to insist that

the medical profession had an equal responsibility to help their dying patients live as full and pain-free lives as possible for as long as possible.

It was a hard battle to win, and, as is clear from her correspondence, published in paperback earlier this year, Saunders recognised the message of palliative care is one that needs constant reinforcement.

In a letter written in 1972, she warned that, "Unless we teach students even more widely than we are doing and continue battling away with those already trained, patients will simply not get the quality of care they should receive."

It was due to her work that palliative medicine was first recognised as a specialty by the Royal College of Physicians in 1987, 20 years after she started St Christopher's hospice as a centre for treatment, teaching and research.

Robert Twycross, who worked as a research fellow at St Christopher's, from 1971 to 1976, says "When Cicely first became involved, doctors largely neglected the dying. There was no systematic approach to pain and symptom management and the idea that patients had to 'earn' their analgesia was still prevalent."

Twycross, now emeritus clinical reader in palliative medicine at Oxford University, says that as well as being "an excellent physician and a charismatic figure with a superb brain... she was extremely effective at engaging powerful allies and spreading the knowledge she had gained."

Saunders, he says, saw the benefits of pain relieving drugs being given regularly, pre-empting pain. She initiated research which showed the effectiveness of morphine and spread what she had learned.

"She was a visionary and also a



ST CHRISTOPHER'S HOSPICE

She was a great advocate for research and made the case that morphine is the gold standard

propagandist and disseminator of knowledge. She always said she didn't found the hospice, it found her, and certainly it was an idea whose time had come. But without her in the background there would not have been a recognition of palliative medicine as a specialty.

"She was also a gifted teacher. Her concept of 'total pain', introduced in an article in 1964, encouraged students and health professionals to consider the mental, spiritual and social dimensions of the patient's feelings.

"Cicely was never just a symptomatologist," he says.

PAIN AND PALLIATION

Twycross' research at St Christopher's in the 1970s showed that morphine was as effective in preventing and

relieving pain as the mixture of diamorphine, cocaine and anti-emetic in chloroform water, then known as 'the Brompton cocktail'. Importantly, it also showed that there were no problems of addiction when morphine was given for pain relief.

"In the 1970s we killed the Brompton cocktail and were essentially using morphine in tap water and an anti-emetic in selected patients," recalls Twycross. This had considerable implications for pain control in countries where diamorphine could not be prescribed.

Saunders had already seen the benefits of pre-empting pain by giving drugs regularly when she worked as a volunteer nurse in the evenings at St Luke's hospital, in central London between 1948 and 1955. But the

practice was not widespread, and she saw that part of her task was to act as a catalyst to promote better care both in the UK and beyond.

Her background gave her a special perspective from which to do this. Forced to give up nursing because of a back problem, she trained as a hospital almoner (medical social worker) and worked at St Thomas's hospital (south London), on a cancer ward, before starting medical school at the age of 33, qualifying in 1957, at the age of 38.

Some of her first articles, written well before the opening of St Christopher's, were for the nursing press in the 1950s, and her writings stressed the role of nurses in hospice care. She believed it was the nurses at St Luke's who came up with the idea



“You matter because you are you, and you matter until the last moment of your life”

of giving drugs regularly to patients with advanced cancer to prevent pain.

It was Saunders' concept of 'total pain' that sparked the modern palliative care movement, according to Phil Larkin, lecturer in palliative care at the National University of Ireland in Galway and vice-president of the European Association of Palliative Care (EAPC).

“She could speak to a number of levels, and as a nurse she hugely validated the role of nurses in palliative care. She was also a great advocate for

research and made the case that morphine is the gold standard,” he says, adding that some doctors still need to be reminded that prevention is better than trying to treat pain when it has already occurred.

PAIN IS STILL A PROBLEM

However, regulation is still hampering effective palliative care in many parts of the world, he says. “Despite clear evidence that morphine remains the gold standard for pain relief and may be administered safely

and with relatively little expense, excessive and unnecessary regulation of opioids still prevents its use where it is most needed.”

Geoffrey Hanks, professor of palliative medicine at the University of Bristol, and honorary president of the EAPC, agrees that many patients with cancer pain still do not benefit from the advances made many years ago. “We have the knowledge to relieve pain in about 80–90% of patients with cancer. But the prevalence of unrelieved cancer pain is 50%.”

He argues that pain relief is still poorly understood by many, and that some patients are wary of taking morphine. "Our problem is still the inadequate use of powerful drugs by non-specialists. And the reluctance of patients to take these drugs."

But while it may be depressing to see how little has changed for some cancer patients since Saunders started her campaign, a head of steam is clearly building up to force a change of attitudes at the highest level. A group of pain specialists from 16 countries, known as the Opioids and Pain European Network of Minds (OPENMinds), is calling for "a positive educational programme to change attitudes on the medical use of opioids, extending from the core curriculum of medical students to patients taking opioids and their families."

In a report to the European Parliament in June, the group pointed out that many European countries demand special prescription forms for strong opioids, different from those for other drugs.

In Italy, Poland, Portugal and parts of Spain, doctors must travel to regional offices in order to access the prescription forms used to prescribe strong opioids. In Austria, Germany, Portugal, Italy and Switzerland triplicate forms must be filled in.

The report concludes that "These unnecessary regulations reinforce an outdated viewpoint associating these medicines with addiction, abuse and death, despite considerable evidence showing the efficacy of their use in managing chronic pain," and it calls for a loosening of bureaucratic regulations that restrict doctors' freedom to prescribe effective pain relief.

A GLOBAL VIEW

While wanting to spread the idea of high quality care for the dying as

widely as possible, Saunders always stressed that the pattern of services, should be determined at a local level. She lectured widely and fostered international networks and received thousands of visitors to St Christopher's, but did not want it to be taken as a global template, saying her main aim was "to encourage people to do

this work in whatever way is most suited to their circumstances."

Later in her career, reviewing global developments in hospice care, Saunders said: "a worldwide spread has shown that the basic principles can be interpreted in widely differing cultures and with few resources other than the family values of the developing world."

CICELY SAUNDERS

Cicely Saunders was born in London on 22 June 1918, the eldest child of a successful estate agent. Educated at Roedean, a girls' private boarding school, she went to Oxford to read philosophy, politics and economics, but left when war broke to train as a nurse at St Thomas's Hospital, South London, qualifying in 1944. Forced to give up nursing because of a back problem, she trained as an almoner (medical social worker) and it was while working at St Thomas's in 1948 that she met David Tasma, a 40-year-old agnostic Polish Jew who was dying of cancer. In the months before his death, she fell in love with him. They discussed the needs of the dying and he left her £500 and said "I'll be a window in your home."

Soon afterwards she went to work as a volunteer in the evenings at St Luke's hospital, in central London. It was at St Luke's, which had been founded as the Home for the Dying Poor in 1839, that she saw the benefits of pain relieving drugs being given regularly. When she told a surgeon colleague that she wanted to go back to nursing, he said: 'Go and read medicine, it's the doctors who desert the dying.' At the age of 33, with no background in science, she was accepted to read medicine at St Thomas' and qualified in 1957, at the age of 38. Two years later, having worked at St Joseph's Hackney, a hospice established by the Irish Sisters of Charity in 1905, she drew up a plan for her own hospice at an estimated cost of £200,000. St Christopher's opened in 1967.

1944 Qualifies as state registered nurse

1945 BA (war degree) Oxford

1945 Diploma in Public and Social Administration

1947 Works as an almoner (medical social worker) at St Thomas's Hospital

1957 Qualifies as a doctor

1958–1965 Works at St Joseph's Hospice, east London

1967 Founds St Christopher's Hospice and is awarded the Order of the British Empire

1974 Becomes a fellow of the Royal College of Physicians

1980 Is made Dame of the British Empire

1980 Marries Marian Bohusz-Szyszko. She was 61 and he was 79

1989 Is awarded the Order of Merit

1981 Is awarded the Templeton Foundation Prize

2001 Is awarded the Conrad N Hilton Humanitarian Prize

2002 The Cicely Saunders Foundation is established at King's College London

2005 Dies in St Christopher's Hospice, July 14



ST CHRISTOPHER'S HOSPICE

The entrance to St Christopher's hospice, founded by Saunders in 1967

Carl Johan Furst, director of the EAPC Centre For Palliative Care Support in Eastern Europe, hopes that her emphasis on local patterns of care, forging international links and learning from each other, will be maintained by her successors.

Colleagues in eastern Europe need support to fight for recognition for palliative care and basic drugs, he says. "The main issue is morphine availability. Basic morphine tablets costing about 10 cents are just not available."

He hopes forming links with centres in eastern Europe and inviting healthcare professionals to conferences will strengthen the development of palliative care services. "And surely we in western

Europe can learn too. How do you provide palliative care without the basic drugs? What sort of qualities do you draw on?"

In his introduction to her letters, Canadian oncologist Balfour Mount says Saunders "has been the catalyst for a paradigm shift in global health care." The lessons from her work on pain and symptom control may need constant reinforcing to successive generations, but there can be little doubt that she had a huge effect on attitudes to care of the dying. Her focus was on quality of life, listening to the patient, helping them to feel safe and involving the family. "You matter because you are you, and you matter until the last moment of your life. We will do all we can, not only to

help you die peacefully, but also to live until you die," she said.

Looking back on her own therapeutic journey, which began on the wards of St Thomas's in 1941, she concluded, "Whatever happens it will still matter that we go on listening and we continue our questioning. Above all, my experience emphasises that the practice of medicine includes more than specific treatments."

Marilene Filbet, president of the EAPC and director of the palliative care unit at the Centre Hospitalo-universitaire, Lyon, France, believes Saunders was responsible for 'a silent revolution' and that her focus on listening to and comforting the patient is a model which could be applied to a wide variety of settings, including care of the elderly, people with AIDS and the severely disabled. "Before, we had the paternalistic model of medicine with the doctor deciding what was good for you. Cicely Saunders' stress on communication, team-working, listening and freedom of choice for the patient and holistic care was revolutionary."

Filbet remembers being somewhat taken aback when she met Saunders. "I had somehow expected someone gentle, and was struck by her dynamism and force of character. This was clearly someone who had battled..."

Saunders would not demur. When someone observed in her last portrait (now in the National Portrait Gallery in London) a look of "love and steel" she said: "Love and steel, how kind. Anyone doing hospice work will need plenty of both."

A new European report calls for doctors to be given the freedom to prescribe effective pain relief

What's coming up in breast cancer?

Experts piece together the big picture

→ Mary Rice

In a follow-up to the first Breast Cancer Observatory, held in 2004, international names in radiotherapy, surgery, medical oncology, genetics and patient advocacy gathered again in Milan this June to predict the major changes for the year ahead.

With so much new information published every week on every aspect of cancer research and cancer care it is enough of a challenge for clinicians and researchers to keep up to speed in their own specialist area. Yet the implications of the new knowledge can be lost if it is not seen in the context of what is happening in the field as a whole.

To try to address this problem, last year, the European School of Oncology initiated an Observatory session at the annual Milan Breast Cancer Conference hosted by the European Institute of Oncology. The Observatory provides a platform where experts from many fields can present an overview of where they feel the most significant progress can be expected in the coming year.

This June, a second Observatory was held, which brought together leaders in their fields from all over the world, representing surgery, radiotherapy, medical oncology, basic science, clinical trialists, and patient groups.

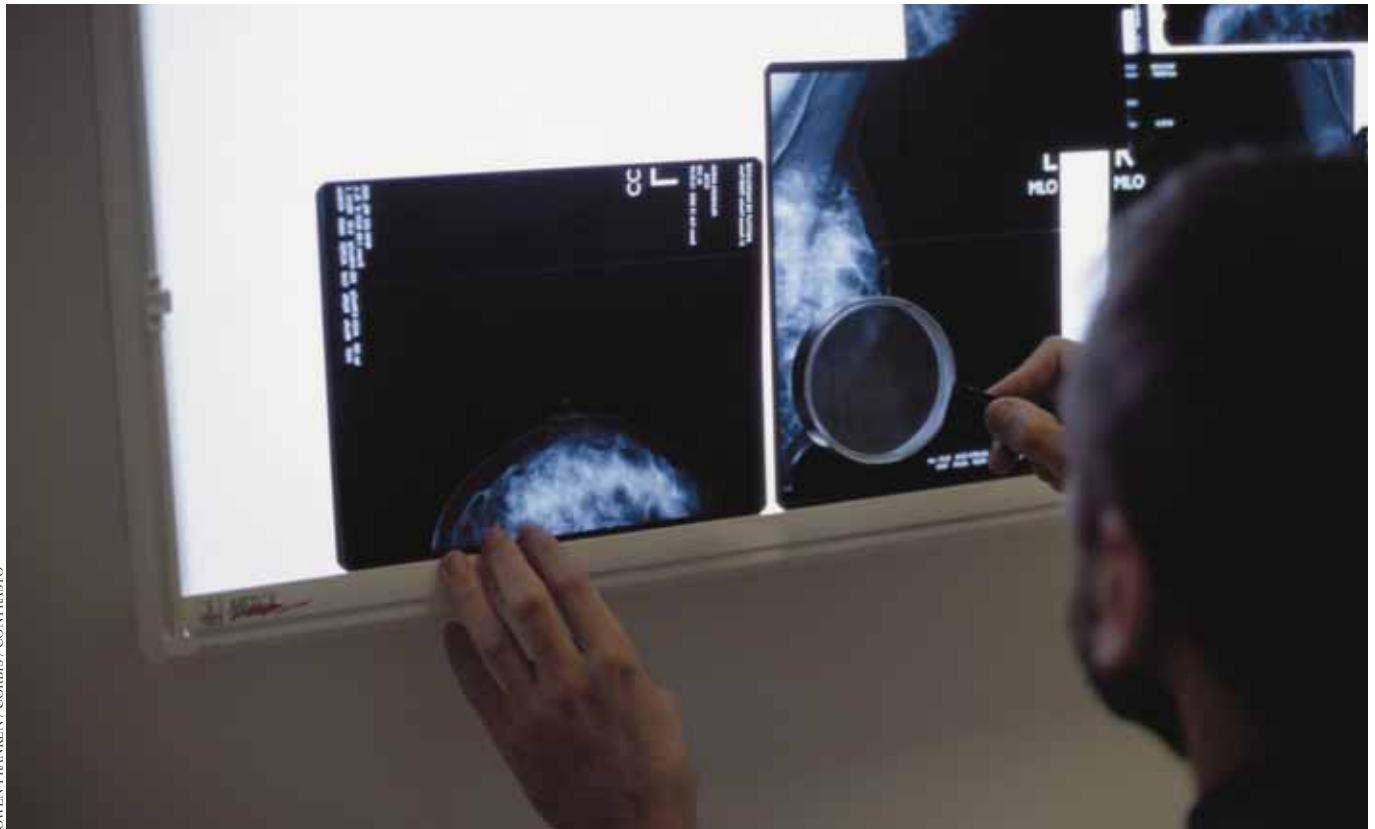
This year's Observatory revealed a sense that the molecular biology approach to cancer is finally beginning to make itself felt in the clinic in the areas of diagnostics, prognostics, treatment selection, and available therapies. As it does so, the financial implications of this new high-tech era are becoming an increasing factor in access to top quality cancer care.

Benefits from recent developments in 'targeted' radiotherapy, which concentrates the dose on the malignancy, sparing healthy tissue, were also flagged up, as was the slow but steady progress in greater patient involvement and in implementing European guidelines and recommen-

dations for improving breast cancer screening and care.

FROM DESCRIPTION TO PREDICTION

Patrick Borgen, of the Memorial Sloan Kettering Cancer Centre, New York, predicted that, overall, the trend in 2006 would be towards disease class prediction. The traditional descriptive definition of breast cancers will be replaced by a functional one, with cancers being defined according to risk of recurrence, allowing treatment to be tailored to individual tumours. Crucially, new testing technologies that can be conducted in a pathology lab are set to bring genetic fingerprinting of tumours into everyday clinical use. Tests such as Oncotype DX, which are just coming into use in the US, use polymeric chain reaction (PCR) to identify tumour genetic signatures



OWEN FRANKEN / CORBIS / CONTRASTO

“Breast cancers will be defined according to prediction of risk of recurrence”

based on a very limited number of genes. At a current cost of around \$3,200–\$3,500 (euros 2,750–3,000) a go, they are much cheaper than the microarray technique being used in clinical studies.

Aron Goldhirsch of the European Institute of Oncology, Milan, agreed that using specific targets via molecular and pathological identification remains the great hope for 2006. “Genetic signatures and other molecular characteristics, like altered proteins, will aid in the definition of

types of cancers according to prediction of response to specific therapies,” he said. “These features, together with age, will radically change the way treatment decision making for individual patients is performed.”

Tumour markers and genomic profiles have a number of other uses, he added.

They can help improve monitoring treatment effects and might aid assessment of efficacy for pre-operative systemic therapies, providing

more women with the chance of breast preservation. They can also be used to identify sub-groups of patients at high risk of recurrence in order to modify treatment. This may help in identifying patients with in-situ carcinoma, who should be spared radiation therapy after tumour excision. “Avoiding unnecessary damage to normal tissue is vital,” he emphasised.

COMBINATION THERAPIES

New opportunities for improving the

“There will be increased use of aromatase inhibitors and trastuzumab at all stages of disease”

use of therapies for patients with advanced breast cancer by using the novel targeted treatments together with cytotoxic agents are becoming available, said Goldhirsch. Novel agents with several biological targets, which include overexpressed receptors, cellular pathways particularly active in tumour cells, and molecules responsible for tumour vessel formation (angiogenesis) have all shown some efficacy in controlling disease progression.

The role of some of these new compounds, used as single agents or in combination with cytotoxics, is already being tested in women with advanced disease. They include tyrosine kinase inhibitors like erlotinib (Tarveca), targeted to the epidermal growth factor receptor (EGFR), or lapatinib, a dual EGFR and ErbB-2 (Her2/neu) inhibitor, and anti-angiogenic antibodies such as bevacizumab (Avastin). Their potential impact as an effective adjuvant treatment will be explored in the very near future.

ADJUVANT THERAPY

Roberto Labianca of the Ospedali Riuniti, Bergamo, Italy, talked about the implications for adjuvant therapy. Not so long ago, whether or not to prescribe adjuvant treatment was decided on standard criteria such as age and menopausal status, and the spread of disease.

In the near future, he said, whether or not a patient needed adjuvant treatment on a more personalised or ‘tailored’ basis would be decided by looking at the biology of the tumour and its genetic profile. Key to this would be access to genomic testing, such as the new Oncotype DX test. This ‘new biological frontier’ would spare many women from unnecessary chemotherapy and lighten the burden on health budgets.

Novel biological compounds, such as the monoclonal antibody trastuzumab (Herceptin) will soon enter the adjuvant setting. Targeted treatment will therefore go beyond the domain of endocrine therapies.

More work will be needed to address the issue of resistance.

Alan Coates from the University of Sydney, Australia, said aromatase inhibitors, either alone or in sequence with tamoxifen, will become the standard adjuvant treatment for women with steroid hormone-receptor-positive breast cancer. “There will be increased use of aromatase inhibitors and trastuzumab at all stages of disease,” he said, adding that adjuvant chemotherapy regimens will continue to be refined with particular attention paid to the selection of drugs and dosage, and to the treatment schedule.

TARGETED RADIOTHERAPY

Following the huge advances made in breast-conserving surgery, there is now a great deal of interest in finding ways to minimise the amount of tissue exposed to radiotherapy.

One way this is done is to minimise the irradiated area. Jacques Bernier, from the Institute of Oncology in Bellinzona, Switzerland, said, “Until fairly recently the idea was widespread that surgery to the whole mammary gland was the right way to go. With surgery now often limited to the index quadrant, this means that we can limit radiation treatment to that area.” This, says Bernier, will have a major effect on quality of life, not to mention economic benefits to healthcare systems.

Increased use of high-conformality radiation therapy is another way in which clinicians are trying to spare healthy tissue. By delivering doses

OBSERVATORY PANEL

- **Jacques Bernier**, radiotherapist, Switzerland
- **Patrick Borgen**, surgeon, US
- **Alan Coates**, medical oncologist, Australia
- **Alberto Costa** (chair): European School of Oncology, Italy
- **Aron Goldhirsch**, medical oncologist, Italy
- **Marie Claire King**, geneticist, US
- **Stella Kyriakides**, patient advocate, Cyprus
- **Roberto Labianca**, medical oncologist, Italy
- **Umberto Veronesi**, surgeon, Italy



With intraoperative radiotherapy, patients will be spared the need to report for daily treatment for several weeks following conservative surgery

breast unit accreditation process, Stella Kyriakides, President of Europa Donna (the European Breast Cancer Coalition), also predicted greater patient involvement in the planning of clinical trials. Advocates are being asked more often to sit on trial committees, she said, but further work is needed to ensure that their input is valued and taken into account in all appropriate areas.

Coates predicted that details of the outcomes of clinical trials will become more available to the general public, and patients would be increasingly interested in participating in trials.

ECONOMIC TOXICITY

One warning note raised by some speakers was the cost of improvements in cancer therapies and the likely social repercussions. Borgen, from the Memorial Sloan Kettering, presented some chilling figures. Treating one patient who metastasises with breast conservation, chemotherapy and tamoxifen costs between \$50,000 and \$75,000 (41,000 and 62,000 euros). But treatment with the angiogenesis inhibitor bevacizumab alone could be as high as \$130,000 (107,500 euros) a year. That cost will multiply if treatment is with cocktails of different types of targeted and non-targeted drugs.

from many different angles it is becoming possible to target the radiation increasingly precisely on tumour while sparing surrounding areas. This is particularly important in avoiding cardiac damage to breast cancer patients.

There are also moves to try to define more closely patients who really need post-mastectomy radiation, in order to spare patients who are unlikely to benefit. A study looking at the impact of radiotherapy to the axillary nodes in patients at intermediate risk post-mastectomy, is set to start later in the year.

Another highly significant development Bernier pointed to is the introduction of intraoperative radiotherapy. Early trial results, he said, are very encouraging, though the technique is not suitable for all patients.

“We can irradiate the surgical bed for 20–25 minutes, and once again this has major advantages for the patient in terms of quality of life as well as in terms of savings to healthcare providers.”

ORGANISATIONAL CHANGES

Changes were predicted in the way care is delivered and the way clinical trials are planned. Coates predicted that patients will be treated in ever greater numbers in specialist centres offering multidisciplinary treatment planning and care. Formal accreditation of breast units throughout Europe will be done by the European Society of Mastology (EUSOMA) through a codified process including site visits and with the full participation of the patient advocacy group Europa Donna.

In addition to their role in the

“Intraoperative radiotherapy has major advantages
in terms of quality of life”

“Patients will be treated in ever greater numbers in specialist centres”

Add on to that the costs of the increasingly high-tech investigations needed to characterise the cancer in order to establish which therapies may be appropriate, and real questions emerge about whether societies with universal public health systems will be prepared to foot the bill, opening the possibility that these therapies may be available only to those who can afford to pay privately. Health insurance systems may start offering two-tiered premiums, restricting expensive targeted treatments to patients paying the higher rate.

However, better selection of the patients could offset some of the higher costs of the therapies, by ensuring that therapies are used only in patients who are known to be likely to respond. In both developed and developing countries, clinical predic-

tion for the appropriate use of specific drugs in cohorts of patients with a predictable highest yield of treatment will become increasingly important. This may help access to appropriate medical care even for the less cared-for populations.

ETHICAL TOXICITY

Goldhirsch made the point that with so much at stake, the pressure for unethical marketing will increase. “There are people out there pushing information who have a financial or political interest in ‘breakthroughs,’” he said. The point was reinforced by Borgen, who referred to the case of a woman with bone metastases refractory to hormone ablative strategies who qualified for an experimental trial of taxane plus Avastin (bevacizumab).

Her comments that she suffered no side effects and that her quality of life was much improved were widely reported. However, later it transpired that she had transferred her entire investment portfolio into Roche, the company that makes Avastin, raising questions about how impartial her comments about the drug really were.

A MESSAGE OF HOPE

Observatory Chair Alberto Costa, from the European School of Oncology, summed up the changes expected in the fields of medicine, radiotherapy, surgery, diagnostics, clinical research and organisation of care (see box). “The overall picture,” he said, “is hopeful – for better working together, learning from each other, and providing the very best service to the patient.”

10 PREDICTIONS FOR 2006

- Breast cancer will gain more acceptance as a genetic disease. Technology will detect more mutations; competition will start among testing technologies
- Research will tackle the issue of interactions between tumour and stroma and normal tissues, looking for new targets for therapies
- Interest in the value of local control will increase, leading to more diagnoses of ductal carcinoma in situ (DCIS)
- Assessment of tumour characteristics to guide therapy choice will become increasingly common and accurate
- Systemic therapies will continue to become less toxic, the use of cytotoxic chemotherapy in patients with small node-negative breast cancers will decrease
- Use of trastuzumab (Herceptin) and studies of Avastin will expand quickly and dramatically. Taxanes will be monitored.
- The issue of treatment duration and maintenance of response will be tackled separately for endocrine responsive and endocrine non-responsive tumours
- Competition and cross-fertilisation will increase between partial breast (PBI) and whole breast irradiation (WBI)
- The real impact of post-mastectomy irradiation will be challenged, biological response modifiers will be back
- Formal accreditation of breast units will start in Europe through a codified process, including site visits and with the full participation of advocates

Switzerland's cancer president

→ Peter McIntyre

When it comes to fighting cancer, coordination is key. And in the fiercely autonomous cantons of Switzerland, that coordination is provided by a network of institutes, leagues and foundations that covers everything from prevention and fundraising to clinical research. They all have one man in common – **Giorgio Nosedà**.

The outside world sees Switzerland as a well-ordered country at the heart of Europe, famous for its neutrality, precision watches and the excellence of its chocolate, industry, medicine and trains.

But Switzerland is complicated. Physically it is indeed at the heart of Europe. But Switzerland has never joined the European Union. It is home to the World Health Organization and other UN bodies. But it only became a full member of the UN in 2002.

It is a neutral country with more soldiers under arms proportionately than any other European country. It is a democratic country that did not give all women the vote until 1971. It is a small country of seven million people, but it has four official languages and a federal system of government that gives huge autonomy to its 26 cantons (regions).

These contradictions can be seen in the Swiss health-care system, which is the responsibility of the cantons, rather than the federal government. The health system is a mix of compulsory insurance and public funding, with large

variations in funding by cantons. There is excellence in every aspect of cancer surveillance and treatment somewhere in Switzerland and the Swiss pharmaceutical industry is a leading producer of anticancer drugs. However, the Swiss system of cancer prevention, surveillance and care is patchy and lacks coordination and equity.

In terms of treatment, Switzerland is amongst the leaders in Europe. According to the EURO-CARE 3 study (2003), Switzerland stands fifth overall in terms of cancer survival, and tops the European league for treatment of rectal cancer in men. However, since Swiss cancer registries cover only 55% of the population, the EURO-CARE data may not be completely accurate.

Treatment needs to be good. The Swiss population has a higher risk of cancer than the average of the (former 15-country) European Union. Half of Swiss men (50%) and almost a third of Swiss women (32%) experience cancer at some point in their lives. For men in these 15 countries, only France has a higher rate, while Swiss women have the highest risk in all 15 countries.



TICINO MANAGEMENT

A NATIONAL PROGRAMME

The first ever Swiss National Programme Against Cancer, published earlier this year, points out that with 31,000 new cases a year and 15,000 deaths, cancer is responsible for the greatest number of lost years and biggest loss of quality of life.

The programme says, “A large part of the Swiss population is poorly informed about cancer. Even the scientists and the politicians in

charge are not familiar with all the specific causes. In addition, equality of opportunity has not yet been achieved: the chance of being affected by cancer or of having a tumour diagnosed varies by region, canton and social and cultural grouping.”

Part of the blame is placed on the variety of political approaches to health, especially to prevention and screening. The programme criticises “vaguely formulated” legal structures that leave responsibility with the cantons unless there is a provision to the contrary. The financial situation is equally difficult. “Cantons have few resources to undertake new activities, to an extent that they have to do their best while limiting their spending.”

In October 2001 the Federal Department of Public Health (OFSP) and the Swiss Conference of Directors of Health for the Cantons (CDS) gave the job of drawing up a national cancer programme to Oncosuisse, an umbrella organisation of Swiss cancer associations and institutes.

And this is where Professor Giorgio Nosedà comes in, as he is president of Oncosuisse, and also president of other key groups developing the fight against cancer. And, since this is complicated Switzerland, naturally he is not an oncologist.

Giorgio Nosedà is a cardiologist at the Lugano Hospital (Ospedale Civico), in the Italian part of Switzerland, the canton of Ticino.

“The chance of being affected by cancer varies
by region, canton and social and cultural grouping”

He recalls the deputies trooping outside to smoke, after the law took effect

His life has been twin tracked. On one path his own successful career; and on the other, the pivotal role he has played in helping to tackle the lack of cohesion in Swiss cancer services.

Noseda studied in Zurich and in Paris in the 1960s. His cardiology training was completed at the Hammersmith Hospital in London and as senior registrar at Berne. In 1974, he became chief of internal medicine at the Regional Hospital Beata Vergine in Mendrisio, in Ticino. Soon afterwards, he was elected a member of the cantonal Parliament, the Gran Consiglio. His beliefs in liberalism and society (“liberté, égalité et fraternité, et société, aussi” as he puts it) located him in the social democratic grouping, but no party. He was in the Canton Parliament from 1975 to 1989, and responsible for two significant laws.

LAWMAKER

The ‘sanitary’ law in 1987 set out to improve public health, regulating the quality of food and water and, radically for the 1980s, limiting smoking in restaurants to special smoking areas. It also banned smoking in the Parliament. Noseda recalls the deputies trooping outside to smoke, after the law took effect.

The hospital law of 1982 was less eye-catching, but just as important. It brought together all 10 hospitals in Lugano, Bellinzona, Mendrisio and Locarno under one administration, covering hospital care for the whole of Italian-speaking Switzerland. Ticino stole a march on the rest of Switzerland with an ability to plan and rationalise hospital services.

During this period, Noseda was persuaded to join the Ticino League Against Cancer. As he was a visiting professor at Berne University Hospital, he was also deputed to be the representative to the national Cancer League in Berne, mainly on the grounds that he would be there anyway!

The work to improve cancer prevention,

detection and treatment caught Nosedá’s attention. In 1989, he gave up his seat in the Gran Consiglio to become president of the Swiss League Against Cancer. He saw that although many individuals and organisations were working on cancer, there was no single voice. Not even the Swiss Cancer League had functioning leagues in every canton. He worked towards the idea of a centre in Berne that would bring together the leading organisations.

Nosedá learned from Ticino, where Franco Cavalli had started an oncology division in Bellinzona, which grew into the Institute of Oncology of Southern Switzerland (IOSI). Cavalli was then a member of the same regional Parliament as Nosedá. He had persuaded politicians in Ticino to take cancer services seriously, and attracted leading practitioners to work with him.

Nosedá says, “Franco Cavalli set up a comprehensive cancer service with a centralised structure at Bellinzona, and units in every public hospital in the canton, a network which includes translational research and basic research. Most cantons do not have that.”

Understanding what could be done with better coordination, Nosedá was the inspiration behind what he calls “a cancer house” in Berne. This opened in 1996 as a home for a number of organisations that were beginning to work more closely together. They include the Swiss Cancer League, the Swiss Institute of Applied Cancer Research (SIAC) and the International Breast Cancer Study Group.

SIAC itself consists of three partners, the Swiss cancer registries (there are nine of them), and two clinical cancer research organisations: SAKK, responsible for research in adults, and SPOG, its paediatric counterpart. SAKK and SPOG each have nine centres around the country.

The centre at Berne is now home to about 100 people who are trying to coordinate and

develop the fight against cancer. Nosedá says, “This was the first step towards my idea for a network of institutions that would address the problem of the fragmentation of services in Switzerland. And I was lucky to secure funding, particularly from this region.”

Eventually these organisations formed Oncosuisse, an umbrella group that allows them to speak with one voice while they retain their autonomy. Nosedá, president of Oncosuisse, thinks of it like a holding company that can focus on strategic work. Oncosuisse also works with other leading Swiss institutions such as the Swiss Institute for Experimental Cancer Research (ISREC) in Lausanne.

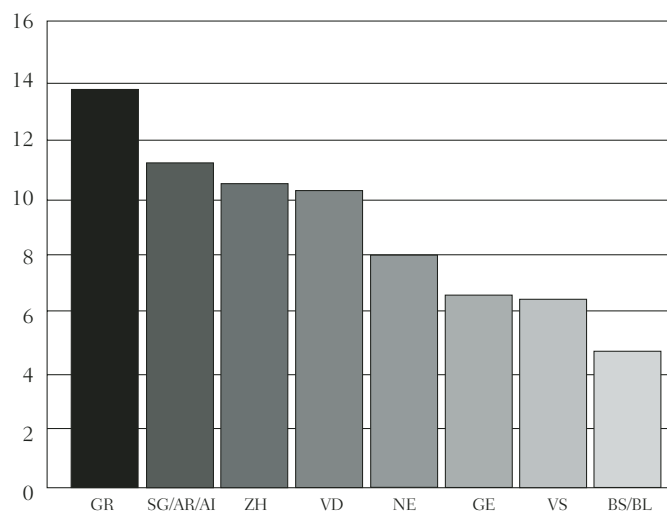
A PATCHY PICTURE

In the bumpy graph that charts inequalities in Switzerland, the different rates of breast cancer are particularly striking. In the francophone part and Italian-speaking Ticino, survival of women with breast cancer is better than in the German east. The superior rates in the French areas can be explained in part by the fact that five French-speaking cantons set up a breast screening system. Ticino, however, got there by a rather more haphazard route.

Nosedá says, “We have good screening in Ticino, but no programme. The public is very educated, and women go to the gynaecologist and ask for screening. But gynaecologists make too many diagnostic procedures. In a controlled programme, mammography is every three years. In our canton, many women have mammography every one or two years. Results are good but we spend a lot of money unnecessarily.”

There are other anomalies. Graubünden in the east has twice the cervical cancer incidence of Geneva and three times that of the area around Basel. “Because health is a cantonal issue, we have 26 different health laws, says Nosedá. “In Graubünden region there is no oncology centre. Other parts of Switzerland have centres based at the Universities of Zurich, Basel, Berne, Geneva and Lausanne. In the south of Switzerland we have the Institute. This explains some of the inequality of treatment which exists in our country.”

The Swiss National Programme Against



Cancer incidence varies greatly across Switzerland. You are three times more likely to develop cervical cancer if you live in Graubünden (GR) than if you live in Basel (BS)

Source: Bouchardy C et al (2000), quoted in the Swiss National Programme Against Cancer, 2005

Cancer, written by Reto Obrist and Doris Schopper with the collaboration of many specialists, was published at the beginning of 2005 with five aims:

1. Better prevention
2. Early detection
3. Better quality diagnosis and treatment throughout Switzerland (better homogeneity)
4. A cancer register in all cantons with better national coordination to improve the epidemiological knowledge
5. Improved research, especially clinical research

The Swiss National Council has been asked to adopt a national law especially for prevention and early detection to back the fight against cancer. Nosedá says, “Now we are awaiting a decision. The Swiss Government and the cantons have built up a platform named the Swiss Health Policy. We hope that through this we can receive money for our programme. But it is very difficult, because some cantons want to preserve their autonomy.”

Nosedá has a vision for a network of oncology centres across Switzerland that will carry out screening and collaborate on treatment and

While many individuals and organisations were working on cancer, there was no single voice

clinical research. But this will take money as well as political agreement.

Along with others, he created Swiss Cancer Research (KFS), which gives SF 10–12mn (6.4–7.7mn euros) each year for research. Before Christmas, KFS will send out two million letters appealing for money, reaching almost every family in Switzerland. As president of KFS as well as Oncosuisse, Noseda is the public face of this campaign. However, despite raising these large sums, he says there is not enough money for all they want to do.

In 1996, Zurich banker Thomas Hoepfli set up the Swiss Bridge Foundation to win support for the fight against cancer from the Swiss private banking sector. In 2004 Swiss Bridge raised more than SF 3mn (almost 2mn euros) for research in Switzerland and abroad. Its scientific committee is headed by Gordon McVie, and its board of patrons includes Umberto Veronesi. Giorgio Noseda is president of the Board of Trustees. One of the Swiss Bridge projects close to his heart is Biobank Suisse, a Swiss national tumour bank, which will collect biological materials from cancer patients, from biopsies and blood and urine samples, together with clinical data. Noseda was one of the originators of this project, which is run by Reto Obrist, Director of Oncosuisse.

AN INTERNATIONALIST

Oncosuisse also started an International Collaborative Cancer Research Project to fund collaborative projects between Swiss and foreign institutions.

Switzerland is home to important collaborative work. The International Breast Cancer Study Group, built up by Aron Goldhirsch and Monica Castiglione, now includes 35 countries in Europe, the USA, Canada and Australia.

The Foundation for Treatment and Research in Lymphomas, part of IOSI, hosts

the International Conference on Malignant Lymphomas every three years. Initiated by Cavalli in 1981, this has evolved into the world's most important meeting for the study and treatment of lymphomas. The International Extranodal Lymphoma Study Group (IELSG) established by Cavalli at Bellinzona now has 133 participating institutes, from Europe, Australia, north America, Asia and Latin America, and pools data from almost 3,400 patients.

Noseda is also president of the Foundation Council of the Institute for Research in Biomedicine (IRB), which opened in the year 2000 in Bellinzona, to foster collaboration among research groups studying basic mechanisms of immune defence against bacteria, viruses and tumours, molecular biology and basic cell research. Led by Antonio Lanzavecchia, the IRB has about 60 researchers, with more research teams expected to join. The Laboratory of Experimental Oncology, part of Cavalli's Institute, has a team of more than 20 researchers in the same building working on molecular pharmacology, drug development, cancer genetics and molecular biology.

International collaboration involving Swiss institutes is becoming more organised. The European School of Oncology runs an increasing number of its courses at the Oncology Institute of Southern Switzerland.

For his part, Cavalli is in no doubt that Noseda has played a pivotal role in the development of awareness and funding about cancer in Switzerland. "I have been collaborating with Giorgio in various organisations, in a variety of situations, for more than 30 years. As chief of medicine, he was the first to have the idea of creating an 'oncology service' at the beginning of what has now become the Oncology Institute of Southern Switzerland (IOSI). He is a great

organiser, a superb fundraiser, and moreover has a genuine interest in oncology.

“He has played a key role in reshaping the Swiss Cancer League and in creating Oncosuisse, the derivation of all organisations dealing with cancer in Switzerland. Because of his engagement with cancer, it is today easier for me to discuss cancer control planning and even cancer research with him than with many ‘pure’ oncologists!”

A BUSY RETIREMENT

Now aged 66, Professor Nosedo will retire from his post at the Lugano Hospital at the end of 2005. His plans, however, do not sound like retirement. He will be a practising physician two days a week, and has a number of projects to develop.

He has plans, for instance, to create a Swiss Institute of Epidemiology, beginning by networking the existing nine cancer registries, then establishing new registries in all the other cantons and culminating in a more general epidemiology institute, probably attached to a Swiss University. “At present, teaching and research in epidemiology and the evaluation of patterns of care are weak. You have to have a base to fight against cancer. Only if you know the causes and the epidemiology can you do good prevention work. And our policy is to prevent cancer.”

He is also under pressure to help with other people’s plans. Cardiologists, bemused that their colleague had become the public face of cancer prevention and fund raising in Switzerland, have asked him whether he might switch his attention to heart disease, which faces many of the same problems. They would like him to help in the formation of an organisation to be named CardiovascSuisse

“I was invited by the Swiss Heart Foundation to speak at a conference in 2002 – Could we have an Oncosuisse for cardiology?”



The proportion of women over 40 who reported having had a breast scan at least once ranged from less than 32% in the east, to more than 60% in Ticino in the South and in Vaud, Geneva and Jura in the French-speaking part of Switzerland

Source: Swiss health survey (1997), cited in the Swiss National Programme Against Cancer, 2005

They invited me to change, but I have a public image as the face of oncology. I write the letters and they have my photograph on them. I cannot change now.”

However, he believes his work will benefit heart disease as well as cancer. “My vision when I built this cancer house in Berne would be to enlarge our centre and to have the same system for cardiology in Switzerland. My vision is that in the same centre there would be Oncosuisse and CardiovascSuisse, because prevention is about the same messages.”

The reality is that the cardiologists already have a great deal for which to thank Nosedo. Because one effect of the numerous organisations he has helped found or support, has been to foster the sort of national perspective and collaboration that are so essential in tackling all complex chronic diseases. In a country of cantons proud of their idiosyncratic differences and fiercely protective of their autonomy, this is no small achievement.

A national law for prevention and early detection is being proposed, to back the fight against cancer

Radiotherapy report sets new targets for Europe

→ Anna Wagstaff

Radiotherapy is the most cost-effective treatment for many cancers. Now radiation oncologists have adopted an evidence-based approach to assessing need throughout Europe. And the league table for meeting that need reveals some surprising results...

Radiotherapy is involved in the treatment of an estimated 40% of all patients who are cured of cancer. As well as being effective, it is less expensive than both surgery and chemotherapy. However, the latest linear accelerators (linacs) cost millions of euros each and require skilled staff, so countries need to plan ahead if they are to acquire and maintain sufficient capacity to meet demand.

In an effort to promote such forward planning, the European Society for Therapeutic Radiology and Radiation Oncology (ESTRO) has taken it upon itself to establish, on a country-by-country basis, the level of radiotherapy need in Europe and how it matches up with capacity. This is the purpose of the QUARTS project – Quantification of Radiation Therapy Infrastructure and Staffing Needs – which has been funded by the European Union.

In June 2005, QUARTS published some fascinating figures (*Radiother Oncol* 75:355–365) comparing the need for linacs in each European country with existing supply. QUARTS calculated need by looking at the

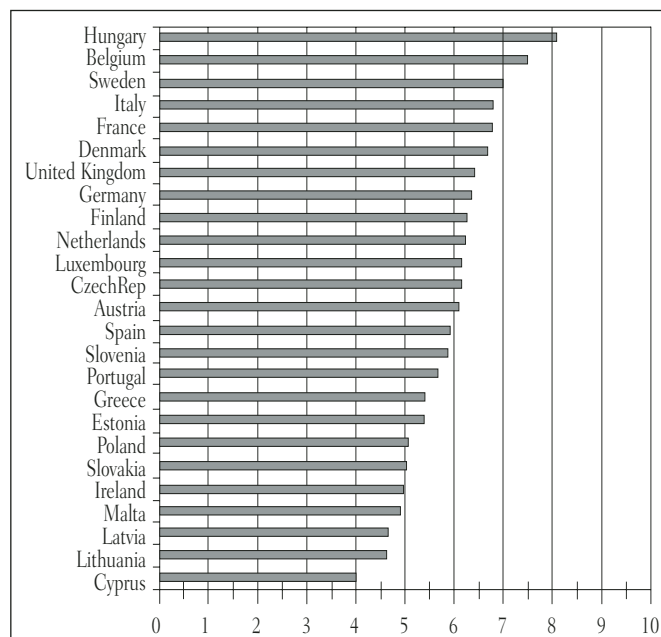
incidence rate for different cancers in each country, and using the best available evidence about the proportion of patients with each type of cancer who need radiotherapy. By estimating the number of treatments that each unit can deliver, the authors reached an evidence-based estimate for the number of linacs per capita needed by each country.

QUARTS then mapped this estimate of need against existing capacity, enabling health ministers, clinicians and patients to see at a glance how adequate (or inadequate) the provision of radiotherapy is in their country.

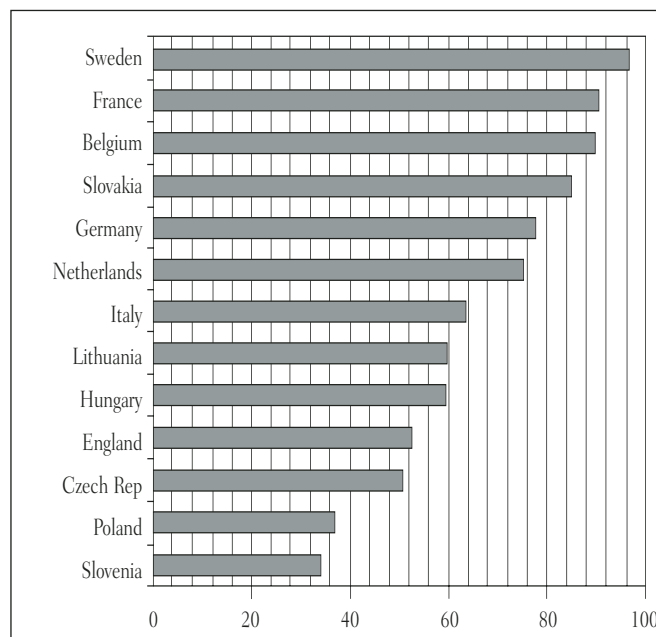
The result is displayed in two league tables – one showing the need for linacs; the other showing the percentage of need that is met by each country.

Some of the findings come as a surprise. Hungary tops the 'need' league, requiring twice as many linacs per head of population as Cyprus, reflecting a combination of lifestyle, environmental factors, and the population age profile. Hungary's high level of need can partly be explained by its particularly high incidence of head and neck cancers, which require a

THE EUROPEAN LEAGUE TABLES



QUARTS estimates of the number of linacs (megavoltage radiotherapy units) needed per 1 million people in the 25 EU states, based on incidence rates and the appropriate rate of radiotherapy for each type of cancer



The ratio of actual number of megavoltage radiotherapy units (linacs and Cobalt units) to the evidence-based required numbers derived by the QUARTS study in 13 European countries where reliable data were available

Source: The above figures and the figure on p35 are reprinted from *Radiotherapy and Oncology*, vol 75, pp355-365. Søren M. Bentzen et al. Towards evidence-based guidelines for radiotherapy infrastructure and staffing needs in Europe: the ESTRO QUARTS project. © 2005, with permission from Elsevier

relatively high number of treatment episodes; Cyprus's low level is largely a factor of its young population profile. In general, it is age profile that accounts for the greatest variation in need across Europe: with the exception of Hungary, it is the wealthier countries with the older populations that have the greatest need.

The important question for policy makers is how far their current capacity matches the evidence of need. Unfortunately, information about capacity is only available for 13 of the 25 countries. Sweden, which increased its radiotherapy capacity following a domestic survey in the 1990s, does best in this league table, meeting more than 95% of estimated need. France and Belgium are not far behind, and Slovakia also makes a strong showing, providing around 85% of estimated required capacity. The Czech Republic, however,

once part of the same country as Slovakia, is now limping along at 50%, but is still ahead of Poland (38%) and Slovenia (34%). England, despite having increased capacity by 20% between 2002 and 2004, meets little more than 50% of the demand indicated by the QUARTS estimates.

BEHIND THE STATISTICS

So what lies behind these apparent variations in radiotherapy provision? Are the differences in capacity really as bad as they look, and if so, are the Swedes and the French, who top the provision table, overtreating, or are patients in Poland and Slovenia really being denied the treatment they need?

Brian Cottier, one of the authors of the QUARTS report, believes some of the differences in the figures for capacity may be

“Some countries have a lot of equipment, some of which is probably used below maximum efficiency”

overstated, because there may be significant differences between countries in how intensively the equipment is used. The study assumed that each linac is used at a uniform rate of 450 treatments a year. (This is high compared with the actual rate achieved in Sweden of 338 treatments per machine per year, or in the Netherlands, at 410 treatments a year.)

But Cottier says that not enough work has been done to establish an evidence-based figure. “It is not yet clear how many people you can treat on a linear accelerator per day, while maintaining professional and safety standards. Some of the countries have a lot of equipment, some of which is probably used below maximum efficiency, while others have very little, which are probably utilised beyond reasonable use.”

He adds that some private sector units in some countries appear to be financially viable with extremely low throughput, while publicly funded units give more priority to a high throughput. This means that the difference between the capacity gap in England and that in Germany or France may not be as great as it appears. Linacs in France are distributed between 179 centres, and in Germany 210, many of which are private practices with a relatively low throughput. Radiotherapy units in England, by contrast, are concentrated in only 53 centres, only two of them in the private sector.

Another possible source of bias is that the older cobalt machines were assumed to be equal to the more modern (and expensive) linacs, which the authors justified on the basis that, with appropriate streaming, a cobalt machine could achieve similar throughput. However, Hana Stankušová, head of brachytherapy at Motol teaching hospital in Prague, thinks this assumption is unrealistic. Cobalt machines still form the bulk of capacity in the Czech Republic, and she says one linac is effectively worth two cobalts. If this is the case, then the variations in provision across

Europe may be even wider than the QUARTS figures suggest.

If defining capacity was a challenge, defining radiotherapy need was no less so, as there are no universally agreed guidelines about which cancer patients should be treated with radiotherapy and how. Since Leopold Freund began therapeutic irradiation in November 1896, in Vienna, and wrote the first textbook about radiotherapy in 1903, different protocols have been established by different units and modified in the light of new knowledge and technology. There have been sporadic randomised clinical trials, which have resulted in new patterns of treatment for certain indications. QUARTS gives examples of the introduction of preoperative radiotherapy for rectal cancer, and the switch to single rather than fractionated doses for painful bone metastases. Developments in surgery and medical oncology, and the focus on multidisciplinary approaches have also influenced the use of radiotherapy.

However, a number of attempts have been made in recent years to establish evidence-based indications for radiotherapy. QUARTS studied two literature surveys by the Swedish Council on Technology Assessment in Health Care (1996 and 2003) and drew on studies from Canada and Australia. These are in the form of decision trees indicating whether or not radiotherapy is required for each type of cancer patient.

The results determine an “appropriate rate of radiotherapy” (ARR), which can then be used, together with incidence rates, to calculate overall need. The QUARTS estimates of need are largely based on the Australian study, which itself uses guidelines taken from “reputed national and international institutions” and cross-checked its results against the guidelines used by the Canadian study.

To be on the safe side, however, the QUARTS authors also looked at what would have happened to their estimates had they used

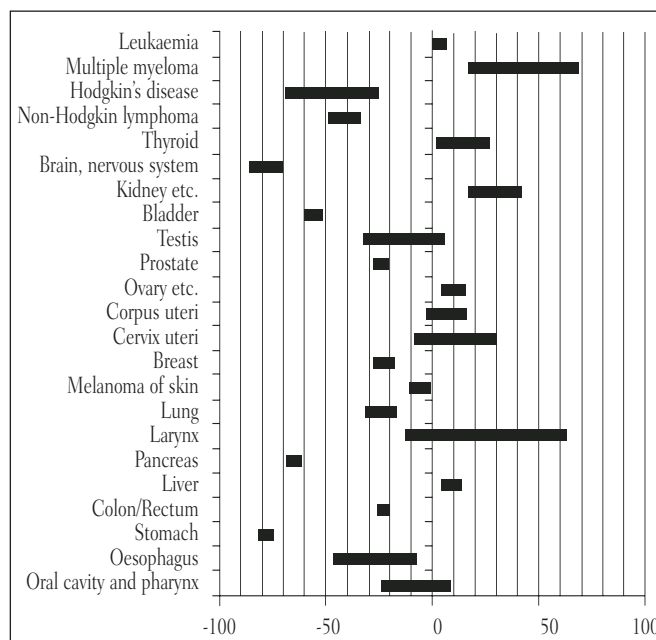
the slightly lower Canadian rates for colorectal, breast, lung and prostate cancer. The effect was to reduce average per capita requirement for the 25 EU countries by 10%, still leaving all but three countries short of required capacity.

The QUARTS study also compared the Australian ARR to the actual use of radiotherapy recorded in Sweden – the country that topped the league for radiotherapy provision. The results, illustrated in the figure opposite, indicated that far from doing too much, Sweden tends to use less than the estimated appropriate rate for many cancers; there are 11 cancers for which the usage rate is clearly below the ARR (the zero line) and only five that are clearly above. There are also seven where the 95% confidence interval line touches zero (meaning that they might be in line with the ARR).

HEY, MINISTER!

Taken as a whole, the QUARTS project falls only just short of a complete customised proposal to bring Europe's radiotherapy capacity up to the required level, and it makes its sales pitch well. It addresses the question of value for money, a central concern for Health Departments as cancer incidence rates head relentlessly upwards. QUARTS cites estimates indicating that, of cancer patients who are cured, 49% are cured by surgery, 40% by radiotherapy (alone or combined with other treatments), and 11% by chemotherapy alone or in combination.

European figures from the 1990s show the average cost of a course of radiotherapy among EU Member States to be 3,000 euros, compared with 7,000 euros for cancer surgery and 17,000 euros for chemotherapy. Seen in this light, and given the way the price of cancer drugs has been rising, radiotherapy looks like a bargain. Indeed, recent figures from Sweden, the country with the highest radiotherapy



Difference between the estimated appropriate rate of radiotherapy and the estimates of actual utilisation in Sweden. The horizontal black bars indicate the 95% confidence limits of the actual utilisation estimate

capacity, indicate that radiotherapy accounts for less than 6% of the total cost of oncology.

But with a squeeze on health budgets all over Europe, will this be enough to persuade governments to provide the necessary funding? Stankušová, in Prague, certainly hopes so. Many patients in the Czech Republic wait four to five weeks before starting radiotherapy, because there are not enough linacs. Worse still, some patients don't even make it to the waiting lists because their clinician avoids referring them for treatment for which there is a long delay.

"It depends very much on where they are treated," says Stankušová. "A responsible radiation oncologist will refer the patient to radiotherapy even if the waiting list is long. But if the patient goes through a clinical oncologist, who is not a radiotherapist, but maybe a urologist or

Given the way the price of cancer drugs is rising,
radiotherapy looks like a bargain



London's Royal Marsden Hospital bids farewell to its first SL25 linac, which had been state-of-the-art when it started service 20 years ago. The machine was pensioned off this June as part of a major revamp of the UK's radiotherapy services

a gynaecologist, they may simply give the patient additional chemotherapy, even though this is not the best treatment.”

The Czech Society of Radiation Oncologists has been trying for years to persuade the Ministry of Public Health to invest in more linacs. Stankušová believes the QUARTS study will strengthen their hand. “For us, it is an important tool to be able to say that, now we are in the European Union, we should be able to provide our patients with a radiotherapy service that is comparable to other European countries.”

Cottier, from the QUARTS team, who was formerly a clinical oncologist and is now head of Cancer Services Analysis for England at the Department of Health, is also hopeful that the study will have an impact. QUARTS, he says, is the first attempt to quantify variations in radiotherapy services between and within European countries, and gives countries the potential to plan future spending objectively rather than

responding only when demand becomes obvious and overwhelming. “Many countries have now adopted an evidence-based approach to clinical practice within medicine. A logical extension to the process is to adopt an evidence-based approach to service planning.”

In the short term, he argues, QUARTS data can be used to analyse gaps in provision within each country and formulate an investment strategy to eradicate variations across Europe. In the medium term, an investment strategy should include a programme to replace equipment with up-to-date technology, as each machine comes to the end of its working life.

Cottier hopes the project will now go one step further and become a sort of annual report card to check on whether and how fast the capacity gaps are being filled. “What I’d like to see is an annual web-based census of all equipment in Europe, to monitor whether we are moving towards and maintaining an equitable provision of services.”

“Now we are in the EU, our radiotherapy service should be comparable to other European countries”

How the hostage-taking of Twist hit the mass media

Ioanna Soufleri writes for the Greek daily newspaper *To Vima*. In a series of articles that jointly won her the 2005 ACE (Awarding Excellence in Cancer) Reporter's Award, she has shown that progress in cancer can make fascinating reading without resorting to misleading talk of 'wonder drugs' and 'breakthroughs'. Below we reprint a sample of her work.

An unexpected finding has changed, yet again, our perception of the origin of cancer (or, at least stomach cancer). American scientists have discovered that stomach cancer originates from bone marrow-derived cells, rather than stomach cells!

Taken together with recent advances in the field, the above finding, which was reported in *Science* (26 November 2004), illuminates a new aspect of this multi-faceted disease. And while nobody is suggesting that we know everything about it, more often than not scientists are now expressing the belief that cancer will soon become a chronic disease.

It's been 15 years since scientists linked stomach cancer to infection with *Helicobacter pylori*, the ulcer-causing bacterium. Now, through ingenious experimentation, American scientists have shown that the cells that become cancerous do not belong to the

stomach. Instead, they are bone marrow cells that "have been invited" to the stomach to help restore the damage caused by the *H. pylori* infection.

Working with mice, Jean Marie Houghton and Timothy Wang initially destroyed the animals' bone marrow. Subsequently they transplanted into the mouse bone marrow cells expressing a fluorescent protein. This enabled the scientists to follow those cells as well as their progeny through the body.

Infection of the animals with *Helicobacter felis* (which is the animal equivalent of *H. pylori*) resulted in the development of ulcers, as was expected. A few weeks after the infection, bone marrow cells started appearing in the area of the

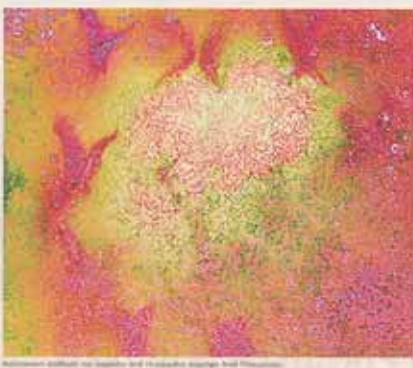
destroyed gastric epithelium and, while they tried to adopt the character of the traumatised cells, they exhibited some pre-cancerous alterations. When tumours were finally formed, their fluorescence betrayed their bone marrow origin.



THE BHMASCIENCE

ARTICLE BY ASSOCIATION 2004 017

Το κεντρικό θέμα της έρευνας, για τον τρόπο που οι κύτταροι...
Το κεντρικό θέμα της έρευνας, για τον τρόπο που οι κύτταροι...



Ο καρκίνος; Μια... χρόνια νόσος

Εάν ο καρκίνος...
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This article originally appeared in the Science section of the Greek national daily, To Vima, on 5 December 2004, under the title Cancer: On the road to becoming a chronic disease?

Metastasis is not an easy process, because cancerous cells have to overcome a number of obstacles: they have to free themselves from the tumour, enter the circulatory system (by squeezing themselves through tiny blood vessels) and then exit again and establish new colonies in a different and hostile environment. The whole process is so complex that one wonders how cancerous cells are able to adopt all the different behaviours that are necessary for them to succeed.

Last summer, a team from the Whitehead Institute gave an answer (or at least part of the answer) to the above question. It seems that cancerous cells can resolve all their problems at once by re-activating a mechanism that normally operates only during embryogenesis (a period during which massive cell movement takes place).

According to their article (Cell, 25 June 2004), breast carcinoma cells "take as hostage" a protein named Twist. Under normal conditions, Twist is only functional during embryogenesis, controlling the movements of cells by activating the right genes at the right moment. The reactivated Twist works as a key to all doors for cancerous cells: it triggers the expression of genes that are needed for every stage of cell movement (entrance to and exit from the circulatory system, establishment of contact with new tissues etc).

The American scientists worked with mice and confirmed the activation of the protein in highly metastatic human breast carcinoma cells. Now they are looking for a molecule capable of inhibiting Twist. Such a molecule could prevent metastasis, rendering cancer a chronic disease. Their findings are also important for another reason: they have attracted the attention of other scientists to proteins with functions similar to that of Twist (which are known to scientists from developmental studies). In other words, a whole new variety of possible target molecules for anticancer medications have come to light.

According to Timothy Wang, "Bone marrow cells arrived at the stomach epithelium in order to heal the tissue. But chronic inflammation conditions prevented them from developing normally, so they progressed down the road to cancer." Indeed, Houghton and Wang's findings contribute to the notion that chronic inflammation favours tumour formation. True, the American scientists worked with mice, and their findings need to be confirmed in humans. But it is expected that the same principle will apply to a variety of human cancers that develop after chronic inflammation (such as colon cancer, lung cancer or liver cancer). A possible common mechanism for the formation of those tumours could lead to a common way of treating them.

Another finding that could lead to the development of a generalised strategy for the treatment of cancer concerns metastasis, the transport of cancerous cells and the subsequent development of tumours in tissues different from the tissue from which they originated.

Lung cancer: spotting the symptoms

→ Alex Mathieson

New research reveals that lung cancers could be picked up much earlier if only the public and health professionals learnt how to recognise the critical symptoms.

IT is often considered a given in the cancer world that people with lung cancer present late in the disease, when the chances of curative treatment are very limited. The reason commonly cited is the lack of obvious symptoms that might trigger the patient's visit to the doctor at an earlier stage. But new research from England suggests this may not be the case, and that patients experience a range of symptoms up to two years before a diagnosis is reached.

The research, reported in *Thorax* (vol 60, pp 314–319), was carried out by Jessica Corner and colleagues from the School of Nursing at the University of Southampton, UK. Their exploratory study involved interviewing 22 patients recently diagnosed with lung cancer about their symptoms, together with the responses of their general practitioners (GPs) prior to diagnosis.

Patients' recollections of their history enabled the research team to pinpoint when symptoms started. For some people, it was more than two years before the diagnosis was confirmed. For others, it was only four months, with the median being 12 months. But the interviews revealed

that the symptoms (most commonly cough, breathing problems and chest pain) had to be severe – such as coughing up blood, or, as one patient put it, a cough that “could be lived with no longer” – before patients went to the doctor.

These results turned out to be something of a surprise for Corner, who is also Director of Improving Cancer Services at Macmillan Cancer Relief, a leading UK charity.

“I had a hunch from previous work that lung cancer patients do experience symptoms some years before diagnosis, but rarely have them systematically investigated,” Corner says. “We found that patients did have symptoms, but didn't appear to link changes in health with the prospect that they might be ill – there seemed to be no connection, even with respiratory symptoms.”

Patients attributed their symptoms to some minor ailment that didn't warrant medical attention, or to “getting older”, the study states. It wasn't until they had moved into the investigation process with the doctor that it occurred to them that they might be ill.

“This was all completely counter-intuitive for us,” Corner continues.

“We didn't expect such significant delays in going to the doctor, and were even more surprised to find that the reason wasn't fear of the diagnosis, but was based on the notion that they weren't really ill. We need to look into this more.”

Corner suspects that people who develop lung cancer do not tend to be proactive about their health, which may dissuade them from seeking medical advice early. “It might also be about lung cancer awareness among the public not being as great as, say, awareness of breast cancer,” she adds. “There isn't a quick check for lumps you can do in the shower.”

Perceived stigma about smoking may be another important issue. Negative portrayals of smoking and its relationship to lung cancer, typified in a government campaign in England which features stark images of terminally ill patients, may lead some smokers to feel ‘undeserving’ of medical care, according to the study. “We have evidence from at least one person we interviewed that this was the case,” says Corner.

“There is a real issue about how lung cancer is portrayed socially, and we should be careful not to make it worse,” she continues. “Anti-smoking



Jessica Corner: Anti-smoking messages are very important, but we must be careful not to deter people from coming forward for early diagnosis

messages are very important – there is no better thing to do than stop people smoking – but we must be careful not to do anything that might hamper people coming forward early for diagnosis.”

INADEQUATE GUIDELINES

Lung cancer awareness may also be lacking among the medical community, according to the study. GPs in England and Wales have been issued with referral guidance for suspected cancer from the National Institute for Health and Clinical Excellence (NICE), detailing signs and symptoms they might expect to see across a range of conditions. The guidelines, however, may not be sufficiently sensitive to allow doctors to identify symptoms that characterise lung cancer.



Jesme Baird: We must get the message across that every symptom requires a diagnosis – there's no such thing as a 'smoker's cough'

Chest pain, for instance, typically has a very different presentation in lung cancer than it does in heart disease, but patients in Corner's study who complained of chest pain were referred for heart checks.

“Because they had pre-existing heart disease, it was assumed to be a cardiac problem,” she explains. “It wasn't – it was lung cancer. You just feel that if the pain had been interrogated more thoroughly, it would have been quickly identified as non-cardiac.” Corner believes a similar situation applies with cough, the pattern of which is very different in lung cancer than it is in infections or asthma.

The exploratory study was small and patient recollection has limitations as a research method, but Jesme Baird, Director of Patient Care at the

Roy Castle Lung Cancer Foundation in the UK, feels the project raises some important questions that justify further study.

“There is a real lack of research in the pre-diagnostic area,” Baird says. “We know that patients present late with lung cancer, but there hasn't been any work looking at why this is the case.

“The assumption has always been that the disease is very advanced by the time symptoms appear, but some of the patients in this study, even those with operable cancer, had symptoms for up to two years and thought nothing of them. If that attitude is more general, we have a big challenge on our hands in educating the public to report symptoms.

“There may be lots of factors associated with patients' delay in going to the doctor, and the study hasn't been able to go into a lot of detail about them,” Baird continues. “But there are definitely big learning points about raising public awareness and getting messages across that every symptom requires a diagnosis – there's no such thing as a 'smoker's cough'.”

Corner's team is now set to move onto bigger studies that can delve deeper into many of the issues raised by these latest research findings. They have already started work aimed at understanding more about patients' behaviour, thoughts and feelings around symptoms, and projects to help GPs differentiate lung cancer symptoms from others are in the pipeline.

“Patients did have symptoms, but didn't appear to link them to the prospect that they might be ill”

NEWS ROUND

Selected press reports compiled by the ESO Cancer Media Centre

Drug can reduce hot flashes for women with breast cancer

→ The Lancet

A drug called gabapentin could reduce the incidence of hot flashes in women with breast cancer by 46%, according to a randomised trial published in the *Lancet*.

Hot flashes are a collection of symptoms including sweating, palpitations and anxiety. They are the most commonly reported symptoms in women receiving chemotherapy or hormone therapy for breast cancer. Treatment with oestrogen and progestagen can improve these symptoms. However, such hormone replacement therapy may increase the risk of breast cancer recurrence.

Gabapentin is an anticonvulsant drug that is often prescribed by doctors to treat epilepsy and control seizures. It has also shown potential for the treatment of bipolar disorder, anxiety disorders, and substance use disorders.

Researchers wanted to see if it could help alleviate the symptoms of hot flashes in cancer patients.

Kishan Pandya (University of Rochester Cancer Center, USA) and colleagues recruited 420 women with breast cancer who were having two or more hot flashes a day onto the study. Participants were randomly assigned to placebo, 300 mg/day gabapentin, or 900 mg/day gabapentin for 8 weeks. Each participant kept a self-report diary on hot flashes before and during treatment.

At 8 weeks, data were available for 347 patients. The percentage decrease in hot-flash severity score between baseline and 8 weeks treatment was 15% in the placebo group, 31% in the gabapentin 300 mg group and 46% in the gabapentin 900 mg group.

Pandya states: "We believe gabapentin [900 mg/day] can be added to the list of nonhormonal agents for the control of hot flashes in women with breast cancer, and the effects of doses higher than 900 mg/day merit further study."

■ Gabapentin for hot flashes in 420 women with breast cancer: a randomised double-blind placebo-controlled trial. KJ Pandya, GR Morrow, JA Roscoe, et al. *Lancet* 3–9 September, 366:818–824

Scientists develop screening method for pancreatic cancer

→ University of Liverpool

Scientists at the University of Liverpool have found a way of identifying families at high risk of pancreatic cancer. The team has developed a new way of testing for pancreatic cancer that will enable doctors to treat the disease at its earliest stages. They can also show how the risk of cancer for these patients will change with age.

The Liverpool-based study group known as EUROPAC (European Registry Of Hereditary Pancreatitis And Familial Pancreatic Cancer), working in collaboration with a similar group in Germany, has shown that familial pancreatic cancer develops at

an increasingly younger age as it is passed down generations – a phenomenon known as 'anticipation'.

In the largest study of its kind, the team surveyed 600 families with a history of pancreatic cancer and identified a subgroup of over 80 families whose lifetime risk of developing the cancer was 50%.

Bill Greenhalf, from the University's Division of Surgery and Oncology, said: "Of those families with the highest incidence of pancreatic cancer, we found that members developed the disease at a younger age in each generation. As well as giving important clues about the nature of the disease, this allows a more accurate estimate of the risk an individual faces of developing cancer in the short term so we can treat the cancer as soon as possible."

The team led by Greenhalf has developed a method of analysing pancreatic juice, taken from patients in families with a history of pancreatic cancer. By analysing DNA, scientists are able to identify specific genetic mutations that indicate the chances of a patient developing the disease in the short term, ranging from a 0.1% chance to a 90% certainty.

Greenhalf added: "Our research has provided strong evidence that anticipation and pancreatic juice analysis are the most effective means of screening for pancreatic cancer in families with a history of the disease. We intend to carry out further trials of these techniques and hope the results encourage more widespread adoption of these screening methods."

■ The research is published in two separate papers in the journals, *Gut* and *Gastroenterology*

Link found between euthanasia requests and depression

→ **Journal of Clinical Oncology**

A study from the Netherlands has found that cancer patients who are depressed are four times more likely to request euthanasia. The study published in the *Journal of Clinical Oncology* demonstrates a link between depressed mood and the number of terminally ill cancer patients who request euthanasia.

Traditionally, it is thought that patients request euthanasia or physician-assisted suicide because of the unbearable pain associated with terminal illness. However, this theory has not been proved by clinical studies. This latest report suggests that euthanasia is not always a carefully thought through, rational request.

The Dutch study was conducted on 138 cancer patients with a life expectancy of 3 months or less. Patients were asked to complete a self-screening questionnaire that measured depression and anxiety. The patients' moods were then evaluated according to their score.

Depressed patients were four times more likely to request euthanasia than those without depression. Of 138 patients, 32 patients were depressed and 30 patients (22%) made an explicit request for euthanasia. The data collected also showed that patients' depression was not the consequence of a poorer prognosis.

The problems of treating depressed patients with terminal illness needs further consideration. Oncologists are often unsure how to treat depression, as Ezekiel J Emanuel points out in an accompanying editorial. "In general, physicians are poor at suspecting, identifying and diagnosing depression. Indeed oncologists themselves recognize that diagnosing and treating depression is not one of their better clinical skills."

Further investigation is needed to see whether depression can be adequately

treated in terminally ill cancer patients and if so whether it would lower the incidence of requests for euthanasia.

■ Euthanasia and depression: A prospective cohort study among terminally ill cancer patients. ML van der Lee, JG van der Bom, NB Swarte, et al. *JCO* 20 September, 27:6607-6612

New technique is better at clearing indwelling ports and lessening morbidity in cancer patients

→ **ECCO**

The use of normal saline solution and a technique that relies on positive pressure is more effective at cleaning indwelling ports than heparinised solution according to a new study presented at the European Cancer Conference.

Cancer patients are often fitted with a port, which is used to give continuous or weekly intermittent infusions of chemotherapy drugs. In order to keep the vein available for multiple access, the port is usually washed out with heparinised solution. However the drug does not always work and can block and close up the vein. On top of this, not all hospitals allow nurses to handle the drug heparin, and incorrect doses to patients can cause thinning of the blood.

The study conducted at the European Institute of Oncology in Milan discovered that using a simple saline solution and a technique called 'positive pressure' gave much better results than the traditional heparinised solution. The positive pressure approach is a simple technique that causes a slight vacuum and increases pressure inside the tube. The saline solution is obviously a lot less toxic than using a drug to carry out the same process.

The study looked at nearly 200 patients aged 18 and over with solid tumours. Each time they visited the clinic for treatment, the same procedure was used, and a total of 1,935 episodes were

annotated. The nurses were taught how to wash the port with 20 ml saline solution and had to maintain positive pressure during the procedure. Almost all patients (99%) experienced normal functioning of the port – a better result than using heparinised solution. Only one patient of 157 showed two consecutive partial occlusions. Hospitals should now be looking at implementing this procedure, which is less toxic for patients, less expensive for the hospital and easier for community nurses to maintain.

■ Positive pressure and normal saline instead of heparinized solution when washing indwelling ports in patients with cancer. Presented by Alessandra Milani at ECCO 2005

Radiotherapy after surgery is best option for prostate cancer patients

→ **The Lancet**

Giving prostate cancer patients radiotherapy after surgery could help prevent the progression of their disease, concludes an article in the *Lancet*.

When cancer is confined to the prostate, removal of the organ can successfully control the disease. However, for patients with cancer extending beyond the prostate, the risk of recurrence after surgery can be 10–50%. Michel Bolla (CHUA Michallon, Grenoble, France) and colleagues tested whether immediate radiotherapy after surgical removal of the prostate (prostatectomy) improved progression-free survival for patients at risk of relapse. Between 1992 and 2001, the investigators recruited 1,000 patients who had undergone radical prostatectomy from 37 centres in Europe. Half were assigned to radiotherapy after surgery and half to monitoring. After a 5-year follow-up, the researchers found that 74% of patients in the radiotherapy group had biochemical progression-free survival compared with 53% in the monitored group.

Biochemical progression-free survival refers to the patient's concentration of PSA. The investigators also found that clinical progression-free survival was significantly improved in the radiotherapy group.

Bolla concludes: "Our results show significant improvement in biochemical progression-free survival with immediate postoperative irradiation. Long-term follow up is needed to assess if postoperative irradiation affects the occurrence of distant metastases, survival, or both."

In an accompanying comment, Stefan Hocht (Charité University Hospital, Berlin, Germany) states: "Michel Bolla and colleagues report on a large study from the European Organisation for Research and Treatment of Cancer (EORTC) that is likely to change patterns of care in locally advanced prostate cancer . . . although the superiority of adjuvant radiotherapy is to be expected, we did not have direct proof of this hypothesis. The question still to be answered is whether adjuvant irradiation is superior to early salvage treatment as soon as prostate-specific antigen rises."

■ Postoperative radiotherapy after radical prostatectomy: a randomised controlled trial (EORTC trial 22911). Michel Bolla, Hein van Poppel, Laurence Collette, et al. *Lancet* 13–19 August, 366:572–578

Survival rates of black women may be affected by other diseases

→ JAMA

Black breast cancer patients may have shorter survival rates than white patients because of higher rates of other diseases, such as diabetes and hypertension, according to a study in a recent issue of JAMA.

Although breast cancer survival has improved over the last 30 years, differences in breast cancer survival between black and white women have not declined and remain sizeable. Several causes have been identified,

such as advanced cancer stage, lack of access to medical care, inferior treatment, and lower socioeconomic status; however this disparity still remains unexplained.

Scientists from Canada looked at the records of over 900 women who had been diagnosed with breast cancer between 1985 and 1990. The results showed that black breast cancer patients have more cancer recurrence/progression and shorter overall survival. Overall, 62% of black women died compared to 50% of white women.

Over 62% of all deaths were attributed to competing causes. Proportionally more black women than white died of competing causes. In 86% of black women, one or more comorbidities were reported compared to 66% of white women. A total of 77 adverse comorbidities were associated with reduced survival. Diabetes and hypertension were particularly important in explaining the survival gap. However comorbidity was not associated with recurrence/ progression or breast cancer-specific survival.

The results indicate more black breast cancer patients die of competing causes than of breast cancer. Effective control of comorbidity in black breast cancer patients should help improve life expectancy and lead to a reduction in the survival rate gap.

■ Comorbidity and survival disparities among black and white patients with breast cancer. CM Tammemagi, D Nerenz, C Neslund-Dudas, et al. *JAMA* 12 October, 294:1765–1772

Chemotherapy regimen may help preserve limbs in 90% of young people with osteosarcoma

→ Journal of Clinical Oncology

A new study has found that high doses of chemotherapy may improve a patient's chance of preserving a limb with osteosarcoma. The joint findings by the Italian and Scandinavian sarcoma groups will be published in the *Journal of Clinical Oncology*.

Osteosarcoma is the most common type of bone cancer, and the sixth most common type of cancer in children. Patients are usually given a course of chemotherapy before surgery or radiotherapy to shrink the tumour and make it easier to remove. The study followed 182 patients from March 1997 to September 2000 with localised osteosarcoma of the extremity. They were given a mix of chemotherapy treatments before and after surgery.

Initial chemotherapy consisted of two blocks of high-dose ifosfamide, methotrexate, cisplatin and doxorubicin. After surgery the patients received two cycles of doxorubicin, and three cycles each of high-dose ifosfamide, methotrexate and cisplatin. Granulocyte colony-stimulating factor support was mandatory after the high-dose ifosfamide/cisplatin/doxorubicin combination.

The study found that no disease progression was recorded during primary chemotherapy, and 92% of patients underwent limb-salvage surgery. With a median follow-up of 55 months, the 5-year probability of event-free survival was 64% and overall survival was 77%, whereas seven patients (4%) experienced local recurrence.

The study concluded that although the addition of high-dose ifosfamide to methotrexate, cisplatin and doxorubicin before surgery is feasible, there were major renal and haematologic toxicities. The survival rates were similar to those obtained with four-drug regimens using standard-dose ifosfamide. So it appears there is little advantage in using the higher doses. However the study showed that in a multi-centre setting, more than 90% of patients with osteosarcoma of the extremity can undergo conservative surgery.

■ Neoadjuvant chemotherapy with high-dose ifosfamide, high-dose methotrexate, cisplatin, and doxorubicin for patients with localized osteosarcoma of the extremity: A joint study by the Italian and Scandinavian Sarcoma Groups. S Ferrari, S Smeland, M Mercuri, et al. *JCO* 10.1200/JCO.2004.00.5785, published online 24 October

The news is bad... the message may be worse

→ Rhonda Siddall

Despite recognised regional differences in how doctors and patients deal with bad news, recent research shows every country has patients who seek information and others who avoid information, and doctors need training to cater for them all.

Telling a patient that cancer has spread is emotionally challenging. Torn between the desire to soften bad news and the duty to keep a patient informed, there is a risk of failing to communicate the gravity of the situation or alarming the patient to the point where it impacts on their care.

Too much information may bewilder and confuse; too little can leave the patient feeling lost and unsure. Too blunt a delivery seems cold and uncaring, while a gentler approach risks becoming patronising.

Patients differ in their attitudes to illness and their expectations of treatment.

However, Lesley Fallowfield, director of Cancer Research UK's psychosocial oncology group at the University of Sussex, UK, says there should be a presumption in favour of the truth. "Many doctors censor information on the basis of a misguided assumption that this is being kind."

Heide Preuss, aged 61, from Selm in Germany, was diagnosed with breast cancer in January 1995. She helped to set up the Mamazone group for women with breast cancer

who want to know as much as possible about their disease. Preuss said, "Doctors do not always understand the needs of their patients for information. Some doctors do not like their patients asking too many questions, so it is important that patients have other outlets for information."

However, Francesco de Lorenzo, president of the Associazione Italiana Malati di Cancro Parenti ed Amici (AIMaC), an Italian support group, says that patients vary in their need for information. "Some patients prefer to know everything, others would rather know nothing, and in between there are patients who want some information but only about certain aspects of their disease."

Given these scenarios, it is difficult for physicians to judge how much information is wanted.

While it has become accepted that most cancer patients want some influence over the management of their condition, patient surveys suggest that most prefer decision-making to be shared, with medical professionals making the final clinical decisions, after taking patient preferences into account.



LWADANN TARDIF / CORBIS / CONTRASTO

DOCTORS' PERCEPTIONS

Physicians are not always well equipped to determine exactly what their patients do want. Indeed, doctors' own attitudes often differ according to their training, cultural background, specialty and the stage and type of cancer they are treating.

This issue was highlighted earlier this year in a qualitative market research study on the management of bone metastases carried out for Novartis (*Zometa Insight Mining Research*. Synovate Healthcare, 2005). The study involved group discussions with oncologists, haematologists, gynaecologists and urologists from the UK, France, Germany, Italy and Spain, and one-to-one interviews with patients.

The discussions with doctors revealed wide regional variations in attitudes. Physicians in Spain were reluctant to use words such as 'cancer' or 'metastases'. One oncologist said:

"The word metastasis would scare them half to death even though most don't know what it is." In both Spain and Italy, physicians said they often give more information to the family than to the patient. Some doctors felt that the patient picked up messages from the doctor beyond the words being used. An Italian doctor said: "The patient will realise it is serious because my expression will change. I'll use a grave tone."

By contrast, doctors in the UK and Germany tended to focus on the facts. A UK oncologist said: "I'm a big believer in facts. You knock the patient down, then you build them up. You need to be honest." A German oncologist agreed. "It's important the patient understands exactly what is happening."

Antonella Surbone, who sits on the Educational and Ethics Committees of the American Society of Clinical Oncology

Some patients said people were less supportive once they heard the cancer had spread

(ASCO), believes that differences in the approaches taken by physicians reflect different cultural perspectives on the role of individuals and families.

“Truth telling to cancer patients is definitely related to cross-cultural differences. In countries such as the US, the UK and Germany, there is a strong emphasis on individual autonomy, which in the patient-doctor relationship is interpreted to mean patients expect to be fully informed and to be engaged with as equals. By contrast, in other cultures, more emphasis is placed on community and family values. Thus, in many countries, including Italy and Spain, doctors are expected to involve the family and to have a protective role towards their patients, especially when they are severely ill.”

BREAKING BAD NEWS

The Novartis study showed that information was usually provided ‘on demand’, and many physicians admitted to fudging or softening the truth to spare their patients’ feelings. The stronger the anticipated emotional reaction, the less the explanation.

Few physicians used any form of educational material. Many feared this would confuse or scare their patients and, instead, preferred tailored, personal explanations from healthcare staff. It was also felt that written materials would be only of benefit to younger and better-educated patients.

In the study a number of factors were shown to have influenced the way physicians broke bad news including:

- Age – younger patients tended to be better informed
- Gender – women tended to be better informed
- Socio-cultural level – higher-level groups tended to get more information
- Tumour type – information for breast and prostate cancer patients tended to be more upbeat, as it was felt these patients had better

prospects than those with multiple myeloma or lung cancer

- Cultural context – cancer becomes increasingly taboo towards southern Europe

Some physicians admitted that they found announcing the detection of bone metastases more difficult than delivering the original diagnosis of cancer, and expressed the desire for better psychological support for their patients.

Perhaps doctors could do with such support themselves. Most physicians admitted to ‘rationalised negativity’ in which initial feelings of disappointment, frustration and powerlessness quickly gave way to a determination to focus on positive aspects.

Oncologists appeared to be more willing than urologists to look on the bright side. The patient’s primary tumour type and the location and extent of the metastases also had a strong bearing on the doctors’ outlook. Physicians tended to be pessimistic about patients with lung cancer, while they felt there was still hope for women with breast cancer, even after metastasis. In the case of prostate cancer, many oncologists expressed frustration that they had seen these patients too late after the initial diagnosis.

PATIENT ATTITUDES

A parallel qualitative study of patient attitudes was carried out as part of the study. Thirty-seven breast, prostate, lung cancer and multiple myeloma patients with bone metastasis from the same five European countries were interviewed. Most understood that metastasis was an extension or spread of the original cancer, but their knowledge varied with their socio-economic level. The seriousness of metastasis was generally appreciated, though not always overtly acknowledged.

Italian and Spanish patients felt strongly supported and, to some extent, shielded by family, who often held more information than the

patient. German patients were most likely to have an idea of how long they could expect to live.

Patients found a diagnosis of metastases devastating once they understood its importance. Older patients were more likely to feel resigned, whereas younger patients expressed feelings of anger, resentment and a determination to fight the disease.

When the patients were asked about the impact that this form of advanced cancer made to their quality of life, most mentioned pain, fatigue and impaired mobility. There was a heightened fear of losing their independence. Patients felt that their condition would reduce their ability to participate in social activities and were acutely aware of the impact this might have on their partners and families.

The strong family support experienced by patients in southern Europe was felt to make living with advancing cancer easier. Patients in northern Europe often found that it put an unbearable strain on their family relationships.

Some patients described the news that the cancer had spread as like crossing an invisible line, after which support, even from other cancer patients, was likely to diminish. Many patients felt that advocacy/support groups were of little use, as they were mainly focused on 'survivors'.

AVOIDERS AND SEEKERS

Patients divided into two distinct groups: the avoiders and the seekers.

Most patients, especially those in Italy and Spain, were classified as 'avoiders'. These patients openly said that they did not want to know. "I can't cope," was one reaction. "It will just remind me of being ill. It will scare me. It will depress me." These patients tended to be older, relied on a relative to find out about their condition and were not interested in support groups.

The minority, who were described as 'seekers', tended to be younger and better educated

and often arrived at consultations bearing articles or lists of questions. These patients:

- Were keen on using the Internet and the media
- Read all the brochures
- Would seek out opinions from different doctors
- Were more likely to go to support groups (but only a minority found them useful)

Despite being well informed, these patients would usually defer to the doctor. However, the relationship between doctor and patient was not always easy.

Most patients use their doctor as their sole source of information, and indeed, the minority who used the Internet often found this information difficult to interpret.

Patients in the UK were more likely to use educational materials such as leaflets, booklets and videos. Cancer charities were also an information source for patients in the UK, Germany and Spain.

WHAT SEEKERS WANT TO KNOW

The questions asked by information seekers included:

- What are my chances?
- How long will I live?
- How much time do I have left?
- How bad can it get?
- Will I go downhill fast?
- What can be done to control it?
- What are the risks associated with this complication?
- Will I be able to continue my daily activities and hobbies?

They also expressed a need for simple language and visual support.

Most patients reported a generally good relationship with their physician, using terms such as 'complete trust', 'unconditional obedience', 'respect' and 'admiration'.

However, very few felt they had much influence over their treatment, either because

Patients divided into 'avoiders' and 'seekers'.

'Seekers' tended to be younger and more educated

they felt unable to make clinical judgments or because they were rarely presented with alternatives.

A QUESTION OF TRAINING

This patient survey suggests that physicians should improve their communication about metastatic disease to patients and families. Physicians should work with patients, family members and caregivers to determine the best methods of support, and tailor information to the individual patient. Patients want clear, understandable information about potential treatment options to improve mobility and independence.

The physician survey suggests that oncologists are generally correct in their assumption that most patients do not want to be involved in every single clinical decision. However, most patients want to retain independence and autonomy for as long as possible.

The survey also raised questions about the

actual words that doctors use. If patients do not know what metastasis is, should this word be used in doctor–patient discussions? Even if some patients do not want to be confronted with facts in too blunt a way, can it ever be justified to hide behind medical jargon? On the other hand, patients reported that the language used by their doctors was often very simple and ‘quite vague’.

Overall, the study confirms that many doctors make decisions on how much and how to tell patients based on their own temperament and professional experience, without a lot of external input. It concludes that a discussion of approaches and practice in breaking bad news should be a part of every doctor’s basic training, and their postgraduate education and continuing education. This could help ensure that while the level of information given varies according to the wishes of the patient, it won’t be dependent simply on the wishes of the doctor.

What we tell them

- I never ever say what the damage is to the patients, only to the family, aside... I’ve had too many reacting extremely badly before, so I shut up now – *Spain*
- In the USA people usually demand more info because they have to pay for their health care, so they want to know what they’ve got But not here! It is both because of cultural and economic factors – *Spain*
- It’s a bit like informed consent – you have a certain obligation to supply information – *Italy*
- The patients will realise it’s serious because my expression will change, I’ll use a grave tone – *Italy*
- We don’t want to put worrying ideas in their heads. It’s pointless to upset them like that – *France*
- Patients often don’t appreciate the significance of bone metastases, so you have to try to explain without frightening them – *UK*
- I’m a big believer in facts. You knock the patient down, then you build them up – *UK*
- I try to be upbeat, to say things in a non-dramatic way, how to confront issues and see what we can do – *UK*

What we want to know

- I only wanted to know where we would go from here, what would happen next – *Germany*
- The doctor consoled me and told me that she didn’t like to say it, but I prefer to know what I have – *Spain*
- I may not have been sufficiently clear in my questions, but the oncologist never responded clearly. He just said it was a consequence of my cancer, which I already knew – *France*
- I don’t want to know that much about my condition. It’s depressing and frightening. I want to forget cancer – *Italy*
- She was sweet, but she didn’t hide the severity of the condition. In any case, she reassured me that current treatments are very effective in combating this bone weakness and controlling pain – *Italy*
- I went crazy searching on the Internet and contrasting all the information – *Spain*
- I prefer not to know anything, my sister is more up on things – *Spain*

Specialist centres: can surgeons heal the wounds?

→ Anna Wagstaff

The policy of specialist centres for certain cancers is backed by research on outcomes. But surgeons in hospitals denied the right to treat cancer patients can find themselves cut adrift. Much of the UK has recently gone through the upheaval of regional specialisation. Are there lessons to be learnt from that experience?

In the late 1990s a UK Department of Health report (the Calman-Hine Report) recommended a complete change in the way that cancer services were provided in England and Wales. Radical changes would see the formation of Cancer Centres for specialist diagnosis and treatment, including radiotherapy and specialist surgery. Cancer services at small district general hospitals would be designated Cancer Units, and these would not undertake major cancer surgery. These changes were driven by the growing evidence that high-volume hospitals obtained better results. Over a decade later, England and Wales are seeing the implementation of this centralisation process for cancer surgery starting with gynaecological cancer and moving on to upper gastrointestinal, hepatobiliary, urology and head and neck cancers. Breast and colorectal cancer are still treated in every hospital. The effects of this change have been profound for hospitals, doctors and patients.

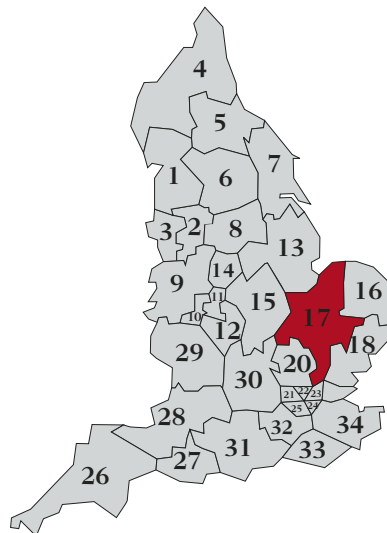
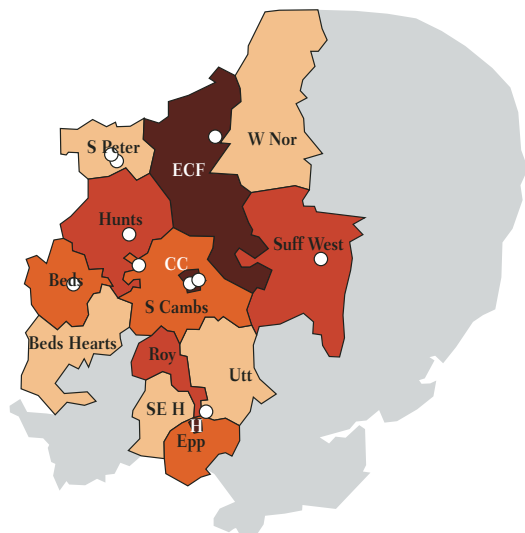
This article looks at how the change was managed in just one specialist area of cancer – upper gastrointestinal (GI) – in a relatively rural

area of England – the western part of East Anglia. It looks at the obstacles, the lessons learnt and the implications for other European countries, which face the same hard choices.

In 2001, had you been diagnosed with oesophageal or gastric cancer while living in one of the rural English counties around Cambridge, now covered by the West Anglia Cancer Network (WACN), you could have been referred to one of five district general hospitals (Bedford, Peterborough, Huntingdon, Bury-St-Edmunds, Kings Lynn), or a teaching hospital (Addenbrooke's) or a specialist thoracic hospital (Papworth). All of these hospitals provided upper GI surgery, some doing as few as three such operations a year, others as many as 30.

But in September that year, faced with overwhelming evidence that patients' chances of survival are seriously reduced if treated by surgeons who operate infrequently, the Strategic Health Authority implemented national guidelines to concentrate upper GI cancer services at a single regional centre.

Today, any of the 1.3 million people served



The West Anglia Cancer Network (left) is one of 34 cancer networks covering England and Wales (right), and caters for a population of around 1.3 million. Before 2001, cancer patients might have been referred for upper GI surgery to any one of seven hospitals shown on the map. Today, they would all be referred to the Addenbrooke's/Papworth Cancer Centre (marked CC) near Cambridge

by WACN diagnosed with upper GI cancer is referred to the Cambridge Oesophago-gastric Centre, a joint venture between Addenbrooke's Hospital in Cambridge and Papworth Cardiothoracic Hospital, which are 18 kilometres apart. Potentially curative treatment is conducted by four surgeons and three oncologists supported by a team of gastroenterologists, cross-sectional radiologists, pathologists, specialist nurses and dieticians. Palliative care is still provided mainly in the local Cancer Units.

NATIONAL PLAN

The decision to centralise England's upper GI cancer services had its origin in *Improving Outcomes Guidance* in 2001, which itself stemmed from the Cancer Plan for England. The plan looked at the evidence on the relation between outcome and annual caseload. It arrived at guideline figures for the minimum population that each specialist cancer centre would need to cover to treat a sufficiently high number of patients to develop real expertise. For pancreatic cancer, for example, the population was set at two to four million. For oesophageal and gastric cancers, it was set at the lower figures of one to two million people.

In every region, hospitals were invited to bid for the contract to provide specialist upper GI cancer services for their cancer network. In West Anglia, Addenbrooke's, in partnership with Papworth Hospital, won the contract to become the designated specialist centre.

Having a 'centralised' service spread across more than one site, avoided the need to build a specialist service from scratch, but the split site is not ideal.

Richard Hardwick, who led the Addenbrooke's bid and is now their lead clinician for upper GI cancer, says that the partnership with Papworth – recognised for its excellence in thoracic surgery – has led to a fruitful collaboration that had been conspicuously missing between the two specialties. However, the 18 kilometre gap has limited the extent of this collaboration. This will improve when Papworth eventually moves onto the Addenbrooke's site.

Hardwick says that the separation between upper GI surgeons and thoracic surgeons developed over decades. "Twenty years ago thoracics used to do nearly all the oesophagectomies in this country.

"They worked in a particular way; it was a technical tour de force. The patient was given to them, they did the operation, and handed the patient back, instead of integrating into a multi-disciplinary team and being involved in the work-up and follow-up.

"Many of them believed that an oesophagectomy was the best palliation for patients, but we now know this to be untrue. As multidisciplinary teams were established, it was not too surprising that gastroenterologists teamed up with the upper GI surgeons they worked with regularly, rather than with thoracic surgeons they rarely met."

The upper GI surgeons began to take on more

Hospitals were invited to bid for the contract to provide specialist upper GI cancer services

oesophagectomies and, at the same time, a new generation of dedicated oesophago-gastric upper GI surgeons emerged who had trained extensively in specialist centres around the world and wanted to establish their own teams back home. "An inevitable turf war ensued," says Hardwick. "This conflict has occurred in many parts of the world and is not always in patients' best interests."

As a result of the partnership between Addenbrooke's and Papworth, this breach is being healed and patients can be allocated to upper GI surgeons or to thoracic surgical specialists depending on who is more appropriate. The isolation of the thoracic team has gone and all patients are discussed in weekly specialist multidisciplinary team meetings. "We have produced a cohesive plan of how thoracics and upper GI work together, which we believe to be in the patients' best interest," says Hardwick.



Richard Hardwick: There are winners and losers, but at the end of this process you have to pick up the pieces to make the service work

LOW MORALE

The picture for hospitals that lost out in the bidding process is less rosy. Upper GI surgeons in these hospitals have no cancer resections on their lists. For some, this is a relief, as they did few cases each year and felt under-supported in a small hospital. For others the loss of this work has seriously impacted on their job satisfaction. They are not personally paid per operation, so this has no financial implications for an individual, but it does impact on morale, and that is beginning to cause recruitment problems. Two district hospitals are having trouble filling vacancies for an upper GI surgeon.

With hindsight, says Hardwick, these problems were predictable and should have been foreseen by policy makers. He feels that morale

was damaged unnecessarily by the way the bidding process was carried out. Because of other structural changes – Regional and District Health Authorities were being scrapped in favour of Strategic Health Authorities and Primary Care Trusts (PCTs) – there was not enough involvement from management. "It ended up with the clinicians having to battle it out as to who was going to get the cancer work, and it caused a lot of rivalries and interpersonal difficulties, particularly between surgeons. There are winners and losers, but at the end of this process you have to pick up the pieces to make the service work."

As a result, some upper GI surgeons in district hospitals have withdrawn from diagnosing and staging cancers, which results in some patients having to travel to Cambridge for minor procedures, such as staging laparoscopies or palliative bypasses.

Hardwick believes that it would have been better to create a 'joined-up' service where cancer work moved to the new

Centres at the same time as high-volume benign surgery moved to the smaller district hospitals.

Some surgeons might have been appointed to do both types of work in different places. In the National Health Service (NHS) of old, this could have been done, but changes to the British system now make it difficult. "The reality is that this is not going to happen," Hardwick says, "because we are all individual hospitals competing with each other for work, following the introduction of a new 'payment by results' system for hospitals, which favours low-risk, high-volume and short-stay cases over expensive cancer surgery. Cancer Centres will rapidly be bankrupted

if they do not do these cash cases as well as the cancer work. The NHS is just fragmenting fast.”

In West Anglia the national policy of referring upper GI cancer patients to specialist centres is being implemented, albeit with a few teething problems. It is today the job of Primary Care Trusts (PCTs) – at general practitioner level – to ‘purchase’ care, and PCTs are being given a firm steer in one direction. Hardwick says: “As part of the National Cancer Plan, PCTs in this region have been told by the Cancer Network Policy Board that the decision has been made that oesophageal and gastric cancer will be resected in the Cancer Centre and not at their local district hospital.” As PCTs now control the budget, he adds, they have a responsibility to purchase care in an ethical and responsible manner. If they deliberately flout the policy of the Cancer Network, they could find themselves having to account for their decision if anything went wrong.

SAFE VS LOCAL

WACN can be regarded as a success in terms of the quality of cancer care, yet it belies an uneasy compromise between the medical evidence and political expediency that will be familiar to anyone trying to centralise services in this way. Convincing smaller hospitals that they should stop carrying out these procedures was relatively straightforward, says Hardwick. The difficulties arose with the larger district hospitals that did intermediate numbers.

“The smaller places put their hands up and say: we realise that we only do three gastrectomies a year, and it’s not sustainable. But someone at one of the larger hospitals who does 10 gastrectomies and 10 oesophagectomies a year with acceptable mortality rates will understandably want to carry on doing so. The trouble is that once we’ve put together a big specialised team in the Cancer Centre, we need the work. Each surgeon needs to be doing about 30–35

resections a year to get the best results – and we need about 100 cases going through the department.”

In practice, the Addenbrooke’s/Papworth centre is only just achieving this level of throughput, and Hardwick attributes this to the population pool having been set too low. He believes that the evidence supports a population pool of two to four million for every specialist upper GI cancer service, but the cancer plan opted for the one million figure because it was deemed more politically acceptable.

The pressures to remain as local as possible are obvious. Quite apart from the resentment among surgeons who are denied the right to treat cancer patients, hospitals feel threatened as their patient volume falls, and the patients themselves can find it very hard to get to and from the Cancer Centre. This may be a small issue for someone who is young and fit, but it is a big one for more elderly cancer patients.

“The biggest complaint we get is access. This place is a nightmare for patients to visit. The county council are insistent that we can’t increase traffic onto the site despite continual expansion. Parking is inadequate, the road access is appalling and every single patient that I see finds it an issue. If you are telling patients in Bury St Edmunds they have to go to Cambridge for their treatment, you have got to do things that will facilitate that. ‘Park & Ride’ buses are not what patients and their relatives want to use.”

COLLABORATION WORKS

On the plus side, the introduction of a weekly video conference meeting of the multidisciplinary teams has allowed much better standardisation of the staging and treatment of upper GI cancer patients. This has already resulted in fewer patients being subjected to inappropriate exploratory surgery, and the complete elimination of inappropriate surgery with palliative intent. Much of the palliative care for patients is

Hardwick feels the population pool was set too low,
for reasons of political expediency

Some adjuvant and neo-adjuvant chemotherapy can still be administered closer to home

provided at the district hospital, close to the patient's home. Gastroenterologists and oncologists at the patient's district hospital will also be involved in their care, enabling some adjuvant and neo-adjuvant chemotherapy to be administered closer to home.

Hardwick says, "We sit down and go through every new case each week and all the follow-up cases, reviewing all evidence before agreeing a management plan. This is actually working quite well now so long as clinicians present their patients early on and not half way through the work-up process. This is still a problem with one of our Units, but overall it is working well. In addition, we are able to collect data on a dedicated computer database, the Joint Clinical Information System (JCIS) and collate useful information on an easily accessible web-based system."

LEARNING THE LESSONS

Had WACN been able to design its specialist upper GI cancer service from scratch, it would have ended up with a very different system. But it is precisely because it had to adapt an existing system to fit the new evidence-based requirements of minimum volume that makes the story of interest to health services elsewhere with similar problems.

For example, having a 'centralised' service spread across two, or even more, sites, avoids the need to build a brand new stand-alone specialist service, and is a solution that has been used in other countries, including the Netherlands.

But the logistical challenges are often less of a problem than enforcing implementation of a policy of referrals to specialist centres, when

either individual clinicians or individual hospitals have a self interest – financial or otherwise – that deters cooperation between different parts of the system.

In Hungary, some voices are calling for referrals of certain cancer patients to specialist centres to be made mandatory – as is already the case with HIV patients. The Netherlands – where the policy of minimum volumes and specialist cancer centres has been pursued for almost a decade – has so far relied on persuasion, backed up by a threat of sanctions. Though largely effective, there are still surgeons who insist on trying their hand at the occasional oesophagectomy that comes their way.

In much of Europe it is health insurance systems, rather than public bodies such as the English Primary Care Trusts, that effectively 'purchase' care. Should they too be held responsible for the consequences of continuing to pay for patients to be treated in centres whose annual caseload is below the threshold known to be safe? Insurers in the United States have already started to use outcome indicators to dictate where patients should have certain high-risk operations.

With the latest research from the Netherlands showing that oesophageal cancer patients treated in smaller hospitals are ten times more likely to die than those treated in specialist centres, the pressure on Europe's health systems to provide a quality service based on appropriate patient volumes is mounting. Hopefully, being able to draw on the lessons of previous experience, such as the West Anglia story, will both facilitate and speed similar change elsewhere.

Should health insurances continue to pay for patients to be treated in non-specialist centres?

Cure should also mean care

→ Raphaël Brenner



Enabling cancer patients to talk about their illness, lives and suffering, as unique individuals, is as essential to a patient's recovery as is medical treatment.

Cancer is a serious disease and should be fought on all fronts. This means that, in conjunction with medical treatment, attention should be paid to the psychological issues involved in the illness and the way patients deal with it.

As a psychologist influenced by the work of Carl and Stephanie Simonton among others, and as a pioneer of trans-generational psychotherapy with extensive experience working with terminally ill cancer patients, Anne Ancelin Schützenberger convincingly argues that human beings possess enormous mental and emotional resources and that, with the help of sensitive therapists, they can develop the inner strength needed to confront the disease and even recover from it.

A person diagnosed with cancer cannot help but ask: Why me? Why now? By enabling cancer patients to deal with these questions and express their feelings, anxieties and suffering, therapists help patients to “understand the disease, to breathe, and emerge from the impasse,” writes Schützenberger. The process of delving into their life history enables patients to regain control of their lives and make meaning out of what seems incomprehensible, dark, and

confusing. They regain the desire to live and to fight. They have a project, a goal – to concentrate their energy on recovery with the help of supportive methods such as positive visualisation, art therapy, relaxation or sport.

In the fight against cancer, says Schützenberger, it is important for patients to maintain a positive attitude – hence the need to pamper oneself, to surround oneself with positive people, and understand the role that our beliefs and motivations play in our lives. No less important is

Vouloir guérir L'aide au malade atteint d'un cancer

9th edition

Anne Ancelin Schützenberger

La Méridienne/Desclée de Brouwer,
230 pp, euro 22

Le Coq-Héron, no. 180 Psychisme et cancer

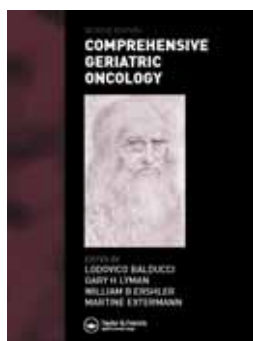
Éditions Érès, 180 pp, euro 16

the belief system of the physician. The enormous faith physicians place in statistics leads them, says Schützenberger, to believe more in the data than in the individuals they are treating. Healing and hope, she notes, also stem from the way

patients are viewed by others. The best present a physician can give their patients, therefore, is to view each of them as an *individual* and avoid imprisoning them in the representation they have of their disease and of themselves.

In the same spirit, the quarterly review *Le Coq-Héron* has produced an excellent issue devoted to the proceedings of the first meeting of the Association “Psychisme et Cancer”. Oncologists, psychoanalysts, nurses and patients discuss the existential suffering and vulnerability of cancer

patients, the role of psychoanalytical therapy, and the need to treat hurts engendered by the disease and the objectifying attitude of the medical world. Referring to Donald Winnicott, Jean-Pierre Lehmann reminds us that, etymologically, ‘cure’ means care, in the sense of *being concerned*. This was the case until the 17th century, when ‘care’ began to acquire the meaning of ‘remedy’. One of the most frightening aspects of oncology today is that ‘cure’ (in the techno/medical sense) and ‘care’ are almost totally dissociated. The two dimensions urgently need to be reconciled if medicine is to survive as a vocation.



Comprehensive Geriatric Oncology

2nd edition

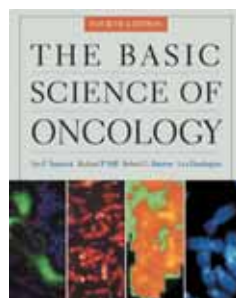
Edited by Lodovico Balducci, Gary H. Lyman, William B. Ershler and Martine Extermann

Taylor & Francis, 896 pp, £160

Cancer incidence disproportionately impacts on the elderly population. Sixty percent of all new cancer cases occur in this group, and the proportion may reach 70% by 2020 if current trends continue. It is therefore not surprising to see geriatric oncology (GO) increasingly recognised as a specialisation in its own right.

Impeccably produced, well researched and fully documented, the editors intend the new edition of this book to become “a frame of reference for the ongoing dialogue in the field of GO,” and it indeed offers a comprehensive review of the subject from the biology of cancer and aging to the management of various cancers in the elderly. The authors remind us that treatment remains an individual issue and a matter of common sense, which must take into account the multidimensional changes caused by age. They also point out a number of deficiencies in GO, such as the under-treatment of elderly cancer patients, especially for breast cancer, and the under-representation of the elderly in clinical studies for new therapies. Supportive measures

such as haematopoietic growth factors for patients receiving systemic chemotherapy are insufficiently used in the elderly population, even though the benefit of such measures can be as great, if not greater than in younger people. Extensive psychosocial support is also essential in managing elderly cancer patients, argue the authors. And importantly, they recognise that this support has to extend beyond the patient to their family and caregivers because, as they point out, “family caregiving for chronically ill relatives is an example of a major life stress.”



The Basic Science of Oncology

4th edition

Ian F. Tannock, Richard P. Hill, Robert G. Bristow and Lea Harrington

McGraw-Hill Medical, 570 pp, \$69.95

Introduction to the Cellular and Molecular Biology of Cancer

4th edition

Edited by Margaret Knowles and Peter Selby

Oxford University Press, 552 pp, £37.50

The unprecedented pace of advance in biology research makes it hard for oncologists – and daunting for non-specialists – to keep up with new discoveries. For the last 20 years, the above two textbooks have helped those interested in the biology of cancer to bridge the gap

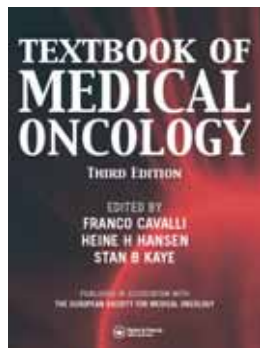
between laboratory work and clinical work, to keep abreast of the tremendous developments that have been made in basic science and apply these appropriately. With similar formats, full indexes, and practical layouts, which include a wealth of illustrations and references at the end of each chapter, these two affordable and up-to-date books cover more or less the same ground. They provide a detailed overview of the process that leads to the development and proliferation of cancer cells, and the current range of therapeutic approaches. The books are written clearly and their length is not overpowering. Where they differ is in their focus and level.

Tannock offers material suitable for a wide range of people interested in the study and treatment of cancer: resident physicians, general practitioners, nurses and students alike. In comparison to Knowles and Selby, it focuses more on medical practice, but provides less basic and less in-depth scientific data. The chapter on apoptosis in Tannock, for instance, consists of 10 pages and 27 references, while the equivalent chapter in Knowles and Selby runs to 18 pages and 55 references (with only one reference common to the two books). In contrast, where Tannock devotes three chapters to chemotherapy (pharmacology of anticancer drugs, cellular and molecular basis of drug treatment for



cancer, drug resistance), Knowles and Selby offers just one short chapter on the topic. Tannock also boasts an excellent glossary, which Knowles and Selby does not.

For readers who have some background in molecular biology or are more research oriented, Knowles and Selby is a good option. The new edition has been expanded from 22 to 30 chapters, to cover new technologies (e.g. transcriptomics and proteomics). When perusing these books, two striking observations emerge: the diversity of types of genes involved in cancer development and the fact that the more we discover, the more we realise that much uncharted terrain still lies ahead.



Textbook of Medical Oncology

3rd edition

Edited by Franco Cavalli,
Heine H. Hansen and Stan B. Kaye
Published in association with the
European Society for Cancer Research
Taylor & Francis,
540 pp, £160 (hardback)

UICC Manual of Clinical Oncology

8th edition

Edited by Raphael E. Pollock
Wiley-Liss, 936 pp, £43.50 (paperback)

Designed for resident physicians as well as for practising physi-

cians and other professionals working with cancer patients, these two textbooks, without being mammoth, provide a comprehensive survey of clinical oncology.

Both books begin with chapters of a general nature, such as the molecular biology of cancer, clinical trials, etc, followed by brief chapters on cancers organised according to their anatomical site. The two books are fully updated and contain useful indexes and references.

As to be expected in view of its price, Cavalli has been beautifully produced, and offers a more pleasant layout and more illustrations than Pollock. Since its subject is solely medical oncology, the basic scientific chapters deal with the principles of systemic therapy and systemic molecular targeted therapies. This is undoubtedly the strongest aspect of the book, as it is highly comprehensive and enables readers to fully understand the rationale for choosing specific drugs and drug combinations. The appendix includes an excellent section devoted to all the agents used in the treatment of cancer (including targeted therapy, endocrine therapies, radiochemoprotectants, growth factors and supportive treatments) and a useful list of abbreviations of drugs and other terms.

An interesting chapter is devoted to the growing field of genetic counseling and the clinical management of families with an inherited predisposition to cancer. Since cancer patients suffer an increased risk of life-threatening events, Cavalli also offers a helpful review of the main medical emergencies that they may experience.

The book's approach is to be commended. Instead of setting out a list of existing results, it offers a critical analysis of current knowledge.

A welcome new chapter on psycho-

oncology and communication (a theme accorded barely one page in Pollock) reminds us that "oncology clinicians tend to underestimate the amount of information that patients would like to receive", and that medical oncology is not simply a matter of mastering the rules of chemotherapy. According to the authors, oncologists themselves suffer from communication difficulties and find it difficult to talk about their own issues and the stresses they suffer from. This is indeed one of the factors that leads to burnout, which is experienced to some degree by 56% of oncologists. Some helpful preventive strategies can be found in this chapter.

The Pollock manual, which has been translated into 12 languages, covers a somewhat broader field, providing essential information on cancer detection, identification, diagnosis, and treatment. It includes important subjects such as paediatric malignancies, cancer in the elderly (missing in Cavalli), multimodality therapeutic strategies and the integration of molecular approaches in both diagnosis and therapy. While stressing the importance of quality of life for cancer patients, which is defined by the authors as "the culture of paying attention to pain and other symptoms," the Pollock manual lacks a global human approach to the subject.

