

John Smyth: unity is strength

→ Marc Beishon

John Smyth likes to get things done. Head of a major research centre and member of EMEA's scientific advisory committee, he argues for closer cooperation between academia and industry. He also wants a stronger voice for oncology in Europe, and hopes to convince his FECS colleagues to opt for greater unity when he takes on the presidency this October.

It's impossible to escape comparisons with the European Union when talking to John Smyth, the incoming president of the Federation of European Cancer Societies (FECS), and professor of medical oncology at the University of Edinburgh, Scotland. While the EU undergoes painful soul searching on its constitution, Smyth's mission for FECS is to bring about a fundamental switch to a single, unified organisation rather than a loose federation of societies. And of course one of the key aims of such unity is to work more effectively at EU level, to influence decision makers in critical areas of cancer research and treatment, such as drug licensing, clinical trials and care standards.

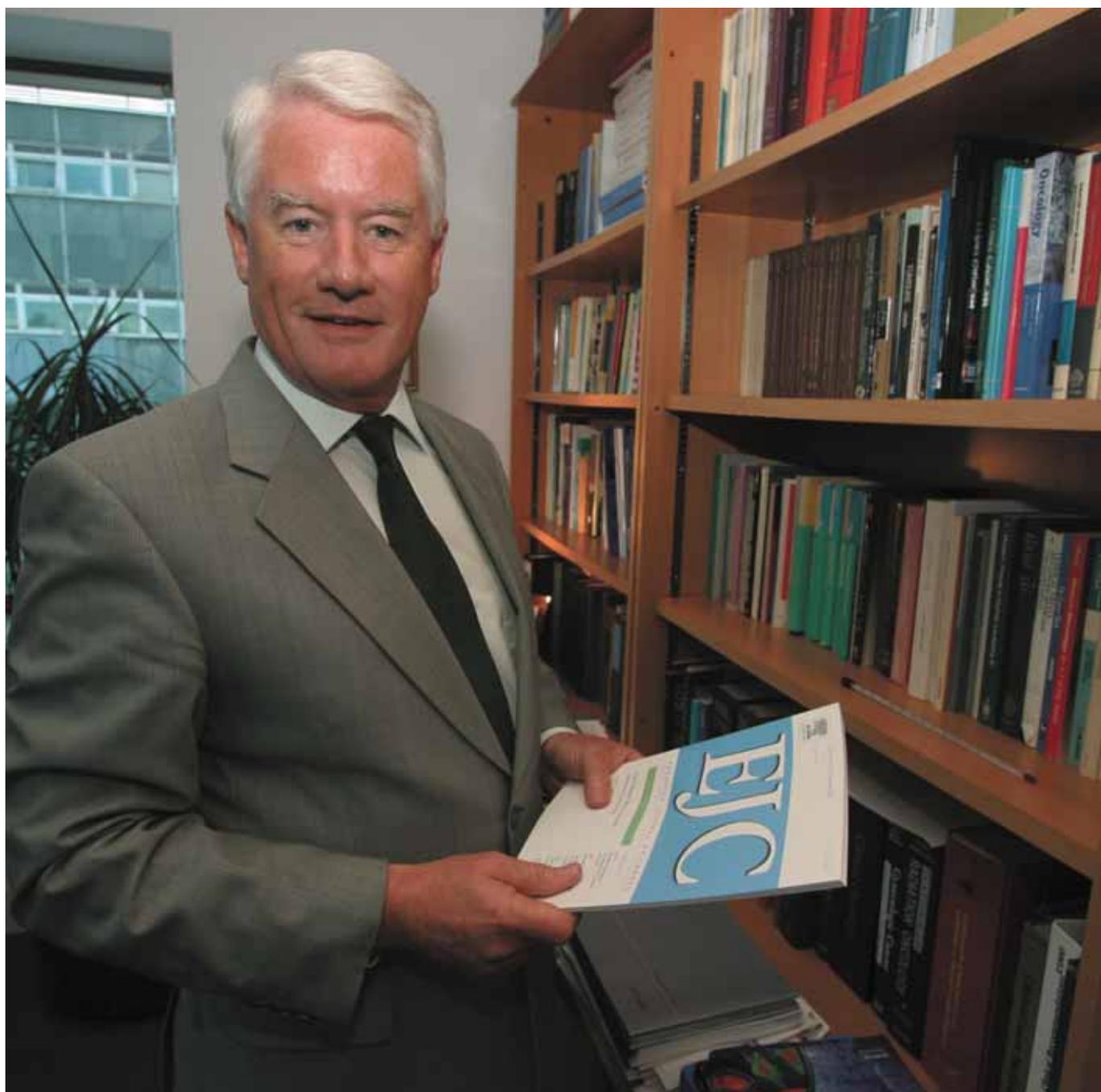
The unity theme extends further, as Smyth has been one of the early proponents of multidisciplinary oncology work that's been developing under his guidance since he took up his post in Edinburgh way back in 1979. He is now also the director of the Edinburgh University Centre for Cancer Research, which is housed in a new building alongside the oncology clinics at the huge Western General Hospital, and links with

several other oncology-related units on site to form one of Europe's major cancer centres.

He's quick to emphasise that this multidisciplinary work does not mean bringing together just say medical and surgical oncology, but also psychology to help treat patients as a whole. In a field where the word 'holistic' is often bandied about, Smyth and his colleagues have a good claim for a strong, all-round patient management programme, which also includes a psychosocial research component.

"There aren't any trivial conversations in cancer, but I tell our trainees that it is possible to help everyone who comes through our door and that patients should feel comforted when they leave the consulting room. Knowing the medical facts is easy – any doctor can learn them – but getting communications right is hard. After all, one of the main reasons people go into medicine is to help others."

Good communications is also the key enabler for Smyth's work and ambition outside Edinburgh. He admits that there still is a lot of talking to do to persuade entrenched interests in



COLIN MCPHERSON / COBBIS / CONTRASTO

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the various cancer societies to share his vision for FECS – and he has of course witnessed at first hand the formation of divisions in the oncology community over the years, particularly in Britain.

Smyth’s present commitments also include being the oncologist on the UK’s Committee on Safety of Medicines, and he’s on the scientific advisory committee at the European Medicines Agency (EMA), where again he stresses the importance of opening up communications lines, particularly between industry and academia. “Most of my research has been on drug development, and the process of approving and licensing medicines is extremely important,” he says, adding that there is too much at stake for ‘snobbishness’ about industry by academics to continue.

He has a platform to explore the academic issues – he is also the current editor-in-chief of the *European Journal of Cancer*, adding to a considerable workload. Apart from the administrative duties of running the cancer centre, and his international work, Smyth continues to see melanoma and ovarian cancer patients, teach undergraduates and direct research programmes (on ovarian cancer, melanoma and drug development). He’s also a governor of the local hospice.

He does this with rigorous attention to time management and delegation, self-expressed “irrepressible enthusiasm and humour”, and probably with the power of a beautifully modulated voice – Smyth was an international singer with the Monteverdi choir under the very demanding conductor John Eliot Gardiner, and he is possibly the only medical oncologist to have sung on

stages from La Scala to the Lincoln Centre. Indeed, he went to the Cambridge University on a choral scholarship, but chose to read natural sciences. “I decided not to pursue music, largely because I had a brother who was a child prodigy on the piano and didn’t want to compete with him.” A second love was (and is) flying – he joined the Royal Air Force at Cambridge, and flies small planes today as a hobby. But thanks to a “general interest in science and people” he found himself studying medicine, moving to St Bartholomew’s (Bart’s) in London, and went on to benefit from a ‘magical’ training before the onset of more structured – and curtailed – development that doctors in Britain have to conform to today, according to Smyth.

“It’s rare now in Britain for anyone to have the experience I did. As an oncology consultant, for example, I did some neuro, thoracic, paediatric, gynae and breast work. It’s quite right now that you can’t be an expert in all these, but I do think doctors have to specialise too soon these days.”

As for medical oncology, Smyth was attracted to this then very new discipline by one of his mentors – and that’s another aspect of his training that is ‘disappearing’ today, he feels. “I’m concerned about the lack of mentoring and apprenticeship for young doctors. I was fortunate in having two mentors who had a profound affect on me.” The first was gastroenterologist Anthony Dawson (who became the Queen’s physician) – “He had an extraordinary capacity to talk to people about chronic illness – I learnt a huge amount from him about talking to patients about cancer as a disabling disease.

“Both men helped me understand that you can face up to apparently appalling situations”

“Then I worked for Gordon Hamilton Fairley, really the founder of medical oncology in Britain. He had a fantastic capacity to talk to people about death. Both men helped me understand that you can face up to apparently appalling situations rather than do what a lot did then in the 1970s, which was not discuss such ‘dark’ matters.”

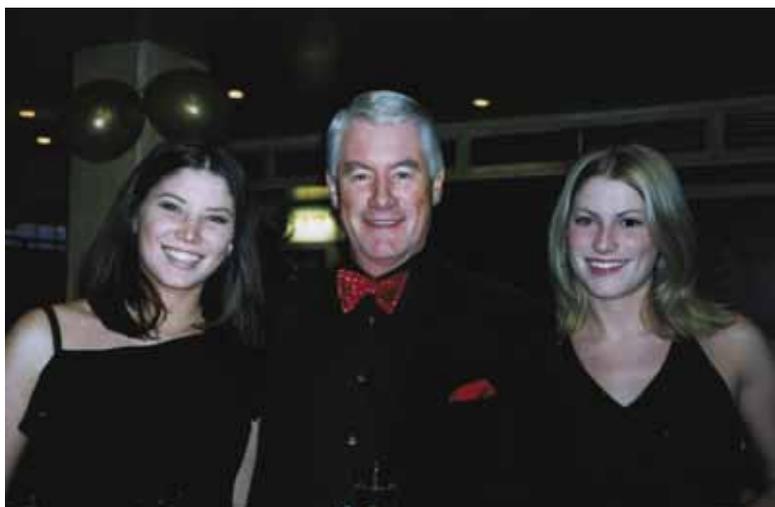
After working for Hamilton Fairley at Bart’s he went to the Institute of Cancer Research at the Royal Marsden, where he did laboratory work and “had one of my few original ideas, about the importance of adenosine in lymphocyte metabolism, which resulted in pentostatin, a drug still used today to treat rare forms of leukaemia and lymphoma. This subsequently led to the widely used lymphoma drug, fludarabine.”

This work got Smyth his PhD and a travelling fellowship to the National Cancer Institute in the US, where he “fell under the spell” of many more mentors, famous names in oncology such as Bob Young, Bruce Chabner and Vince DeVita.

He returned to the Royal Marsden, and then two years later was offered the professorship at Edinburgh, just after his 33rd birthday. “This was very scary, but I was able to draw on my cadre of mentors to help me. I was amazed to get the job – I didn’t expect to have an academic career, as I was always middle-of-the-road in exams, but I was strongly inspired by the people around me in medical oncology.”

Certainly the rigour of the US approach to drug development made a great impression – he says that those who feel the early chemotherapy days failed to deliver misunderstand medical oncology. “The Americans were very protocol driven and very good at publishing evidence, which you need to be when working with a narrow therapeutic index and sailing close to the wind between help and harm. They built up what we would now call an evidence base – and many Europeans went to the US to learn this discipline.”

With hindsight, there was, he adds, a tendency to push on for too long with what worked for leukaemia and lymphoma, and to push therapies to the limit. “But I don’t think anyone was seeking to cure cancer – there has also been confusion for the public who don’t realise that cancer

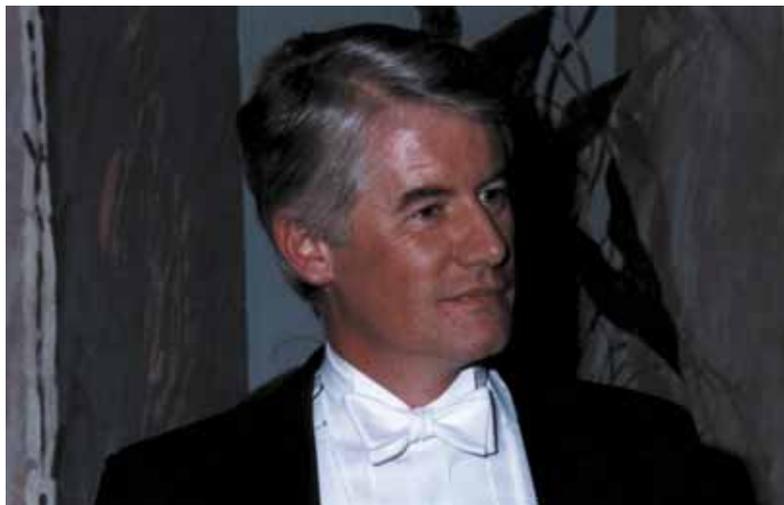


With daughters
Anna and Sarah
at a family
celebration

is a condition of the body, just like getting older.” At Edinburgh, he found that surgical and radiation oncology were already well established, and added the third – medical oncology – component as part of a joint cancer centre effort. “This was partly out of necessity – I couldn’t set up a centre in a big city on my own – but mainly because I believed in multidisciplinary working. It has served us well; we now have 21 consultants, all the clinics are multidisciplinary, and we have some 30,000 outpatient appointments a year.”

Nor did he have to sell the importance of clinical research – there were already ongoing trials and he joined in by setting up a drug development and pharmacology lab, tapping into a high standard of medical expertise in the area that has long been a feature of Edinburgh. A training programme was set up, and Smyth’s group established a good reputation for drug trials and relationships with industry, and became one of the leading British clinical research centres – in fact it was one of only two places earmarked for investment by the then Imperial Cancer Research Fund.

A standout development, and one that Smyth is especially proud of, was work with Glaxo on the first of the 5HT₃ anti-emetic (anti-nausea and vomiting) drugs – his group conducted the first worldwide trials. “This has been one of the greatest contributions to patient tolerance of chemotherapy,” he says. He was also a participant in the now defunct early clinical trials



Appropriate nerves before a live recording at the Salzburg Festival

group at the European Organisation for Research and Treatment of Cancer (EORTC), where he gained a lot of peer support and had fun meeting others – often at people’s houses around Europe.

“While we were very conscious of physical toxicities we also wanted to learn about the emotional experience and what we now call quality of life,” he continues, mentioning that his wife, Ann Cull, a research psychologist, set up a psychosocial oncology group and played a key role with the EORTC in establishing a group of quality of life researchers, with Edinburgh developing assessment tools. On-going work on what he terms “symptoms research” – not just sickness and pain but distress – has a current focus on fatigue (“a complex mix of the physical, emotional and psychological”), and ties in with Smyth’s core interest in patient communications.

Where Smyth feels he has really taken a lead is with the clinical research effort, although it has been a struggle to reach the funding level the centre now enjoys, and also to attract staff. “It’s much more challenging for scientists to work on human material. If you want a paper in *Nature* or *Cell* you work on clean, well-worked systems

that will do what you want, such as yeast.” Britain, he adds, is favouring basic research too much, while universities have become obsessed with research assessment and getting papers published in high-impact journals. “Clinical trials – including our first into man Phase Is – don’t fall into this remit and the research is expensive. Clinicians get paid more than lab scientists, and universities don’t have the resources to provide more lectureships and professorships.”

An example: “We’ve just done some fascinating research on an anti-inflammatory medicine, with Fran Balkwill at Bart’s, that may influence diseases such as ovarian cancer. But the value of such trials will only be realised in the lab, as we are looking at scientific end points.” This drug – infliximab – is used, he says, to treat rheumatoid arthritis, but also inhibits the tumour necrosis factor. “So far it looks very encouraging in treatment of women with ovarian cancer. Applying science in such a dynamic clinical experiment has been very exciting.”

As a centre, Edinburgh now looks to have considerable strengths. In addition to the regional clinical centre, Smyth’s University Cancer Research Centre embraces research programmes on basic genetics and cell biology, a colon cancer genetics unit, research into prostate cancer and leukaemia and a combined programme investigating endocrine sensitivity and resistance in breast and ovarian cancer. Basic science and clinical research are linked by the drug development programme, which translates molecular and preclinical pharmacology to early clinical trials.

There are also ovarian and breast tumour banks, with many tissues having the advantage of full histories: “We not only know where the tissues came from but what happened to the patient subsequently,” says Smyth. “We’ve been harvesting them for years. These tumour banks will be an absolute gold mine over the next ten

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years or so.” Another strength of Edinburgh, he adds, is simply having research people right alongside the hospital clinics. “As I travel the world I’ve found relatively few places where the lab and clinical complexes are physically joined up,” he says.

Many of the successes and problems at Edinburgh will be familiar to those in other cancer centres, but as Smyth points out, one of the fundamental differences between Europe and the US is the former’s wide diversity in patient and professional expectations and experience as you move among countries and regions. “The European oncology world has always been a complex mix, with great intellectual ability and good funding, but heterogeneity is the challenge – it’s no good trying to impose say the British or French way on the rest of Europe.”

FECS, he says, has been addressing issues such as clinical trials best practice and multidisciplinary working through workshops for junior oncologists. But there’s a much bigger picture – the image and accessibility of the European oncology community as seen by healthcare decision makers, politicians, industry and the public. While FECS remains as essentially a ‘talking shop’ – albeit discussing important issues – opportunities to present a coherent voice to the outside world will be lost, says Smyth. As things stand, there are just too many interest groups competing for attention – and a single oncology society may have had a better chance, say, of staving off the worst of the European clinical trials directive, “which has been an absolute disaster for academic research.”

“I realise that people are worried about loss of identity and visibility but I think that you can be an important part of a big enterprise as well as a small one.” Certainly, FECS and other bodies such as the EORTC and the European Society of Medical Oncologists (ESMO) – of which Smyth is a past president – have made concerted

efforts to lobby on issues such as the trials directive and the recognition of medical oncology. But Smyth is angling for the professionalism and clout that a unified society can bring, and comments that there has been too much “amateurish” lobbying work and protectionist behaviour.

A case in point in Britain, he says, stretches back to the 1980s. “With medical oncology still fairly new we formed the Association of Cancer Physicians – and the radiotherapy people were so jealous they set up the British Oncological Association. This year, for the first time, we are finally having a single meeting.” If people are serious about multidisciplinary working, there should be no room for big egos and professional jealousies, he says. That names for disciplines around Europe are confusing and inconsistent – such as what comes under ‘clinical oncology’ – and that some professionals have private practice to protect, makes the situation yet more challenging, he adds.

“We are spending too much time and money duplicating efforts, with people massaging their egos in little fiefdoms,” he says. “Ultimately, this is about improving patient care by providing greater equality of access to drugs and equipment around Europe. We stand a much better chance of doing this as a unified society than by arbitrary lobbying by small groups.”

The situation is compounded too by the proliferation of meetings, which are “seriously out of control”, according to Smyth. This is partly driven of course by the huge increase in industry money over recent years, but he feels professionals are now faced with an impossible choice of events. “I could be away 40 weeks of the year and not necessarily be any wiser,” he says, adding that getting the right mix of new materials and the right people is often hit and miss. But he considers meetings and workshops to be pivotal to professional learning – “Education isn’t about handing out recipes from a textbook or a journal. You

“Education isn’t about handing out recipes from a textbook. You need debate and discussion”

need debate and discussion. Cancer medicine is a very difficult and subtle art form – you add science to the art. It’s so easy to do something that is useless, harmful or just misleading.”

Smyth would like to see fewer meetings, appropriately themed at certain times, and which also open up more balanced debate on the implications of research. Again, he hopes that FECS – or son of FECS – will be able to help streamline events.

He notes the standing ovation given to a Herceptin (trastuzumab) breast cancer trial paper at the last American Society of Clinical Oncology (ASCO) meeting, but is concerned that the ensuing headlines are picked up by patients and lobbyists without prior debate about cost implications and priority setting for treatment and screening. “Glivec is another good example – drugs like this can place huge unscheduled burdens on our health funders. But these ‘irresistible’ drugs don’t come out of the blue – results are known well in advance of the big announcements and we should have systems that allow governments to anticipate research. We have to take responsibility for the hype and curtail it to allow data to settle in a more mature way.”

Part of the streamlining process involves drug licensing and relationships with the drug industry. Smyth’s primary interest in drug development, extensive consulting work and positions on the British and European approval bodies have given him considerable insight into pharma’s workings – although some decisions remain a mystery. “We have to have a more open, honest and practical dialogue with industry. Over 25

years I’ve seen the attitude that academia is ethically pure and industry is commercially tainted. While such views may have had some validity, we have to recognise now that pharma has extraordinary financial resources, some of the world’s best scientists and the best technology. My contact with companies tells me that unless the science is sound and the medicine works they will not try and sell it.”

For EMEA, his hope is that it will offer an equivalent European licensing marketplace for the industry to the US Food and Drug Administration, where most commercial activity is currently focused. This should come about as recognition grows that Europe has different priorities to the US and may offer a better route to market for some drugs. Smyth adds that EMEA’s scientific advisory committee is also very keen to open up dialogue with industry to make sure that ‘pivotal’ Phase III trials are done to a high standard, with the result that medicines are made available faster to the public. “It’s tragic when millions of euros are spent on a Phase III trial that is poorly conceived and we can’t give a licence – not because of the end result, but because the protocol was not well designed. I’ve had recent experience of this, and it is hard to understand why companies set out on expensive trials that are fatally flawed.”

However, while it’s in everyone’s interest to shorten time to market, he adds that he’s not happy with some recent fast-tracking – in particular Iressa (gefitinib), which was approved in the US from non-randomised trials, and which has higher toxicity than anticipated. “The pendulum

“With more treatment opportunities than we can afford, how do we prioritise?”

has swung too far away from our previous very conservative stance,” he says.

While stressing that the oncology world needs to play its part in becoming much better organised, Smyth says that societies – nations, that is – have to create ways of involving the public in healthcare decision making. “It’s one of the things I’m really interested in and it fits in with my remit at FECS and drug licensing – and I’ve spoken on public platforms about it. With so many more opportunities for cancer research and treatment than we can afford, how do we set priorities? It’s absolutely clear to me that such decisions are not for doctors or lobbying groups alone, but in Britain I know of no public forum where we argue the case for healthcare.”

While noting that the EU breast cancer resolution is a good example of effective lobbying, he comments: “You will always find people who support breast cancer for well understood reasons – but it’s a pity if society has to fall back on groups of vulnerable patients and a few spokespeople who can argue their case.”

Meanwhile, healthcare administrators such as hospital directors should not be placed in a position where they have to choose between different cancer treatments. That leaves the politicians – and Smyth has no truck with the “unspeakable nonsense” they spout at election times. Those who do take responsibility have his admiration – such as the Finnish health minister who addressed the last European Cancer Conference (ECCO) meeting. “She said that ultimately she makes the decisions and stands by them.”

He would like to see such debate more closely linked with health promotion efforts, mentioning that Scotland has one of the world’s best melanoma databases – and although incidence in men has trebled in the last 20 years, survival has improved thanks to an allied education programme that has seen people presenting earlier. Prevention is another area he wants to devote more time to, especially strategies that target young people.

If all this sounds like far too much work for any one person, Smyth says his university will be giving him time out to do the FECS work – he’s seen too many colleagues overloading themselves



to make the mistake of stretching himself too thinly. Home life is probably less frantic now that his four daughters have grown up and are safely pursuing non-medical careers, and there’s a country cottage to retreat to. His bass voice is now a bit too ‘old’ to sing on the big stage, but flying is very much on the agenda – he and his wife have recently flown over Mt Blanc and watched whales off the South African coast in a small plane – as he says, you can’t think of any other problems once at the controls.

At 60, his immediate work ambitions lie in two areas. At FECS, in whatever shape it becomes, he’s intending to take a more “harmonious” message to European politicians and professional groups, recognising though that a lot of time-consuming “listening and talking” will need to be done. In Edinburgh, with all the physical and manpower resources in place for a modern cancer centre, the push is on for translational research to be rolled out into clinical medicine and he’s in no doubt that many new treatments will be available. “Also, I hope I’ll be around long enough to see a recreation of interest in academic medicine in Britain,” he adds.

But what really makes him tick are “family, champagne and humour – humour especially is a very important part of life, no more so than to cancer patients, for whom it’s a coping strategy.”

No doubt a few bottles will be opened too if he gets everyone singing from the same European hymn sheet.

**En route
for Mont Blanc
in a plane older
than himself!**