Putting the person back into personalised therapies

The concerns of a head and neck cancer specialist

➜ Simon Crompton

With ever more biological information required to pick the perfect protocol to target an individual's disease, the hopes and the fears, the priorities, wishes and concerns of that individual risk going unheard. Listening and learning remains the key to personalising therapy, says **Jan Vermorken**, who spent a career specialising in the cruellest of cancers.

It is unusual for chickens and elephants to figure prominently in interviews with the modern movers and shakers of medical oncology. But Jan Vermorken's passion for animals is more than an idle pleasure. It's what got him involved in medicine in the first place, and parallels the compassionate model of cancer medicine that he has tried to follow for forty years.

The chickens in question roam around the grounds of the Antwerp University Hospital, where Vermorken runs a clinic once a week as emeritus professor of medical oncology, having officially retired as head of the hospital's medical oncology department last year. He sits in his portacabin office, defiantly dapper against the plasterboard, and talks about how the stubborn cockerels block his route into the car park. "They just look at me," he says. "You will not see me hurt an animal." You can imagine the queue building up behind him.

His garish silk tie, it becomes clear on close inspection, is patterned with elephants and his computer screensaver revolves pictures of the baby pachyderms, provided by his favourite charity, an elephant orphanage in Kenya. Twelve years ago, he saw them at first hand, during a visit to South Africa. "The social interaction between elephants, the way they protect their little ones, is very impressive," he says. "And the way they handle it when one of them is dying: you see them suffer. I think the interaction between them is an example of how humans should be."

Vermorken's career has spanned clinical work, research and education. He has been professor of oncology at the University of Antwerp since 1997, when he arrived in Belgium from the VU University Medical Centre in his native Netherlands. He has carried out major studies on treatments for gynae-

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cological and head and neck cancer, coordinated large trials in breast and colon cancer, and been a leading figure in the Gynecologic Cancer Intergroup (GCIG) and study groups of the EORTC (European Organisation for Research and Treatment of Cancer) and ESMO (European Society for Medical Oncology). Now, in his supposed 'retirement', he has taken up the post of editor-in-chief of ESMO's journal, *Annals of Oncology*, which he wants to change to put more emphasis on translational research and multidisciplinary working.

Looking back at how the treatment of cancer has developed over his career, it becomes clear that while he is excited by the increasing potential to individualise drug treatment, he worries about the way modern health systems work against the individualisation of care. As time-pressed doctors increasingly follow protocols and rigid systems for treating cancer, are they losing sight of that compassionate – maybe elephant-like – need to respond delicately to individual wishes? Even if it comes to hastening a person's end rather than prolonging their life? Vermorken is concerned.

Given his love of animals, it comes as no surprise that Vermorken, now 66, set out into adulthood wanting to be a veterinary surgeon. But when he started training as a vet, he realised that he would often be expected to act in the best interest of the owner, not the animal. That shocked him. In medicine it was always clear who came first, so he started medical training in 1961 so that he could put the patient truly at the centre. He graduated from the University of Amsterdam in 1970.

Maybe, he acknowledges, it was the early death of his mother from ovarian cancer in 1973 that subconsciously made him set a course in cancer medicine, and a specialisation in gynaecological cancers among others. "That was still in the days when patients were being treated with single alkylating agents, and that didn't help my mother a lot. Her quality of life was not, in the last phases of the disease, a good one. So maybe that could have played a role…"

Although his passion for animals might have originated from the regular visits to his grandparents' farm, his family did not directly influence his choice of vocation. The really important figures in his career

appeared when he started his internal medicine training at the VU University Medical Centre in Amsterdam. Vermorken worked under Lopez Cardoso, one of the first internists to be strongly involved in oncology, at a time when oncology was not the most popular option for young doctors. He arranged for Vermorken to work at the Netherlands Cancer Institute in Amsterdam in 1974.

And although Vermorken worried about the emotional toll of working with seriously ill young people, his fears diminished as he began to practise, and he began to realise that combining clinical work with research provided hope as well as variety. His commitment grew as he became a medical oncologist under Bob Pinedo, who was appointed full professor in medical oncology at the VU University and was determined to develop medical oncology in the Netherlands.

Pinedo inspired Vermorken to see the potential of medical oncology, but he also encouraged him to expand his own professional horizons, showing him the importance of the interaction between clinic and lab. This sparked a lifelong interest in translational research, and the need to balance clinical work with research.

Every patient is unique

"Pinedo taught us all that every patient is unique. You have to continually learn as much as possible from each patient, exploring all the possibilities of what you can do for them. He wasn't a man to give up easily."

It was Pinedo who encouraged him to become active in the EORTC – first in the Gynaecologic Cancer Group (GCG), and then in the Head and Neck Cancer Group (HNCG). These were the specialisms that have stayed with Vermorken throughout his career – he has been a member of the EORTC-GCG since 1980 (chairman from 1983 to 1989) and a member of the EORTC-HNCG since 1985 (chairman from 2006 to 2009).

"We did a lot within EORTC in the earlier days," he says. "We wrote an enormous number of protocols. Conducting trials has become very complex nowadays, and it's difficult for EORTC to keep the same pace. But in those days there were far fewer administrative hurdles, and we wrote one protocol after another and also got them running. We were a group of friends who were willing to really work for each other, so it was great, great fun – and very rewarding."

"In the 1980s, there were tremendous changes in the treatment of these cancers. When I started, radiotherapists and head and neck surgeons were certainly the leading figures in head and neck cancer – and they still are to some extent because their therapies are crucial for this disease. But I think that the integration of systemic therapies over time has become more and more important, and medical oncology – which is a young profession – has gained standing."

Head and neck cancers, he says, have never been the most popular career choice for medical oncologists. It's not just the fact that systemic therapies were not so integral to the treatment of these usually late-diagnosed cancers. It's the less palatable fact that these cancers disproportionately affect less privileged members of society – heavy smokers and alcoholics for example – and that the aggressive treatments they usually require are often highly toxic and sometimes mutilating.

And now, he says, the increasing efficacy of cancer drugs to help control the disease is bringing its own problems. "I think it's the worst kind of cancer you can think of," says Vermorken. "For patients with advanced disease – which is about two-thirds of those diagnosed – the treatment has changed from using local therapies only to a combined modality approach, with a tendency in some countries to be primarily non-surgical. Now, as we're seeing the effectiveness of this grow, we're also beginning to understand that the late side-effects of these non-surgical approaches might strongly influence quality of life and might even be killing some."

There have been, he stresses, spectacular advances in the treatment of cancer since he came into oncology, and many have had a positive impact on head and neck and gynaecological cancers. New targeted therapies have a lower toxicity profile and may be combined with existing therapies

He worries about the way modern health systems work against the individualisation of care

"You must learn as much as possible from each patient, exploring all possibilities of what you can do for them"

Inspiring a new generation. Vermorken and his colleagues at Antwerp University Hospital hosted the first Elective Course in Oncology for Medical Students, sponsored by the EU and FECS (now ECCO), August 2005

such as radiation therapy and chemotherapy.

And although, until recently, there had been few targeted drug breakthroughs for head and neck cancers, trials coordinated by Vermorken have shown for the first time that patients with recurrent and/or metastatic head and neck cancer have a significantly improved outcome with the use of the monoclonal antibody cetuximab, when given in combination with platinum-fluorouracil chemotherapy. "I'm very happy that, after 30 years, we've finally found a way to give a better result to these patients," he says.

A different type of targeted care

He argues, however, that the fundamental challenge facing cancer doctors are not changed even by the advent of new targeted therapies. If they really want to serve the best interests of the patient, and to make sure that care is right for the individual, then sometimes the obvious treatment may not be the best option at all. Maybe a different kind of targeted care is required.

"Personally, I think we are sometimes too eager to administer medication to patients. That may be good in the curative setting, but is sometimes questionable in the palliative setting. We know that the biological behaviour of some of the tumour types is quite variable, and it is wise to see how rapidly a tumour is growing before administering medication – because it should be clearly understood that there is no effective medication without side-effects. I have many examples of patients with cancer who came to me for a second opinion, having been advised to receive chemotherapy,

and it was clear that it could be years before they needed it because the tumour was not aggressive."

When the cancer is advanced, the challenge of doing the right thing for the individual becomes even greater. "For people who are dying, the medical oncologist can help these people by not running away when things become difficult. And what I mean is, for example, active euthanasia."

Vermorken remembers the days when physician-assisted euthanasia was not officially legal (it was legalised in Belgium in 2002), and subsequent police questioning: "talking to you as if you were a criminal," he says. But he will also never forget a woman with end-stage head and neck cancer who asked for euthanasia, and said, just before the drugs were administered, "Please do it as quickly as possible."

"She didn't want to gradually go to sleep. What we said didn't matter to her. Her suffering was so tremendous, and that made an enormous impression on me. I'd never seen someone so longing for the end of life, and I think doctors should never walk away from this."

In fact, Vermorken believes that if doctors talk openly to their patients about euthanasia, it worries them less, and they are unlikely to pursue it as an option. "It's a strange thing. The moment you make clear you are not running away from it, and you will be at their side until the end, it's very often sufficient."

It's not that Vermorken is a passionate advocate of euthanasia – which is, of course, not an option in most countries. But the importance of sitting and listening to patients is a permanent theme throughout our interview. "I'm worried that doctors today are so rushed that they can't listen and learn about the individuals they're treating and what they want. But you will only be a good doctor if you do so. Patients aren't a form to be filled in."

These are principles Vermorken carries through to his teaching work. As well as courses in cancer medicine at the Antwerp University Hospital, he has run various summer schools for medical students since 2004, backed by universities throughout Europe, which, he hopes, have stimulated interest in cancer medicine – whether it be surgery, radiotherapy or oncology.

Teaching students to listen

The most enlightening moments on the courses come when students have to interact with patients who tell them about the impact that health care professionals can have at such a difficult time in their life. "You can see the students beginning to lose their fear, and begin to discuss things more openly with patients."

A key theme in his teaching has been the importance of multidisciplinary work. As a specialist in the field of head and neck cancer and gynaecological cancer, where combinations of treatment are often key, Vermorken knows that feeding in the perspectives of different disciplines into decision-making processes can only benefit the patient.

He has little time for the professional turf wars that have been fought in some European countries over, for example, who should lead care in gynaecological cancers.

"There are differences from country to country," he says. "In the Nether-

Still looking ahead. Even in retirement Vermorken remains an important presence at conferences like this one in Beirut, January 2010, where he gave a presentation on future directions in head and neck cancer treatment

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lands, there is the discipline of gynae-oncology – gynaecologists who have specific surgical training and skills in major surgery, such as debulking surgery in patients with advanced ovarian cancer. Preferably, patients with gynaecological cancer should be treated by such specialist colleagues. But when there are many treatment options, these need to be discussed by a panel of experts, each of them making full use of each other's expertise, and entrusting patients to those with most experience in a particular field. The medical oncologist should be part of this decision-making process from very early on."

Although Vermorken has never worked in a laboratory, his research work has been significant, and he's particularly proud of three areas of work. One is the clinical research that led to the first improvement in outcome of patients with recurrent and/or metastatic head and neck cancer. He hopes the successful cetuximab trial will now lead to further treatment developments.

A second area is the introduction of a new form of induction chemotherapy, including docetaxel (the so-called TPF regimen), for patients with advanced head and neck cancer that cannot be removed by surgery. His research on this was published in 2007. The improved outcome of these patients led to a revival of induction chemotherapy in head and neck cancer and has strongly influenced the type of studies now being conducted in the advanced disease setting.

A question of immunology

His third research achievement is possibly the one that has had least impact, but may also have the most potential. In the 1990s, Vermorken coordinated a study investigating whether vaccinating survivors of colon cancers using vaccines derived from their own cancer cells reduced the risk of recurrence. It seemed to, but the findings were never confirmed by others: "For a variety of reasons," says Vermorken. "Logistics, complicated procedure, financial hurdles … But I think it was a proof of concept. It has shown to me that the immunological response in the body to tumour cells is absolutely of importance."

With grandchildren Beau, 7 months, and Claire, 6 months

Vermorken loves working with people and enthusing students about medical oncology, so in his retirement he's as busy as ever – finding a time to speak to him at all is a feat. He's still attending cancer conferences, organising symposia, running an annual international medical oncology course, participating in or running summer schools with ESO and ECCO, running post-ASCO meetings in Belgium and chairing the Belgian Association for Cancer Research. He is also a member of journal editorial boards, and still active in the EORTC-HNCG group and many other committees of national and international cancer organisations.

His family – wife, two grown-up sons, and two grandchildren – understand that his work is his hobby, and always will be. So though he is looking forward to spending more time with his wife at his holiday house in their beloved France, enjoying the good food, he acknowledges that he'll probably be looking through some journal papers while he's sipping his fine wine. And one day he will find time to return to Africa, to meet those formidable, caring elephants again, face to face.