The Biology of Cancer

The Application of Biology to Cancer Nursing

Edited by

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Preface

The application of biology to the delivery of cancer care is playing an increasingly important role in the management of this group of diseases. Although there is a plethora of specialist cancer biology books, they are not aimed at nursing students and practising nurses.

The aim of this book is to be an informative text for students, newly qualified nurses and practising oncology/palliative care nurses. It is also hoped that it will be a useful text for other health-care professionals working in the field of cancer, so that the common questions asked by patients, and their families, can be answered with a clear understanding of the latest advancements in the management of an individual's care.

The aims and objectives of this book are:

- To describe what cancer is, its disease processes and predisposing factors for certain types of malignant conditions.
- To identify the composition of the cell and its functions.
- To discuss the current research that is taking place relating to the biology of cancer.
- To apply research to the management of an individual's disease.
- To summarize current Department of Health guidance applying to care of the individual with cancer.

Janice Gabriel
April 2004

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I would also like to thank Imogen and Bethany for their understanding. I can at last say 'I have finished my homework'.

JAG

Introduction

This book is written for nurses by experienced, practising health-care professionals to provide a 'readable', comprehensive text that can be easily applied to patient care. The book has not been designed 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 disease.

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, i.e. the development of a tumour and metastatic spread. It also seeks to identify and explain why there are predisposing factors linked to the development of some cancers.

The second part looks in detail at the cell, its composition, functions and response to cytotoxic agents. It also looks at the roles of the immune system and genetics in relation to the development of malignant disease. This part also deals with the increasing importance in the role of tumour markers in managing a patient's response to treatment.

The final part tackles the area of research. It takes into account the latest research guidelines and applies these to patient care, so that as practising nurses we can have a greater understanding of the potential implications for those of our patients who are considering participation in research studies.

Nurses are playing an increasing role in the management of cancer care. We therefore have a responsibility to our patients to have a sound knowledge base, reflecting the latest research and the application of this research to patient care.

JAG

PART I
UNDERSTANDING CANCER

Chapter 1
What is cancer?

Janice Gabriel

Cancer is not just one disease, but a generic term used to encompass a group of more than 200 diseases sharing common characteristics. Cancers (carcinomas) are characterized by their unregulated growth and spread of cells to other parts of the body (LeMarbre and Greonwald, 2000). Management of an individual diagnosed with cancer is dependent not only on which type of malignancy they have, but also on the extent of its spread, together with its sensitivity to treatment (Gabriel, 2001).

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 about 270 000 individuals receive a cancer diagnosis each year in the UK, with more than 7.5 million affected worldwide (Cornwell, 1997; DoH, 2000a; Corner, 2001). Sadly, the UK incidence of cancer is expected to increase by 2025 (Cornwell, 1997).

This chapter attempts to provide a clearer understanding of what cancers are, and how they spread (metastasize) throughout the body (British Medical Association (BMA), 1997; O'Mary, 2000). It also looks at the importance of staging an individual's disease before determining their most appropriate management (DoH, 2000a, 2000b).

The definition of cancer

As humans we are made up of many millions of cells. Some cells are specific to certain tissues, e.g. epithelial cells are found throughout the gastrointestinal tract, bladder, lungs, vagina, breast and skin. It is this group of cells that accounts for about 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. The 'tumour' cells are not only confined to localized 'overgrowth' and infiltration of surrounding tissue, but can also spread to other parts of the body via

the lymphatic system and bloodstream, creating secondary deposits known as 'metastases' (Walter, 1977; BMA, 1997). The '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, as a result of microscopic spread. Malignant tumours are often irregular in shape with ill-defined margins (Walter, 1977; Wolfe, 1986). Microscopic spread results in the tissue surrounding the visible tumour appearing unaffected by disease. However, 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. The spread of the malignant cells extends outward from the original tumour and has been described as resembling the appearance of a crab. Historically this has been traced back to the origins of the term 'cancer', which was derived from the Latin word for 'crab' (Walter, 1977). Generally, the earlier that a cancer is detected, the less likely it is to metastasize, and so the more favourable the prognosis for the individual.

Metastatic spread

All cells replicate themselves. This is usually about 50–60 times before the cell eventually dies (LeMarbre and Greonwald, 2000; Corner, 2001). 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 (Walter, 1977; Wolfe, 1986). To ensure that these malignant cells receive nourishment to thrive, angiogenesis occurs, which is the formation of new blood vessels (see Chapter 8) (LeMarbre and Greonwald, 2000).

Lymphatic spread

The malignant cells gain access to the lymphatic system, and travel along the vessels to the 'regional draining' lymph nodes (Walter, 1977). The malignant cell(s) can then establish residency in these regional nodes where they replicate and eventually replace the lymph node with a malignant tumour, i.e. cancer. Malignant cells from this tumour can then spread, 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 commonly spread via the lymphatic system (LeMarbre and Greonwald, 1997).

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, subsequently replicating to form a secondary (metastatic) deposit. The malignant cells can then migrate via the smaller blood vessels, i.e. the capillaries (Walter, 1977). However, there is evidence to demonstrate that only a small percentage of cells entering the vascular systems actually survive to give rise to blood-borne metastatic spread (Walter, 1977). Malignancies that are linked to blood-borne spread include melanoma and small cell carcinoma of the lung (LeMarbre and Greonwald, 2000).

Liver

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

Lung

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

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 as a result of damage of the bone by the malignant cells (Walter, 1977; Wolfe, 1986).

Brain

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

Adrenal glands

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

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. It is commonly seen in the peritoneal cavity, where it is associated with ovarian and colonic malignancies (Walter, 1977; Wolfe, 1986).

Staging of malignant disease

To ensure that every patient can be advised about the most appropriate management of his or her particular disease, it is vital that the extent of the cancer is known, e.g. if a patient presents with a breast lump that proves 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 would already have 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 about the most appropriate treatment option(s).

Most solid tumours, excluding childhood cancers, are 'staged' using the internationally recognized TNM (tumour, node, metastasis) classification system (UICC, 1997). The TNM classification system was introduced into clinical practice in the early 1950s and it aims to ensure that each individual patient is offered the most appropriate treatment for the cancer, depending on 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 cases and their anticipated responses to treatment, e.g. at the patient's pretreatment multidisciplinary meeting (see Chapter 3). By recording this information, future researchers in the treatment of cancer will have a benchmark on which to base assessment of a patient's disease response to potential new treatments (UICC, 1997; O'Mary, 2000).

The TNM classification works by assessing the extent of the primary tumour, the involvement of the lymph glands and the presence of metastases (Table 1.1) (UICC, 1997). A patient diagnosed with a small primary tumour, e.g. T1, will have a more favourable prognosis than a patient with a large primary tumour and widespread metastases.

The staging process will inevitably follow on from the initial diagnostic procedure. This can be a tremendously anxious time for the patient and family members/close friends. The patient has been given a diagnosis of cancer, and will inevitably become concerned about the delay in the start of treatment while waiting for further

Table 1.1 TNM classification system

T = tumour size, e.g.
T0: no evidence of primary tumour
T1, 2, 3, 4: number allocated to size of primary tumour, with '1' representing the smallest size, ranging to stage '4'
TX: primary tumour unable to be assessed
N: regional lymph node involvement, e.g.
N0: no evidence of regional lymph involvement
N1, 2, 3, 4: number allocated to involvement of regional lymph nodes ranging from '1', confined to one group, up to '4' when several groups are involved
NX: regional lymph nodes unable to be assessed
M = distant metastases, e.g.
M0: no evidence of distant metastatic spread
M1: evidence of distant metastatic spread
MX: distant metastasis cannot be assessed

Note that these are examples only. Not all stages are applicable to some cancers. From TNM Classification of Malignant Tumours (UICC, 1997).

investigations to determine the stage of the disease. A patient whose staging investigations confirm a small primary cancer confined to his larynx may well be successfully treated with radiotherapy, as opposed to more radical, surgical treatment by laryngectomy. Conversely, a patient with advanced disease that has already metastasized will not have the 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 Dukes' staging system for colorectal cancer and Clark's classification for malignant melanoma. For haematological malignancies the TNM classifications are not appropriate because of the systemic nature of the diseases. O'Mary (2000) lists a number of classification systems for haematological malignancies, including the following:

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

Diagnostic and staging investigations

Today there are a growing number of tests that can be performed to identify the presence of abnormal cells or an abnormal structure. These tests can initially be undertaken to confirm or eliminate a primary cancer (diagnose), or they can be performed to help in