1 What is Cancer?

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INTRODUCTION

Cancer is not just one disease, but a generic term used to encompass a group of more than two hundred diseases sharing common characteristics. Cancers (carcinomas) are characterized by their unregulated growth and spread of cells to other parts of the body (Corner, 2001; Yarbro, Frogge and Goodman, 2005). Treatment of an individual diagnosed with cancer is not only dependent upon which type of malignancy (cancer) they have, but also on the extent of its spread, together with its sensitivity to treatment (Gabriel, 2001). The total care of the patient will involve assessment of their physical, psychological and social needs, so that a complete care package can be developed to support them and their carer(s) throughout the whole of their patient journey (National Institute for Clinical Excellence (NICE), 2003). (This aspect of care will be further discussed in Chapter 3.)

It is estimated that one in three people in the United Kingdom will develop a malignancy by the time they reach the age of 70, with the incidence increasing with age. This means that approximately 270 000 individuals receive a cancer diagnosis each year in the United Kingdom, with more than 7.5 million affected worldwide (Cornwell, 1997; Department of Health (DoH), 2000a; Corner, 2001). Sadly, as was predicted by Cornwell back in 1997, the UK incidence of cancer is increasing (DoH, 2001a).

This chapter will attempt to provide a clearer understanding of what cancers are and how they spread (metastasize) throughout the body. It will also look at the importance of staging an individual’s disease prior to determining the most appropriate management (DoH, 2000a, 2000b).

THE DEFINITION OF CANCER

As humans we are comprised of many millions of cells. Some cells are specific to certain tissues, for example epithelial cells are found throughout the gastrointestinal tract, bladder, lungs, vagina, breast and skin. This group of cells accounts for approximately 70% of cancers (Venitt, 1978; Corner, 2001).
However, any cell has the potential to undergo malignant changes and lead to the development of a carcinoma. Cancerous cells are not confined to localized ‘overgrowth’ and infiltration of surrounding tissue, but can spread to other parts of the body via the lymphatic system and bloodstream, creating secondary deposits known as ‘metastases’ (British Medical Association (BMA), 1997; Walter, 1977; Wells, 2001). This can occur when ‘normal’ cell control mechanisms become disrupted or indeed fail (Corner, 2001). Surgical removal of the original tumour is not always a successful treatment in malignant disease, due to microscopic spread. Malignant tumours are often irregular in shape, with ill-defined margins (Wolfe, 1986; Walter, 1977). The potential for microscopic spread occurs when the tissue surrounding the visible tumour appears to the eye (macroscopic examination) to be unaffected by cancer. Microscopic examination of the surgical resection margins can reveal the presence of malignant cells. If left untreated, these cells will result in localized recurrence of the cancer and eventual spread (metastasis). The spread of the malignant cells extends outward from the original tumour, and has been described as resembling the appearance of a crab. This is the origin of the term ‘cancer’, which was derived from the Latin meaning ‘crab’ (Walter, 1977). The earlier a cancer is detected, the less likely it is to metastasize, and so the more favourable the prognosis for the individual (DoH, 2000a).

METASTATIC SPREAD

All cells replicate themselves. This usually happens about 50–60 times before the cell eventually dies (see Chapter 4) (Corner, 2001; Yarbro, Frogge and Goodman, 2005). However, as malignant cells replicate, they grow in an irregular pattern, infiltrating surrounding tissue. This can result in infiltration of the lymphatics and/or blood vessels. By gaining access to these vessels, malignant cells can be carried to other sites within the patient’s body, where they will replicate and grow, rather like rodents establishing colonies in various parts of a town by gaining access to sewer systems (Wolfe, 1986; Walter, 1977). In order to ensure that these malignant cells receive the nourishment they need to thrive, angiogenesis occurs. This is the formation of new blood vessels (Yarbro, Frogge and Goodman, 2005).

Lymphatic Spread

Malignant cells gain access to the lymphatic system and travel along the vessels to the ‘regional draining’ lymph nodes (Walter, 1977). The malignant cells can then establish residency in these regional nodes, where they replicate and eventually replace the lymph node with a malignant tumour — that is, cancer. Malignant cells from this tumour can then travel, via the lymphatic system, to the next group of lymph nodes, thereby spreading the malignancy throughout the patient’s body (Walter, 1977). Lymphomas and squamous cell carcinoma of the head and neck are two examples of where cancer commonly spreads via the lymphatic system (Yarbro, Frogge and Goodman, 2005).
WHAT IS CANCER?

**Blood Spread**

As with lymphatic spread, malignant cells can also infiltrate the vascular system and travel along the vessels until they arrive at an area where they can become lodged, and subsequently replicate to form a secondary (metastatic) deposit. The malignant cells can then migrate via the smaller blood vessels — that is, the capillaries (Walter, 1977). However, there is evidence that only a small percentage of cells entering the vascular system actually survive to give rise to blood-borne metastatic spread (Walter, 1977). Malignancies which are linked to blood-borne spread include melanoma and small cell carcinoma of the lung (Yarbro, Frogge and Goodman, 2005).

**Liver.** The commonest site for blood-borne metastases is the liver. Malignancies originating from the gastrointestinal tract, including the pancreas, commonly metastasize to the liver. Other malignancies which can result in secondary deposits in this organ include breast, melanoma, lung and urological cancers (Wolfe, 1986; Walter, 1977).

**Lung.** The lung is the second most common site for metastatic spread. Tumours that are associated with metastasizing here include the breast, teratomas, melanomas and sarcomas (Wolfe, 1986; Walter, 1977).

**Bone.** Bone metastases are commonly associated with malignancies of the breast, prostate, kidney, lung and thyroid. Patients with bone metastases can often present with pain. Pathological fractures are not uncommon due to the damage caused to the bone by the malignant cells — that is, the cancer cells replacing the healthy cells and thereby weakening the bone, making it more prone to fracture (Wolfe, 1986; Walter, 1977).

**Brain.** Brain metastases are closely associated with primary malignancies of the lung, but can also arise from other sites, including the breast, teratomas and malignant melanoma (Wolfe, 1986; Walter, 1977).

**Adrenal glands.** Breast and lung primary malignancies are more frequently associated with secondary deposits in the adrenal glands, compared to cancers arising from other sites within the body (Wolfe, 1986; Walter, 1977).

**Transcoelomic spread.** Transcoelomic spread is the term used to describe invasion of the serosal lining of an organ by malignant cells. The malignant cells trigger an inflammatory response, which results in a serous exudate. This is commonly seen in the peritoneal cavity, where it is associated with ovarian and colonic malignancies (Wolfe, 1986; Walter, 1977).

**STAGING OF MALIGNANT DISEASE**

In order to ensure that a patient can be advised as to the most appropriate management of their particular disease, it is vital that the extent of their cancer
is known. For example, if a patient presented with a breast lump, which proved
to be malignant, it would be inappropriate to offer the patient a mastectomy if
the cancer had already spread to the liver. Removal of the breast would not affect
the patient’s prognosis, because the cancer had already metastasized at the time of
diagnosis. This is why it is so important to ‘stage’ a patient’s cancer before detailed
discussions can take place regarding the most appropriate treatment option(s).

The majority of adults with solid tumours are ‘staged’ using the internationally
recognized TNM (tumour, node, metastasis) classification system (UICC, 2002). The TNM classification system was introduced into clinical practice in the early
1950s. It aims to ensure each individual patient is offered the most appropriate treat-
ment for their cancer, depending upon the exact extent of the disease. It also provides
an indication of the individual’s prognosis, by ensuring that health professionals
have standardized information when discussing specific patients’ cases and their
anticipated responses to treatment, for example at the patient’s pre-treatment multi-
disciplinary team (MDT) meeting (see Chapter 3). This information will provide
a benchmark for future researchers into the treatment of cancer when assessing a
patient’s disease response against potential new treatments (UICC, 2002; Yarbro,
Frogge and Goodman, 2005).

The TNM classification works by assessing the extent of the primary tumour, the
involvement of the lymph glands and the presence of metastases (see Table 1.1)
(UICC, 2002). A patient diagnosed with a small primary tumour, for example TI,

### Table 1.1  TNM classification system.a

<table>
<thead>
<tr>
<th>T = Tumour size</th>
<th>For example</th>
<th>N = Regional lymph node involvement</th>
<th>For example</th>
<th>M = Distant metastases</th>
<th>For example</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>No evidence of primary tumour</td>
<td>N0</td>
<td>No evidence of regional lymph node involvement</td>
<td>M0</td>
<td>No evidence of distant metastatic spread</td>
</tr>
<tr>
<td>T1, T2, T3, T4</td>
<td>Number allocated to size of primary tumour, with ‘I’ representing the smallest size, up to ‘IV’, the largest</td>
<td>N1, N2, N3, N4</td>
<td>Number allocated to involvement of regional lymph nodes, ranging from ‘I’, confined to one group, up to ‘IV’ when several groups are involved</td>
<td>M1</td>
<td>Evidence of distant metastatic spread</td>
</tr>
<tr>
<td>TX</td>
<td>Primary tumour unable to be assessed</td>
<td>NX</td>
<td>Regional lymph nodes unable to be assessed</td>
<td>MX</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
</tbody>
</table>

*a Example only. Not all stages applicable to every cancer.
Source: TNM Classification of Malignant Tumours (2002).
will have a more favourable prognosis than a patient with a large primary tumour and widespread metastases.

The staging process should follow on from the initial diagnostic procedure without any undue delay (DoH, 2000b, 2001, 2004). This can be a tremendously anxious time for the patient and their family members and close friends. The patient has been given a diagnosis of cancer, and will inevitably become concerned about the delay in the commencement of treatment while they wait for further investigations to determine the stage of their disease. A patient whose staging investigations confirm a small primary cancer confined to their larynx may well be successfully treated with radiotherapy, without requiring more radical treatment by laryngectomy. Conversely, a patient with advanced disease which has already metastasized will not have their prognosis improved by undergoing a laryngectomy.

The TNM classification system is commonly used throughout the world for solid tumours, but other classification systems do exist. These include the ‘Dukes’ staging system for colorectal cancer and the ‘Clark’s’ classification for malignant melanoma. For haematological malignancies, the TNM classifications are not appropriate because of the systemic nature of the diseases. Yarbro, Frogge and Goodman (2005) list a number of classification systems for haematological malignancies, including:

- Ann Arbor classification for lymphomas
- French, American, British (FAB) classification for myeloblastic leukaemia
- Rai classification for chronic lymphocytic leukaemia.

**DIAGNOSTIC AND STAGING INVESTIGATIONS**

Today, a growing number of tests can be performed to identify the presence of abnormal cells or an abnormal structure. These tests can simply confirm or eliminate a primary cancer (diagnose), or they can help determine the spread of the malignancy (stage). Essentially these investigations fall into three main groups:

1. Radiology
2. Pathology
3. Endoscopy.

**RADIOLOGY**

Radiology allows for visualization of the internal structures. Images are created, which the radiologist then interrupts. These images can be created in a number of ways:

* X-rays. X-rays or gamma rays are passed through a particular part of the body to generate an image, for example a chest X-ray or mammogram (Yarbro, Frogge and
Goodman, 2005). In order to achieve a clearer image, especially in the gastrointestinal tract, lymphatic vessels, urinary tract and so on, a contrast medium can be used. This involves injecting or, in the case of gastrointestinal studies, asking the patient to swallow a contrast medium. These contrast medium enhances the structures, thereby providing clinicians with more detailed information (Yarbro, Frogge and Goodman, 2005).

Computerized axial tomography (CAT or CT scan). This is an X-ray technique which involves taking a series of X-rays in 'slices'. The images are then analysed by a computer to produce a three-dimensional picture.

Magnetic resonance imaging (MRI). Magnetic resonance imaging does not involve the patient or staff being exposed to ionizing radiation. The patient lies on a couch within a powerful magnetic field and the field aligns the patient’s hydrogen nuclei in one direction. Pulses of radio waves are used to disturb the magnetized nuclei and change their alignment. This results in images being generated, which are captured and analysed by a computer. This procedure is excellent for generating detailed images, especially of soft tissue structures. The procedure from the patient’s perspective is not dissimilar to undergoing a CT scan (Yarbro, Frogge and Goodman, 2005).

Ultrasound. Ultrasound involves the use of high frequency sound waves. The sound waves are directed over a particular area of the patient’s body, via a probe rubbed over the skin, and echoes are ‘bounced back’. These echoes can be interpreted to provide information relating to the density of the underlying structures. This is particularly useful in distinguishing cysts from more solid structures (Yarbro, Frogge and Goodman, 2005).

Nuclear medicine imaging. Nuclear medicine imaging involves the parenteral or enteral administration of radioactive compounds. The radioactive material concentrates in the organs or tissues under investigation. A special camera (gamma camera) is used to obtain images of the specific organ/tissues, for interpretation by the radiologist.

Positron emission tomography (PET). Biochemical compounds, ‘tagged’ with radioactive particles, are administered to the patient. Images are obtained based on the biochemical and metabolic activity of the tissue, and are interpreted by the radiologist (Yarbro, Frogge and Goodman, 2005).

PATHOLOGY

Pathology tests can confirm a clinical diagnosis, and have been used recently to monitor a patient’s disease and response to treatment (see Chapter 9). The types of pathology tests that can be undertaken include:

Biochemistry. Body fluids such as blood, urine and so on can be used to identify values that fall outside the range expected in a ‘healthy’ individual. For example, an
elevated bilirubin and alkaline phosphatase could be indicative of liver disease. A raised calcium could indicate bone metastases (Yarbro, Frogge and Goodman, 2005).

**Monoclonal antibodies.** The production of monoclonal antibodies can lead to the detection of specific tumour antigens, such as HER2 in one type of breast cancer (see Chapter 10) (Cook et al., 2001).

**Tumour markers.** Tumour markers are proteins, antigens, genes or enzymes that can be produced by a tumour. Testing body fluids, including blood, for these markers can be useful in reaching a diagnosis or monitoring an individual’s disease (see Chapter 9).

**Biopsy.** A biopsy provides tissue for histological examination (Yarbro, Frogge and Goodman, 2005).

**Cytology.** Cytology involves looking at cells which have been obtained from fluid, secretions, washings from irrigation of cavities, or brushing from tissues (Yarbro, Frogge and Goodman, 2005).

**ENDOSCOPY**

Endoscopy involves the passage of a long flexible bundle of fibreoptic lights. Images are reflected back to the head of the endoscope, providing the operator with a clear picture of the tissues/organs being examined. It is possible for the operator to obtain samples of tissue for histological examination. A pair of special forceps is passed through the endoscope to the area requiring biopsy. The tissue is then retrieved through the endoscope and sent to the laboratory. Cells for cytological examination can also be obtained via this method.

**CONCLUSION**

Cancer comprises a complex group of diseases, which currently affect one in three people in the United Kingdom. Successful treatment is dependent not only upon advances in medical science, but also on early detection of the disease, careful staging to determine the extent of the cancer at the time of diagnosis, prompt treatment and appropriate support for the patient.