As efforts continue to prevent further leakage from the damaged Fukushima Daiichi power plant, fears about the potential health consequences of radiation exposure are widespread. But in fact, much is known about the effect of unintended exposure to radiation. By a strange coincidence, it is now 25 years since the unprecedented and tragic accident at the Chernobyl power plant in Northern Ukraine, and scientists have conducted meticulous studies into the health of the exposed populations. Most of their findings are reassuring; others are intriguing and could open up new lines of research into, and treatment for, cancer.

Before the Chernobyl accident, the most intensively studied population exposed to man-made radiation was the Japanese survivors of the atomic bombings at the end of World War II. As a result, many feared that the radioactive fallout from Chernobyl, which spread over northern Ukraine, south western Russia and Belarus, would lead to a dramatic increase in leukaemia.

Once it was apparent that this hadn’t happened – but that instead there was a dramatic increase in childhood thyroid cancer – research took an unexpected turn. Gerry Thomas, professor and director of the Chernobyl Tissue Bank (Imperial College London, UK) has brought together the main strands of research on the aftermath of Chernobyl in a Clinical Oncology special issue (Thomas GA et al; doi:10.1016/j.clon.2011.02.001).

The rise in childhood thyroid cancer was predominantly papillary thyroid cancer – the most common type – but, when compared to thyroid cancer in non-exposed adults, initial reports suggested that there was a much higher incidence of RET rearrangement in the childhood cancers post-Chernobyl.

“People thought it must be due to the radiation exposure. But with 25 years of follow up, we have been able to compare this population to those born in 1987 and afterwards – when the radioiodine [released by the reactor] had disappeared from the environment. Proper age-matched studies have shown that in children, there is a higher incidence of RET rearrangement in thyroid cancers, whether they were irradiated or not. In older-onset thyroid cancer in adolescents and adults, the incidence of BRAF mutations increases.

“The interesting thing is that the molecular biology of childhood cancer is very different from the molecular biology of adult cancer. BRAF and RET are mutually exclusive in thyroid cancer, but both act on the same MAP kinase pathway. Obviously there is something different about the physiology of the young- and older-onset tumours which suggests cross-talk with pathways other than MAPK may be important in the development of thyroid cancer at different ages,” she said.

Continued ...
Chernobyl: 25 years on continued...

This wasn’t previously even guessed at, because of the rarity of thyroid cancer. Thomas said that in an early study, when they were looking for a control group they had to look at 30 years’ worth of data from the UK childhood cancer registry to find 80 tumours. “There were so few childhood thyroid cancers, it wasn’t possible to conduct age-matched studies. And it was assumed anyway, that thyroid cancer was thyroid cancer.”

Thomas believes that the effect of age on the development of tumours has been neglected: “It isn’t unknown in other tumours but we haven’t looked at the literature in that way. FLIT3 mutation leukaemia seems to predominate in older age groups, whereas other oncogene rearrangements take precedence in younger age groups. And we’ve done a recent study in breast cancer which suggests there are differences in grade III node-negative cancer in younger, compared with older, women.

“There is something fundamental about biology and the aging process which seems to interact in cancer and it needs more exploration. We might eventually be able to exploit differences and tailor treatment for different age populations, but a lot more work is needed before we get to that stage.”

----Chernobyl tissue bank ----
The Chernobyl tissue bank is at the heart of many of the research efforts which stem from the accident. Researchers are still collecting samples from the cohort that was irradiated and, importantly, from people born after 1st January 1987, when the released radioiodine had expired, who have developed spontaneous thyroid cancer. They make up the control cohort in much of the research.

As its director, Thomas sees it as a paradigm of how cancer research should be conducted. “If you collect a blood sample from a patient, a serum sample and tissue samples both frozen and in paraffin, it gives you the full gamut of things you might want to look at. It allows you to ask questions about germline defects, somatic changes, expression changes – so that we may find things in the germline which predispose you to getting certain somatic changes in a tumour.

‘There is something fundamental about biology and the aging process which seems to interact in cancer’

‘By keeping the bank, you can collate the findings of all groups and start to take a systems biology approach to working out which pathways are critically important’

“By keeping the bank, you have a record of which groups have taken samples of tumours and you can collate all their findings, so that you can start to take a systems biology approach to working out which pathways are critically important in the growth of the tumour.” (Thomas GA et al; doi:10.1016/j.clon.2011.01.503).
Chernobyl: 25 years on continued...

---The human cost---

This research was only possible because of the huge excess of thyroid cancers seen after the accident – and the associated tragedy. But even there, the initial horror seems to have turned out to be less severe with time.

So far, approximately 5000 children developed thyroid cancer following the accident, which often had an aggressive presentation, locally invasive and metastasising to the lungs. Thomas: “Actually it was very amenable to radioiodine treatment; ironically the treatment is the same as the cause. Children appeared to respond well and we don’t expect a huge recurrence rate. Also, when the tumours do recur, we expect them to be iodine-sensitive again so the prognosis is very good despite the initial clinical presentation. (Tuttle RM et al; doi:10.1016/j.clon.2011.01.501).

The irradiated cohort is now aged 25 years plus and will take with it an excess risk of cancer; it’s thought there will be a total of approximately 9000 excess cancer cases because of Chernobyl. But in the same population, there will be 900,000 cancers from other causes. Thomas: “Overall, there are very few radiation-induced cancers in the population as a whole. It’s relatively more in thyroid cancer because this cancer is normally so rare.”

To Thomas, the real human cost is the damage that was done psychologically to the population. “A very rural population which had lived on the land in those areas for generations was uprooted and moved to cities. They had to live with the stigma of being irradiated and the unfounded expectation that there would be birth deformities, leukaemias and wholesale deaths.

Calm, clear reporting of the facts, presenting risk in an understandable and accurate way, would have helped after Chernobyl and should be employed now in Japan. Thomas: “The radiation didn’t cause the predicted damage – far from it – but there is a very real psychological hangover from Chernobyl, and we shouldn’t make that mistake again.”

Helen Saul

For more information, see http://www.journals.elsevierhealth.com/periodicals/chernobyl

‘A very rural population was uprooted and moved to cities. They had to live with the stigma of being irradiated and the unfounded expectation that there would be birth deformities, leukaemias and wholesale deaths’
How to improve end-of-life care in Europe

Cancer experts have presented policymakers in Brussels with a European research agenda to better support end-of-life care for patients. The agenda is the result of a three-year pan-European collaboration on palliative care and a response to increasing cancer mortality, forecast by the World Health Organisation to rise from the current figure of 1.7 million to around 2.1 million deaths a year in Europe by 2020.

The PRISMA project began in 2008, with 1.65 million Euro in funding from the EU’s Framework 7 research programme. A consortium of specialist institutions from nine countries, led by King’s College London [see box], studied the care of cancer patients in their last year of life, and how research is conducted, across Europe.

The objectives included identifying best practices, coordinating national actions, and aiding cross-national policy development. Guidance on how to measure outcomes in end-of-life care has been published.

The research agenda, presented to policymakers from the European Commission’s research and health directorates on 24 March 2011, pinpoints five priority areas to be pursued at EU level: the control of patients’ symptoms and pain; their emotional well being; the choice of where to be cared for; family support measures and the information needs of both patients and carers.

The priorities stem from the consortium’s findings in 36 European countries, published in the EJC and the Journal of Supportive Care in Cancer in 2010, and are corroborated by a novel public survey of the priorities of 9,344 people over 16, in seven EU countries: England, Germany, Italy, the Netherlands, Spain, Portugal and Belgium.

This is the first large scale cross-national public survey of its kind to be conducted in Europe, according to Barbara Gomes from King’s College, who is leading the work on public priorities and preferences. “The existing evidence, nationally and locally, is limited. International recommendations and attempts to co-ordinate international efforts have been made – for instance by the WHO – but with caveats, based on local data,” she says.

Respondents were asked what their priorities would be if faced with less than a year to live. Of those surveyed, 65% had a close friend or relative diagnosed with a cancer
or serious illness and 70% had experienced the death of a friend or relative. Around half had supported and cared for a close relative or friend in their last few months of life. Ten percent of respondents had a serious illness themselves.

A large majority (73% of respondents, on average) in all countries except Italy expressed a preference for improved quality of life during their remaining time over extending that time. In Italy, 40% of respondents thought both equally important. Relief from pain and discomfort were the top priority in England and Portugal whereas keeping a positive attitude ranked highest in the other countries.

Earlier findings show that end-of-life research is currently "fragmented and unsustainable" with data sets that are difficult to compare, according to Stein Kaasa, director of the Department of Cancer Research and Molecular Medicine at the Norwegian University of Science and Technology, leading the PRISMA work on clinical priorities. "A high proportion of research groups consist of one academic and one PhD student. The few larger groups in Europe account for 50% of research publications on palliative care. When it comes to national cancer plans, there is little mention of palliative care, if at all," he says.

Kaasa is calling for better integration of end-of-life care in mainstream oncology. "The observation that there is such little research in palliative care is also a sign of the clinical attention given to it in mainstream oncology. It's very low. Yet more than 50% of cancer patients are receiving oncology care that is not with a curative intention," he explains.

The shift towards targeted therapies in mainstream oncology may not serve these patients well, he says: "Interestingly, these patients are suffering from a series of
symptoms which actually need control and palliation. These are reported very little in
the [targeted therapy] drug studies, which is problematic."

The shift to targeted therapies increases the need for better attuned palliative care:
"As well as incidence rates, prevalence rates are also increasing because the new
therapies increase survival, but patients are not cured. So more patients are getting
cancer and more patients are living longer with cancer," says Kaasa. "

Every nation, and every department of oncology, needs a strategy on how to care for
the increasing number of patients who are not receiving curative treatment. He says
that mainstream oncology and oncology need to join forces:

"It's an issue of how you prioritise in the daily running of a very busy
clinic. Most [oncologists] will say integration is a good idea, but it's a
resource issue. This is a leadership challenge both at the level of
departments and hospitals, and at national level."

EU research commissioner Maire Geoghegan-Quinn was positive
about the consortium's work. "PRISMA is a concrete example of how
EU-funded research on health issues can make a real difference to
patients, not only by developing new treatments but also by providing
data and other tools to support clinical decision-making and
management," she said at the launch.

Despite her acknowledgement, she would not be drawn into indicating
whether the proposed research would be earmarked for further public
funding in the EU's next research programme, due to begin in 2014.

In the meantime, the consortium is developing
research protocols in
priority areas and
approaching potential
funders and partners.
One project aims to
develop a new model for
end-of-life home care.
"The majority of people
want to be cared for at home. We want to look at cost-effectiveness issues
surrounding home care, as the evidence here is limited," says Gomes. The project will
start in Portugal later this year, funded by the Gulbenkian Foundation, but the
consortium would welcome other partners in Europe, to make the venture
international, based on a common measurement framework, and allow comparable
studies of models in different countries.

Saffina Rana
Brussels

The data is available to download from www.prismafp7.eu
The long road to recognition

Since it was founded in 1975, one of ESMO’s key goals has been to secure recognition for the specialty of medical oncology in Europe. In March 2011, the European Commission announced that medical oncology is, finally, to be covered by Directive 2005/36/EC on the recognition of professional qualifications.

Paolo Casali, ESMO Public Policy and European Affairs Chair, discusses the implications of the move.

Why has it taken so long?
It’s probably because of the differences in training programmes across Europe. The basic requirement now is that the training period lasts at least 5 years. Just a few years ago, it was less than this in many countries, and still is, in some. So even though a majority of European countries were strongly in favour of mutual recognition of medical oncology, agreement had to be reached on the training period at least. In a few countries, oncology disciplines are pooled together so that the specialty is clinical oncology rather than medical oncology, but these are exceptions.

What does the move mean for the individual medical oncologist?
In the countries with training periods of at least 5 years, which are covered by the Directive, qualifications obtained in one country are automatically accepted in another. A medical oncologist from Italy is acknowledged as a medical oncologist in France via a simple mechanism. It will make it much easier for medical oncologists to work in other member states covered by the Directive.

Is it effective immediately?
We have to wait a few months for technical reasons; essentially, it will be in place very soon. It is a great achievement but it’s also part of a process and we hope that the Directive will in due course cover all EU countries. It’s important that this decision has been made in Brussels, because now we can progress in a step-wise fashion and individual countries who are not yet covered by the Directive can work towards inclusion.

Continued ...
INTERVIEW continued.

Will the Directive act as a stimulus to extend training in countries not currently covered by it?
It certainly will, although this process had started long before.

What other effects do you expect the Directive to have?
A major problem in some countries is the shortage of medical oncologists and it should now be easier to fill vacancies. That's the easiest change to forecast, and it’s a good thing because increased mobility of physicians tends to diminish disparities in the provision of care.

Will ESMO be monitoring the consequences?
We will try. ESMO will certainly be continuing to work with the national medical oncology societies in those countries not initially covered by the Directive, because our aim is for medical oncologists in all countries to have automatic recognition of their qualifications.

This decision went through at the same time as a Directive on cross-border healthcare (which covers patients opting to travel for treatment). It includes the concept of European reference networks (ERNs), and ESMO will be working on the idea of networks which will enable medical oncologists, in fact all oncologists, to work together, across borders, within a clinical network. We've always had collaborative groups in research, but now we’re talking about networks for the provision of healthcare.

Are you in favour of health migration?
The cross-border healthcare Directive will make it easier for patients to travel to receive the same treatment that they should be able to receive in their own country. Many patients will not want to do this and having physicians move across Europe is better in the sense that it improves the harmonisation of healthcare. But I see both changes in parallel, in principle at least, and as a good thing because both should reduce the disparities in cancer care that are of major concern to us. In addition, the notion of reference networks will contribute to harmonisation, with no need for health migration.

Does the Directive mean solely a practical change?
We always stress the point of principle. Clearly having medical oncology recognised at European level will improve the implementation of the specialty in all European countries, including those in which it is still facing difficulties. Recognition at EU level should improve things on the ground across Europe.
INTERVIEW continued.

Wouldn’t patients be astonished that it wasn’t recognised earlier?
I’m sure they would! Cancer is treated by surgery, radiation therapy and medical therapy and only one of the three treatment modalities was not an EU-recognised discipline. We were aware that the reasons were practical, due to differences in countries’ training rather than to real points of principle, but we needed agreement by a majority before we could progress. So it’s a big achievement for us, both practically and in principle.

Interview by Helen Saul