Vesna Kesic:

exporting excellence in women's cancers

Marc Beishon

Working at a massive hospital in a country with high rates of advanced women's cancers gave Vesna Kesic the ideal opportunity to hone her skills as a gynaecological oncology surgeon. Thanks to her commitment to plugging the widespread gap in specialist training, the benefits of her expertise are being felt by patients well beyond the walls of her own institution and even her own country.

There are few prevention strategies in oncology for which there is virtually unanimous consensus, but screening for cervical cancer is certainly one. It is currently the only cancer screening which has a solid evidence base to show large-scale life saving and where intervention can be minimal – although many have high hopes that breast and colorectal screening will prove similarly effective.

Yet many women are still dying of cervical cancer every year, especially in emerging nations and indeed to some extent in developed countries. Some 490,000 new cases are diagnosed every year worldwide, with 250,000 deaths. Considering that screening and the Pap smear have been available for many years – since 1967 in the UK, for example – suffering and death on this scale should not be happening, as Vesna Kesic, head of gynaecological diagnostics and oncology at the large Institute of Obstetrics and Gynaecology at the Clinical Centre of Serbia in Belgrade, is the first to agree.

"Despite being at the heart of Europe, in 2002 my country had cervical cancer rates twice as high as the world average and three times the rate of the European Union, with the highest incidence in all of Europe," she notes. "This was completely unacceptable as countries with good screening policies do not have a major problem with cervical cancer now."

This neglected disease finally made it on to Serbia's policy agenda after the publication of figures that showed just how dire the situation was: with a population of only 7.3 million, more than 1300 women a year were dying of all gynaecological cancers. Since then Kesic has been instrumental in establishing a screening pilot as part of a new cancer plan. But as she points out, the lessons learnt so far in addressing cervical cancer are critical not only for Serbia but also for other countries in Europe where incidence is also high. According to the European Cervical Cancer Association (ECCA), 30,000 women in Europe are dying each year, while there are 60,000 new and 225,000 ongoing cases. Women in central and eastern European countries are particularly at risk.

But screening is only one part of a story that also involves cultural attitudes and barriers, healthcare organisation, and diagnosis and treatment pathways. As with breast cancer, where mammography can be seen as only one pillar of a multiprofessional

KOCA SULEJMANOVIC

service, cervical cancer screening needs to be integrated into a coherent structure. "It is also only one disease we group together in gynaecological oncology, the other main cancer sites being the ovary, endometrium and, to a lesser degree, vulva and other locations," says Kesic.

The development of the specialist field of gynaecological oncology, she says, is at the centre of the drive to improve outcomes, and she and colleagues both in Serbia and around Europe have dedicated much effort to gaining recognition and improving education and training, notably through the European Society of Gynaecological Oncology (ESGO). "This has been a Cinderella subspecialism in obs/gyn for Serbia and surrounding countries for decades," she says, pointing out that many general gynaecologists treat patients with cancer. "We have seen that treatment by inexperienced surgeons and failure to follow guidelines are associated with increased risk of disease recurrence and mortality."

But oncologists with inadequate specialist skills in gynaecology also pose a problem. "The status of gynaecological oncology ranges from true recognition of gynaecological oncology and strictly defined training, such as in the UK, to complete disorganisation in which an oncologist with just a few months in obs/gyn can treat a patient," she says. Her message is clear – trained gynaecological oncologists must displace both general oncologists and gynaecology practitioners. "After all, we have other well-developed subspecialisms in obs/gyn, such as IVF (in vitro fertilisation) and

"General gynaecologists need to realise they cannot do everything, but they are afraid they will lose prestige"

urogynaecology. General gynaecologists, especially, need to realise they cannot do everything – and they don't need to do everything. They are afraid they will lose patients and prestige, but in practice there are sadly more than enough sick people in the world for us all to find a place in this field."

Like other cancer sites, gynaecological cancer presents as a wide spectrum of tumours, which she says can be very different in cause, biological behaviour and therapy. "Ovarian cancer is the most challenging, because it can arise from any embryological tissue. And more and more we see previously very rare cancer types and multiple malignancies – the profile of gynaecological tumours has significantly changed. But when properly treated, the overall prognosis for most gynaecological cancers is reasonably good."

Kesic's primary expertise is in surgery and diagnostics, but her impression of progress in basic research and in therapies for more advanced disease is that this group of cancers has not seen any major steps recently. There is of course one spectacular advance in prevention – the new vaccinations against the human papillomavirus (HPV) that cause cervical cancer. "It is the major discovery in my speciality in my time and probably is the future for cervical cancer prevention – but the story is very complex and we cannot yet prove that the vaccinations do decrease the number of cancers."

Growing complexity and tensions among practitioners is not a situation unique to gynaecological cancers, of course, but Kesic points out that these tumours are particularly distressing because they can affect women not just physically and socially, as in any disease, but also in sexual responsiveness,

A mission to educate. More than 350 doctors from all over Iran attended demonstrations of laparoscopic-assisted hysterectomy, lymphadenectomy and intraperitoneal therapy, as well as panel discussions of controversial issues, at this three-day seminar in Mashhad in October 2008 – part of a major programme of educational events organised by Kesic with the IGCS and ESGO

body image and, very importantly, fertility.

It was the combination of the intense human side of the work and the knowledge that much disease can be prevented or successfully treated that drew her into the field and continues to fuel a mission to bring multidisciplinary thinking to many places around the world.

In addition to working with the Serbian authorities to get cervical screening off the ground, Kesic has clocked up a number of notable achievements both at home and internationally. She was instrumental in founding the Serbian Society of Gynaecological Oncology in 2003. This October, the Society played host to the ESGO's 16th biennial conference, in Belgrade, landing as keynote speaker Harald zur Hausen, the German virologist who won a Nobel prize last year for uncovering the role of papilloma viruses in cervical cancer.

She also led Serbia into membership of the European Cervical Cancer Association (ECCA) – the first eastern European country to join.

But it is probably her work setting up an ambitious programme of teaching seminars, with both ESGO and the International Gynecologic Cancer Society (IGCS), that has made the biggest contribution to exporting her mission for excellence in gynaecological oncology to all corners of the globe.

It was the obvious needs of Serbian women that kept Kesic in her home country during the dark days of war and sanctions in the 1990s, when she could have escaped to a far better resourced department in the UK or elsewhere. In fact, gynaecology is fortunate to have her at all – obs/gyn was just about the last place she wanted to work on completing her medical degree in Belgrade.

"I did not have any great wish to be a doctor – I think it was just an unconscious desire to help people that saw me study medicine, but then I became very interested in cancer, even spending my summer at our National Cancer Institute rather than going on holiday. I think I saw myself as coming up with the next great leukaemia treatment, or such like. At that time I won an important award for a paper on thyroid cancer. But when I looked for a job I couldn't find one in oncology. After a year, I had to take a post in obs/gyn."

While it can be amazing to be involved in a field where life is being born, says Kesic, obs/gyn can also be very stressful and disruptive. She set about carving out an oncology role within the large Institute of Obstetrics and Gynaecology – a process that proved to be both long and painful. Even though the Institute is the referral centre for the whole of Serbia, and surgically treats the largest number of cancer patients in the country, it still lacks the necessary facilities. Chemo- and radiotherapy, and other specialist treatments, have to be carried out in collaboration with Serbia's National Cancer Institute.

Today, however, not only does Kesic have a unit of her own – diagnostics and oncology – but she also has an obs/gyn professorship at the University of Belgrade medical school.

While benefiting locally from excellent general gynaecological surgical training, her main route to integrating oncology came from a series of visits abroad that she organised herself, starting at London's Hammersmith Hospital under Patrick Soutter, who also guided her PhD topic on lymphocytes in cervical cancer. Claes Trope at the Norwegian Radium Hospital is another key mentor.

"As a result, the heads of department here allowed me to carry out radical procedures much earlier than is usual in Serbia, and my challenge was to explain how we should be using guidelines that just were not followed at that time across the spectrum of gynaecological cancers. For example, radical hysterectomy was not as it is today – many surgeons were not removing all the right tissue, and pathology reporting was poor. I also helped to introduce organ-conserving surgery for the cervix – hysterectomies were often done unnecessarily, and they still are in hospitals that lack good oncology input."

Tailored surgery, introduction of laparoscopy and sentinel node biopsy are the most important advances in surgical gynaecological oncology, she adds. "And to preserve fertility in a woman with a

"My challenge was to explain how we should be using guidelines that just were not followed at that time"

"To preserve fertility without compromising outcome is the most exciting achievement of modern practice"

gynaecological cancer, without compromising oncological outcome, is for me the most exciting human achievement of modern practice."

Kesic is particularly proud of the detailed study she has made over the years of colposcopy, the diagnostic technique used to examine the cervix and other tissues. In combination with cervical smear tests colposcopy can – in the right hands – achieve near 100% accuracy in detecting precancerous lesions and is an important secondary prevention method. "It really does allow us to plan treatment properly and avoid unnecessary hysterectomies," says Kesic.

But it has no fewer than 50 core competencies, as identified by the European Federation of Colposcopy (which was founded in 1999 with the then Yugoslavia, which had set up its own society four years earlier, one of the founding members). Most countries have only recently begun national colposcopy training programmes, which again is why Kesic is so committed – as an authority on the technique – to educational activities, and indeed she helped attract another event to Belgrade, the 4th European Congress for Colposcopy and Cervical Pathology, in 2007.

Just 100 metres from the Institute, a NATO bomb was dropped in error on a hospital building in 1999 – a horrific event that marked the beginning of the end of a long period of Serbian isolation, and when thoughts of international collaboration, such as on multisite research projects, were unthinkable.

"With the airports closed the only way I could leave the country was to take a bus to Budapest and fly from there. Our medical schools did not have the funds even to go to congresses or take up fellowships. Meanwhile we were left with old equipment we couldn't repair properly and not much in the way of antibiotics. There was a time when we had to use ordinary soap to prepare for operations. But most depressing was really the lack of knowledge from the outside world – we were even restrained from getting books and medical journals. Remember, this was before we were on the Internet, which gives easy access to new medical information."

On occasions where she was able to make trips abroad, Kesic says she was pleased to report back that her clinic's skills were up to standard. But she points out a paradox with suffering high cervical cancer incidence. "We are seeing 600 new oncology patients a year and carrying out 450 surgeries just in my unit, which gives us a high volume to evolve our skills. For cervical cancer, even centres in countries such as the UK may be performing many fewer radical procedures a year, thanks to effective screening. It means we can play a major part in driving forward standards and training."

Certainly, a priority in Serbia is sending more patients to larger centres. As Kesic notes, it has long been established in other countries that centralising expertise at high-volume hospitals improves morbidity and mortality in gynaecological cancer. A recent survey she helped conduct in Serbia was not encouraging. "About 45% of general hospitals here are carrying out fewer than 10 and some only a couple of radical procedures a year – that simply is not enough for high quality and to tailor treatment to the stage of disease. Some 70% are not even doing radical procedures, the standard for invasive cervical cancer, and where they do, a classical hysterectomy is not enough to remove the affected tissue."

Omentectomy, which is the standard in ovarian cancer surgery, is performed in only about half of cases, she adds. "And overall, in a third of cases guidelines are not followed at all, and nearly two-thirds of gynecological departments treating cancer have no survival data."

It is no surprise that Kesic is putting so much time into helping the country introduce a national cervical screening programme to start to eliminate cases of advanced disease. Since the political situation stabilised – and with the unwelcome report of Serbia's number one position in cervical cancer publicised – she found the health ministry receptive not only to screening but also to including prevention as part of national plan, Serbia Against Cancer, launched this year.

Team work. Close collaboration with nurses like Olgica Milosavljevic and Ljiljana Mijajlovic, pictured here in the Institute's colposcopy clinic, is both enjoyable and essential for patient care, says Kesic

"The plan has 30 steps, starting with screening for breast, cervical and colorectal cancers – we are also seeing some 4000 new breast cancers as well as 1500 cervical cases, so imagine how many lives we could save. It's hoped we will also be able to cut long waiting times for radiotherapy and introduce much better palliative care through the plan."

Kesic and colleagues carried out a survey about what women knew about cervical cancer to help determine barriers to screening, and with the support of the French government a pilot was put in place in a high-incidence region, and screening is now starting in other areas. As she notes, barriers are formidable, although Serbia does have some advantages.

In common with other post-communist countries there was a legacy of a traditional focus on treatment rather than prevention, and patients had little awareness of basic rights. "But we do have a well-developed primary care system that includes more than 500 gynaecologists, where opportunistic screening was being done, and colposcopy services are extremely good. However, such an approach tends to favour women of reproductive age, while middle-aged and older women are poorly covered, especially in rural areas. We don't have technicians to look at Pap smear tests, because, since the early 1950s, cytology in Serbia has been performed by gynaecologists trained to read Pap smears. So we are having to rely for the time being on the most experienced gynaecologists, those that read at least 2000 tests a year, to serve as cytologists until we train the required number of cytotechnicians. There is no other option at present."

Much will depend on the communication and

"Most depressing was the lack of knowledge from the outside world – we were not even getting medical journals"

"I see the future of cervical cancer prevention as a combination of screening and vaccination"

technical skills of gynaecologists to drive up the number of screened women, in conjunction with government campaigns, and the target is to screen 2.3 million women every three years, initially extending the upper age to 69 rather than the more usual 65, to target better the hard-to-reach older group. At present, only 20% of women visit a gynaecologist.

And as Kesic adds, when more disease is detected the shortcomings in hospital services will be exposed, especially for services such as radiotherapy, which is part of the standard treatment for advanced cervical cancer. "A main message about screening is: 'Don't start if you cannot provide the treatment' – and I'm not sure how we are going to manage this at present."

Does part of the answer lie in the new vaccinations now on the market? Kesic is worried that women may be getting an overinflated view of their capability. "Yes, vaccination will probably be the end of cervical cancer – something we dream about – but it still requires a lot of research and time. Only two vaccines are registered so far, but there are others – and none are yet proved to decrease cancer cases. I'm not happy when companies and the media announce they are infallible. Yes, what we see is that there are fewer precancerous lesions, but for cancer itself we will need another 10 to 15 years to see the real effect on vaccinated groups."

HPV has many types, she notes, with 10 that are high risk for cervical cancer. The majority of cancers – two-thirds in countries such as the US – are linked to HPV types 16 and 18, which are targeted by the two vaccines on the market. "But at least one-third of cases are caused by other types, and HPV infections differ by region – in our country, types 31 and 33 are the most common. In any case, the vaccines only protect for about five years – I know the drug companies would hate me to say this, but the vaccines simply do not protect totally and their effects don't last for ever."

She mentions also concerns that, given the publicity, girls and young women may feel free to engage in more risky behaviour because they feel protected. Not to mention the financial cost, which may be prohibitive for less well-off countries.

For all these reasons, says Kesic, screening should still be carried out. "I see the future of cervical cancer prevention as a combination of screening and vaccination."

The message about strengthening population screening, she feels, is especially important in countries with a high degree of health inequalities, as its lack is clearly a factor that accounts for higher incidence, although HPV infection and sexual behaviour patterns also contribute to geographic differences. Smoking and immunodeficiency are also key factors. Despite strong campaigns, smoking rates remain high in Serbia, and the heritage of stress, poor nutrition and pollution all contribute to impaired immunity, says Kesic.

These and most other aspects of gynaecological oncology have been

Omdurman, Sudan. In a country where 75% of cervical cancers are picked up at an advanced stage, this three-day seminar attracted more than 300 doctors, who found the practical training workshops in colposcopy and cytology particularly helpful

explored by Kesic and colleagues at a major series of workshop-style events around eastern Europe, spearheaded by Kesic under the auspices of ESGO. "So far we have run 34 events in five years, with topics ranging from early diagnostics to controversies in ovarian tumours and fertility sparing treatment – it is up to local people what they want, and the events have been very well supported. We had about 1000 people in Moscow, for example." Eastern Europe had few members in ESGO before these meetings, she adds, and she is also involved with the IGCS, which has run similar events in the Middle East, Africa and Latin America,

She is a huge supporter of education and training wherever and in whatever form it makes sense, having herself benefited from early involvement with the European School of Oncology, the European Association for Cancer Research, the American Society for Colposcopy and Cervical Pathology and other bodies. Running events first in Serbia a few years ago – bringing in experts who could not have come during much of the 1990s – helped to shape the eastern European programme.

One of the main frustrations for Kesic in Serbia now is still the fragmented nature of oncology organisation and inadequate training for gynaecological oncology. She is optimistic, however, that ESGO's accreditation in gynaecological oncology, a recent initiative for hospitals around Europe, will help standardise the quality of care for patients. Indeed, she has made several visits to accredit centres herself – there are now 23 – and says that the criteria are hard to fulfill, such as adequate patient numbers, research capability and especially high-quality training, as the aim is to become certified to offer training.

"We were lucky to have gynaecological oncology recognised in Serbia back in 1994, but it is taught under postgraduate oncology studies. I do have concerns about the educational content, but at least it gives young doctors the concept of the multidisciplinary approach and awareness that not all of us in gynaecology should treat cancer. We need to improve surgical skills by adding basic training in general surgery, urology or vascular surgery. We also need to increase knowledge of science, medical oncology and radiotherapy, and involve doctors more in research."

Certainly, Kesic would very much like to extend her own research interests, working from her expertise as a surgical gynaecologist. However, as patients who have undergone surgery tend to be followed up by the National Cancer Institute, where they receive their adjuvant treatment, it can be difficult to participate in international trials.

Kesic adds that she has no ambition to be a surgeon who also administers systemic therapy – "We have more than enough to do in diagnostics and surgery, and I much prefer to see us strengthening multidisciplinary working with specialists in each part of oncology. And I definitely do not think gynaecologists should get involved in breast cancer management, as happens in some countries."

She lives quietly with her family in Belgrade and is very modest about her achievements. Ian Jacobs, past president of ESGO, says Kesic is "extraordinarily generous, often giving credit to others for her own achievements and minimising the importance of her own contribution. She has made a great contribution to training in gynaecological cancer in Europe and her efforts in this area are admired by her colleagues internationally." In particular, the training programme and meetings in eastern Europe that Kesic has organised have been a major achievement carried in a very short time, he says.

Above all, Kesic emphasises that in cervical cancer, professionals can only do so much on their own, and that engaging governments and the media is crucial. The work of the ECCA in raising awareness of cervical cancer around Europe is pivotal, she says. The European Cervical Cancer Prevention Week, first held in 2007, is a great chance to promote cervical cancer prevention. "We have to work closely with the media, because they are powerful and can deliver our messages much more effectively than we can by meetings, lectures or roundtables."

And in the case of cervical cancer, where so much unnecessary suffering persists, her message to policy makers and the public is simple and direct: "Cervical cancer is a disease of health inequities – its incidence in a country is an indicator of how much that society takes care of its women."

"Engaging governments and the media is crucial"