

# CANCER SURVIVORSHIP – THE IMPORTANCE OF ONGOING CARE. PART 2

In this second article\* on the issues facing people who survive treatment of cancer, the authors discuss the late consequences of anti-cancer treatment and propose primary care management strategies to identify and manage those at risk.

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## Can we differentiate between acute effects and long term effects?

Oncologists strive to achieve optimal rates of cure while minimising long term toxicity. Acute effects of oncological treatments usually develop within eight weeks of treatment. Because radiotherapy and chemotherapy impact upon the cell's ability to reproduce, acute effects tend to be more apparent in those tissues with the fastest cellular turnover (skin, gut and bone marrow). Tailoring the dose of treatment means that there is usually full recovery from acute effects.

It is the more slowly reproducing tissues (lung, kidney, heart, liver, CNS, connective tissue) that tend to show late effects of treatment, and recovery might not be complete. The skin can show both acute and late effects.

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## Late consequences of treatment

Long term consequences are generally accepted to arise anything from a few weeks or months after treatment to many years later. The rate of development of late consequences does not seem to fall off with increasing survival time after treatment, and the reverse may even be the case, particularly for second tumours.

Physical effects include fatigue, weight gain, lymphoedema, neuropathic pain, heart damage leading to an increased risk of cardiovascular disease,

lung damage, bowel and bladder dysfunction and increased risk of osteoporosis. In addition, there is a significant risk of cancer survivors developing a second cancer, either as a result of pre-existing genetic or environmental predisposition, or as a consequence of their previous cancer treatment. Many patients also suffer psychosocial consequences of their cancer, including anxiety and depression, memory loss and problems with concentration, leading to lower educational attainment for childhood and adolescent cancer patients, and increased risks of job loss, financial problems, marital breakdown and divorce.

The late consequences of surgical treatments for cancer are perhaps better recognised, including lymphoedema (breast), urinary incontinence and sexual dysfunction (prostate, colorectal), and stoma incontinence (colorectal).

## Cardiovascular disease

Cancer treatment for children and adolescents, and also for adults, is a risk factor for cardiovascular disease in later life. In particular, radiotherapy to the left side of the chest and some chemotherapy agents such as anthracyclines (commonly used for breast cancer, sarcoma and haematological cancers) are known to increase the risk of the patient subsequently developing cardiovascular disease, including heart failure. For example, in those women who have been treated for breast cancer and survived more than five years, there is an increased risk of heart failure (hazard ratio 1.95) or coronary artery disease (HR 1.27).

As treatment for childhood cancer has become more successful over the past decades, we can expect to see rising numbers of patients who are at increased risk of developing ischaemic or valvular heart disease as a result of their treatment. Presentation may be at an earlier age than those who have not had such treatments.

## Osteoporosis

Hormonal treatment, including the use of GnRH analogues for prostate cancer and aromatase inhibitors for breast cancer, is associated with an increased risk of bone fractures due to osteoporosis. NICE recommends

\*The first part of this feature on the GP's role in cancer survivorship appeared in BJFM May/June

that women with early invasive breast cancer should have a baseline DEXA scan to assess bone mineral density and increasingly urologists are adopting the same approach with men with metastatic prostate cancer. Osteoporosis, when identified, should be treated with bisphosphonates, after consideration of the risk of osteonecrosis of the jaw.

## Embarrassing bowel and bladder problems

Approximately 17,000 patients undergo pelvic radiotherapy with curative intent annually in the UK. From this, it has been calculated that there are around 80,000 cancer survivors with a history of pelvic radiotherapy. About half will have bowel and/or bladder problems and half of these will have severe problems including diarrhoea, faecal urgency and incontinence. These symptoms are highly stigmatising, and many patients are reluctant to describe themselves as incontinent, preferring to use words such as leakage or soiling instead. A significant proportion of patients with faecal incontinence will not seek medical advice, being either too embarrassed or believing that medical care will not help. Other patients are able to deny their faecal incontinence because they take drastic measures, such as not leaving their home or not eating for some hours before going out.

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Side effects are frequently missed or overlooked because the current priority of cancer care follow up is to perform surveillance for recurrent disease. Individual GPs are unlikely to have many patients with complex problems after cancer treatment and so will require guidance if these patients are to be optimally managed.

Some patients who have had pelvic radiotherapy will also complain of symptoms of radiation cystitis and sexual dysfunction (including erectile problems), particularly when prompted, and it is therefore important to find the time and opportunity to enquire about these symptoms during the course of consultations; otherwise they may be ignored, left untreated and significantly affect quality of life.

## Risk of second tumours

Because they may have an inherent genetic risk, some people who have had cancer are already at increased risk of another cancer. The development of a second cancer is also a rare but serious consequence of radiotherapy, and often there is a long latent period – for example, leukaemias occur most frequently after 6-8 years, and solid tumours 10-30 years after radiotherapy. These second cancers are particularly likely to occur in the breast and thyroid gland, especially in those receiving radiotherapy as children or young adults.

Some chemotherapy agents also increase the risk of second tumours (alkylating agents, etoposide).

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It is worth remembering that 5-10% of all childhood cancer survivors develop second malignancies, and those people successfully treated for Hodgkin's disease have a high incidence of leukaemias, non-Hodgkin's lymphoma and solid tumours (especially lung, breast and thyroid).

## Other late effects

Primary care practitioners and other generalists should be increasingly aware of the possibility of other late effects of cancer treatment including:

- Metabolic and hormonal consequences (e.g. pituitary hormone deficiencies after whole brain irradiation, adrenal insufficiency resulting from prolonged use of steroids, thyroid and parathyroid dysfunction following radiotherapy to neck)
- Adverse lipid profile and metabolic syndrome (for example insulin resistance, dyslipidaemias, hypertension and abdominal obesity after bone marrow transplantation)
- Fertility consequences
- Neuro-psychological effects
- Neuropathy
- Endometrial disease (for example resulting from tamoxifen treatment)

**How can GPs contribute to the care of long term survivors?**

Lifestyle advice is as important for long term survivors of cancer as it is for the general population, if not more so. Advice on diet, physical activity and smoking cessation has an important role in this group of people, who share the same high risk for other non-malignant chronic conditions. There is accumulating evidence of the benefits of maintaining a physically active lifestyle, both in improving quality of life measures and reducing the risks of developing further disease, including recurrence of some cancers (particularly for breast, prostate and colon cancers).

We need to be aware of the possibility of late effects for patients with a history of cancer and to think of them when the patient presents with new symptoms; are the symptoms related to the past cancer, its treatment or possibly the development of a new cancer? This is why it is so helpful to ensure that patient records are clearly coded with past oncological treatments and, if possible, also coded as ‘At increased risk of...’ if appropriate. And it is essential that significant events in the medical history are not lost with each new summarising of records.

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Cancer specialists can also help here by being clear in the information they provide to both patients and to GPs about possible long term consequences of treatment. Practices can create a register of those who have had oncological treatment, including radio- and chemo-therapies, so that those patients can be highlighted on their computer system and alerts set.

It is good practice for primary care clinicians to proactively ask patients about possible treatment-related problems and also potential psychosocial effects as part of any regular review and to consider offering patient information on long term effects. Applying this anticipatory care is similar to the prevention and early detection and management of exacerbations and adverse effects of treatment in other long term conditions.

**TABLE 1: LATE EFFECTS OF SYSTEMIC ANTICANCER TREATMENTS (CHEMOTHERAPY AND HORMONE THERAPY): SOME ORGAN-SPECIFIC PROBLEMS**

Causal treatment	Impact
Anthracyclines Trastuzumab (Herceptin)	Dilated cardiomyopathy (reversible) reduced cardiac function
Bleomycin (for germ cell tumours)	Pulmonary fibrosis (dyspnoea, unproductive cough, chest pain)
Cisplatin, Aminoglycosides (often used in neutropaenic sepsis)	Chronic renal impairment
Platinum agents; aminoglycosides	High frequency sensorineural hearing loss; tinnitus
Cisplatin; taxanes; vincristine	Neuropathy (usually sensory)
High dose steroids	Cataracts, Sjogren's syndrome Osteoporosis
LHRH analogues	Coronary disease; osteoporosis; obesity; sexual dysfunction

**TABLE 2: ORGAN-SPECIFIC LATE EFFECTS OF RADIOTHERAPY**

Organ	Impact
Skin	Atrophy, fibrosis, telangiectasia
Oral mucosa	Dry mouth – can persist if a large volume of salivary glands have been irradiated
GI tract	Mucosal ulceration, fibrosis/obstruction, necrosis
CNS	Demyelination effects at about 2-6 months after treatment causing somnolence (brain) or shooting pains (spinal cord) Irreversible neurological deficit due to radiation necrosis can occur at 1-2 years
Lung	Radiation pneumonitis (2-6 months) and irreversible lung fibrosis (6-12 months)
Kidney	Radiation nephropathy with proteinuria, hypertension and renal failure
Heart	Self-limiting pericarditis (6-24 months); cardiomyopathy and conduction blocks (>24 months)

Second cancers are more common in patients who have already had one previous cancer. It is therefore important not to focus solely on treatment of the primary cancer but to offer strong lifestyle advice to all cancer patients to reduce the risk of second cancers. In those patients likely to develop cardiovascular disease or osteoporosis, primary care practitioners have a major role to play in proactively identifying and managing risk factors and it is important that a previous history of cancer is considered in the calculation of risk for these patients.

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In the future, patients are more likely to be discharged from medically-led hospital follow-up. Primary care is well-placed to manage continuing care, putting in place systems to ensure those that identified at increased risk of long term consequences of cancer or its treatment are given appropriate care and support to lead as healthy and active a life as possible, for as long as possible.

Primary care teams need to be aware of the possibility of late effects, given that as many as 40% of cancer patients are not aware of the possibility of long term physical side effects, while almost 80% admit to experiencing one of these in the previous 12 months. Many patients indicate that GPs would be their first port of call if they did develop symptoms.

## Conclusion

It is no longer acceptable for patients to have to endure the consequences of treatment, unrecognised and unsupported, grateful that their life-threatening illness has been successfully treated. Information given around the time of initial diagnosis and treatment needs to acknowledge the likelihood of late effects, and further research needs to be undertaken into prevention and optimal management strategies. We must strive to ensure that the care we offer leads to the best possible quality of life for patients in the years following successful treatment of their cancer, irrespective of the type of complications that can arise – an aim to which primary care can contribute effectively by knowing which patients are at risk, being alert to the possibility of late effects and signposting and referring appropriately.

## 'TEN TOP TIPS' FOR IDENTIFICATION AND MANAGEMENT OF LATE EFFECTS

- 1 Many cancer survivors will experience long term consequences, both of the disease itself and its treatments (as treatment becomes more successful we can expect to see unexpected and varied late consequences)
- 2 Long term consequences can arise a few weeks, months or many years after treatment
- 3 Cancer patients have increased risk of second tumours, especially children and young people
- 4 Pelvic radiation has a high risk of causing chronic disease and disability. Symptoms include diarrhoea, faecal urgency and incontinence
- 5 Hypothyroidism is increased in young cancer patients and after head and neck radiotherapy, and high risk patients should have TFTs checked annually
- 6 Hormonal treatments carry cardiovascular and osteoporosis risk and patients need to be considered for cardiovascular risk assessment (cholesterol, blood glucose, blood pressure) and DEXA scanning
- 7 Cancer patients are more at risk of chronic illness of earlier onset and may be more receptive to lifestyle intervention
- 8 Be aware of the possibility of late effects when a cancer patient presents with new symptoms
- 9 Accurate coding at time of treatment will help identification of those at potential future risk of late effects (see BJFM May/June p.31)
- 10 Once late effects are identified, much can be done to mitigate these, including information for patients, non-drug and drug treatments and/or specialist referral

## Further Reading

- Khan et al. *British Journal of Cancer* (2011) 105, S29–S37. doi:10.1038/bjc.2011.420 [www.bjcancer.com](http://www.bjcancer.com)
- Andreyev HJ et al. *Gut*. 2012 Feb;61(2):179-92. doi: 10.1136/gutjnl-2011-300563. Epub 2011 Nov 4
- SIGN 132 Long term follow up of survivors of childhood cancer - A national clinical guideline March 2013 <http://www.sign.ac.uk/pdf/sign132.pdf>
- Pelvic radiotherapy possible late effects. How will this change your practice? <http://macmillan.org.uk>
- Cure – but at what cost? Long-term consequences of cancer and its treatment, July 2013 [http://www.macmillan.org.uk/Documents/AboutUs/Newsroom/Consequences\\_of\\_Treatment\\_June2013.pdf](http://www.macmillan.org.uk/Documents/AboutUs/Newsroom/Consequences_of_Treatment_June2013.pdf)