The Biology of Cancer

Second Edition

Edited by
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Nurse Director
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Preface

Every day we, as cancer nurses, care for patients with life-threatening conditions, and every day we are responsible for the delivery of complex treatments to our patients. We witness at first hand the impact a diagnosis of cancer has for an individual and those around them. We also see how determined our patients are to overcome their diseases. The delivery of treatments to patients in our care necessitates us to have an understanding not only of what they entail, but also of how they work.

The application of biology is playing an ever increasing role in cancer care. There are a number of texts and specialist papers available about the biology of cancer, but they are not, in the main, aimed at cancer nurses, that is the health professionals who actually deliver the majority of treatments. The aim of this book is to be an informative text for students, newly qualified nurses and practising oncology/palliative care nurses. It will also be a useful text for other health care professionals working in the field of cancer, for example radiographers, physiotherapists, dieticians and so on, so that some of the questions asked by patients and their carers can be answered with a clear understanding of what the latest advancements are in the management of an individual's illness.

The aims of this book are:

- To describe what cancer is and its disease process.
- To identify some of the predisposing factors for certain types of cancer.
- To identify the composition of the cell and its functions.
- To discuss the current research and developments relating to biology of cancer.
- To apply the research to the management of an individual patient.
- To summarize current Department of Health guidance to improve access to and quality of cancer care.

Janice Gabriel
March 2007

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I would like to dedicate this edition to Imogen and Bethany – the more you learn, the more you grow – and to my colleagues and patients in the Central South Coast Cancer Network.

Janice Gabriel

Introduction

Every member of the cancer multidisciplinary team plays a crucial role in the management of their patient. Therefore, each of us has a responsibility to our patients to ensure we have a sound knowledge base, reflecting the latest research and the application of this research to patient care.

This book is written by experienced, practising health care professionals to provide a 'readable' and meaningful text that can easily be applied to patient care. The book is designed not to overwhelm the reader with excessive information on the disease process, but to illustrate how the developments relating to the understanding and application of the biology of cancer can be applied to the management of an individual's care.

The book is divided into three parts, all of which are evidence based and fully referenced. The first part looks at cancer generally and discusses the disease processes, that is the development of a cancer and metastatic spread. It also seeks to identify and explain why there are predisposing factors linked to the development of some cancers, and concludes with a summary of how Department of Health guidance has improved access to cancer services in England.

The second part looks in detail at the cell, its composition, functions and response to cytotoxic agents. It also examines the roles of the immune system and genetics in the development of cancer. This section of the book will also discuss the increasing importance of 'tumour markers' in managing a patient's disease, including their response to treatment.

The final section of the book will tackle the area of research. It takes into account the latest research guidelines, including storage of pathology material, and applies these to patient care so that health care professionals can have a greater understanding of the potential implications for those patients who are considering participating in research studies.

Janice Gabriel

Part I Understanding Cancer

1 What is Cancer?

JANICE GABRIEL

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).

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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).

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 gastrointestine, 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 treatment 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 multidisciplinary 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]

T = Tumour size	
For example	
T0	No evidence of primary tumour
TI, II, III, IV	Number allocated to size of primary tumour, with 'I' representing the smallest size, up to 'IV', the largest
TX	Primary tumour unable to be assessed
N = Regional lymph node involvement	
For example	
N0	No evidence of regional lymph node involvement
NI, II, III, IV	Number allocated to involvement of regional lymph nodes, ranging from 'I', confined to one group, up to 'IV' when several groups are involved
NX	Regional lymph nodes unable to be assessed
M = Distant metastases	
For example	
M0	No evidence of distant metastatic spread
MI	Evidence of distant metastatic spread
MX	Distant metastasis cannot be assessed

[a] Example only. Not all stages applicable to every cancer.
Source: TNM Classification of Malignant Tumours (2002).