Basics of Oncology

Second Edition

Frederick O. Stephens Karl Reinhard Aigner



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particularly satisfying to be able to help people with this most distressing and worrying health problem. Most patients are cured but for some cure is not a possibility with our present state of knowledge. All can be helped.

Working in oncology is a very satisfying career. It is

with our present state of knowledge. All can be helped. In most cases our patients become our friends and some become very special friends. They honour us with their

than worthwhile, indeed a special reward.
We are also grateful for our teachers of the past and for our present colleagues without whose cooperation our work would be of limited value and progress would be difficult.

friendship and trust, and this makes our work feel more

Like all teachers, we are inspired by our students. We not only pass on knowledge to them, but we also learn from them. To have interested and enthusiastic students is a real stimulus and privilege.

As is obvious from the authorship of this book, we have been privileged to make close and lasting friendships across national borders and across borders of traditional disciplines. We treasure these friendships dearly from their personal aspects as well as being able to learn from each other and to stimulate each other in clinical work and research. It is sad that so much cancer is still with us, but the constant mutual commitment to

improving methods of care and discovering new

information on prevention and treatment for the betterment of people everywhere is itself a reward, which we all share with respect and gratitude.

Finally we acknowledge that our work is demanding of time and energy. This is time and energy in which our wives, families and friends have so often had to make allowances for our absence. Without their love, support and acceptance of the conditions of our work, this work and our efficiency would be severely compromised. They have often joined us and at other times have had to stand by without us when we were concentrating on other things we could not always share with them. We especially owe our loved ones a debt of thanks and gratitude.

We proudly dedicate this book to all of these people.

Preface

Who Should Read This Book

In Western societies and other developed countries, cancer is the leading cause of death, after cardiovascular disease. It is therefore a major component of medical undergraduate curricula and of primary concern to nurses and allied health workers.

Presently most undergraduate students learn about cancer from a broad range of general and specialist books and journals. Medical students read about cancer in textbooks of surgery, pathology and cancer medicine as well as in general and specialist journals and from time to time in newspaper reports, in magazines and from various other sources.

We the authors teach, practise and conduct research in different specialty areas in different parts of the world. We agreed that we should write this book as an easily understood and general overview of cancer for students of medicine, nurse oncologists, students of medical sciences and other health professionals in all parts of the world. It is intended to serve as a basis for more detailed or specialised studies that will be needed in different areas of practice and in different countries. Different countries will emphasise different aspects according to their more specific community needs, incidence, traditions and available healthcare facilities and systems.

What This Book Is About

This book is intended to give an introduction to the scientific and clinical aspects of cancer, that is, the broad range of concepts of causes, pathology, clinical features, possible investigations, treatments and outcomes both for cancers in general and for the common cancers in different countries. It should be a basis for further study as appropriate for all areas of oncology no matter where it is practised or in what particular professional discipline. The purpose of this book is not to cover all social, personal, environmental or financial aspects of cancer nor to discuss details of supportive services available. These important aspects will differ in different countries with different social, medical and administrative services and facilities as well as different traditional practices and requirements. Ideal comprehensive facilities and

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services may or may not be available. Other books, specifically written for students and practitioners in different countries with different curriculum requirements, may be needed to cover these aspects.

Objective of This Book

The objective of this book is to develop graded information from very basic to more sophisticated understanding of present knowledge about cancer. For some students, this may well meet all their needs, but for students wishing to undertake further studies in cancer, this book will serve as a sound basis for more detailed or specific studies.

To achieve this, the book will:

- Cover basic medical, scientific and clinical aspects of cancer.
- Explain how and why people develop cancer.
- Indicate how the body reacts to cancer.
- Describe how cancer presents.
- Outline principles of cancer prevention, investigation, diagnosis and management.

This information applies in all countries. It is the essential requirement for understanding cancer no matter where studied or practised. We believe this basic information about cancer is best introduced early in a student's career before other details of personal, psychological, social and management practices and traditions are studied in detail in different communities.

More detailed and comprehensive information on specialised areas of knowledge, research and practice is expanded in more specialised books and publications, some of which are listed in the final section of this book.

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Burghausen, Germany

Karl Reinhard Aigner, MD

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Part I The Cancer Problem

What Is Malignancy?

In this chapter you will learn about:

- · Prevalence of cancer
- · Benign and malignant tumours
- · Dangers of malignant tumours
- · What causes malignancy

A malignant growth is characterised by a continuing, purposeless, unwanted, uncontrolled and damaging growth of cells that differ structurally and functionally from the normal cells from which they developed.

The commonly used term for a malignant growth is a cancer – cancer is Latin for crab. The condition was called cancer in ancient times because an advanced cancer was thought to resemble a crab, with "claws" reaching out into surrounding tissues.

Cancer is Latin for crab.

All living plants and animals are composed of living cells that often need to divide to produce more cells for growth and development and also to replace cells that have been damaged or have died. The process of cell proliferation (cell division and cell growth) is controlled by genes in the DNA of the cell nucleus. The genes are inherited from parents and bestow particular features in the offspring, including height, colour, weight and countless other distinctive features and functions of the tissues. The process is normally under remarkably well-balanced control. A cancer forms when this genetic control is damaged or lost in one or more cells, which then continue to divide and divide again, producing more abnormal cells that continue to divide and increase in number when and where they should not. The masses of unwanted dividing cells cause damage to other cells and tissues in the body. They are no longer controlled by normal genes that stop division after normal body needs have been met. They just go on dividing in spite of causing damage to other tissues and body functions. This is a cancer. All the causes of cancer are now known to directly, or indirectly, damage these normal genes that regulate cell division.

One obvious factor is that the longer we live, the more chance there is for the genes that regulate cell proliferation to become damaged by exposure to agents that damage the genetic blueprint, DNA. So most cancers become more common the longer we live; most cancers are more common in old age. Another factor is the rate of division for growth and replacement of tissues. Tissues like skin, bowel lining or lining of air passages (especially in the lungs) and blood cells are constantly being shed and replenished. Breast cells are constantly changing due to hormone activity over a woman's years of fertile life. With all this constant cell proliferation, there is more likelihood of mistakes being made in the process of copying the genetic blueprint to daughter cells, especially as the process becomes less accurate as we get older. A mistake or error in copying the genetic blueprint is called a genetic mutation. These then are the tissues most likely to undergo malignant change. Bone growth is greatest in growing young people, and testicular activity is greatest in young adult males, and these are the periods of life most prone to cancers of these tissues. As men grow old, the slow but constant changes in the prostate gland make it more likely that factors causing a change in cells might go wrong after years of exposure to the driving force of male hormones. So prostate cancer becomes increasingly common in old age.

The remarkable thing is not that something goes wrong from time to time in the delicate process of cell division but that things don't go wrong more often. In all life, there is a continuous delicate living process involving countless generations of cell division. The better we care for our bodies with good living practices, the greater the likelihood of preventing something, possibly uncontrollable, from seriously going wrong.

These good living practices include having good nutrition, healthy exercise, safe sex and avoiding exposure to potentially damaging agents in our environment. All of these practices serve to reduce the exposure of the genetic material in cells to agents that could cause changes in the genetic blueprint.

In the normal genetic make-up, there is a braking mechanism to stop cell division when the need for more cells has been satisfied.

Whilst most normal body tissues are composed of cells that have the ability to grow or reproduce, they normally only do so when there is a need. When this need has been satisfied, they stop reproducing. In the normal cell, there is a braking mechanism to stop cell division when the need for more cells has been satisfied. Cells in such tissues as the skin or blood or the lining of the mouth, throat or alimentary tract wear out quickly and are constantly being replaced. They are normally replaced only to meet the immediate need of the body, after which reproduction stops. Also, after injury or cell death, surrounding cells reproduce to replace and repair damaged tissues, but there is an inbuilt mechanism that stops the cell reproduction once the injury has been repaired and the wound has healed. The "switch-on" and "switch-off" mechanisms are governed by two different types of genes, whose functions are either to promote or to suppress cell division and cell growth. These are called proto-oncogenes and tumour suppressors. Proto-oncogenes respond to growth signals and are positive regulators of cell proliferation, only in the presence of appropriate growth signals. Tumour suppressor genes conversely act

as negative regulators of cell growth and suppress or check the unregulated growth of cells. So in the normal cell, the "switch-off" mechanism is the response to the absence of specific growth signals.

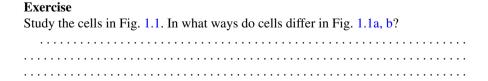
Some, but not all, body tissues retain a lifelong ability to replicate themselves to meet the body needs. For example, after surgical removal of as much as three quarters of a normal liver, the remaining liver will grow back to its original size within about 6 weeks and then stop. The nature of the "switch-off" mechanism is not fully understood – but it is clearly a critically important process that is normally under genetic control.

In the case of a malignancy, there is no "switching-off" mechanism. Some of the proto-oncogenes have now acquired mutations that mean they promote cell growth even in the absence of appropriate growth signals, i.e. they become oncogenes (cancer-promoting genes), and some of the tumour suppressor genes are inactivated, such that abnormal growth goes unchecked. Abnormal and unwanted cells then invade into surrounding tissues and possibly blood and lymph vessels, or body cavities, thereby spreading to other parts of the body, where they establish new damaging colonies of unwanted growing cells. These colonies are called secondary or metastatic cancers, known as *secondaries* or *metastases*.

1.1 Nature of a Malignancy

A malignancy is therefore totally different from an infection, which is caused by organisms from outside the body invading body tissues and causing damage. The body defences recognise invading organisms as foreign and protective measures are set in train to destroy them. Invading cancer cells, on the other hand, are abnormal cells that have developed from the body's own cells and are therefore allowed to further develop and infiltrate other tissues without the control normally provided by natural body defences.

Cancer cells also have different features and take on a different microscopic appearance from the cells from which they developed. Cancer cells become bizarre in size, shape and other features. As a rule, the more bizarre they become, the more aggressive and malignant is their behaviour. Cancer cells are usually derived from a single original cell and are said to show a clonal origin. The nucleus is often irregular, larger and darker in colour and may even be duplicated in the one cell. The cytoplasm is often relatively smaller, irregular in size and shape and without the special features of the cell of origin. There may be cells not only of different sizes and shapes but also with different staining properties (pleomorphic). These changes are brought about by changes in the tumour suppressor genes and oncogenes that are responsible for the control of cell division.



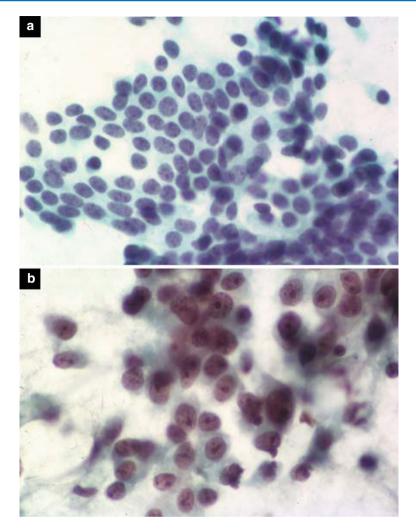


Fig. 1.1 Photomicrographs showing (**a**) breast cells of normal appearance aspirated from a benign breast lump and (**b**) highly malignant anaplastic breast cancer cells aspirated from a breast cancer (400×)

1.2 What Is the Prevalence of Cancer?

Cancer is known to occur in all societies and in all parts of the world. It affects animals as well as man. In humans, cancer is known to have been present in ancient times as well as in modern communities. However, the types of cancer

most prevalent in a community will vary with the age, sex distribution and race of people in the community, as well as the geographical situation, the economic and environmental situation and the habits of the people including their diets. (See Appendix showing incidence of different cancers in different countries.)

In developed countries, cancer is responsible for about 25–30 % of deaths. It is second to cardiovascular disease as a cause of death. Young people in developed societies are much more at risk of dying from causes other than cancer such as infectious diseases (including AIDS) or as a result of trauma (especially accidents in homes or on the roads, gunshot wounds or suicide) than from cancer. Although cancer can occur at any age, it is relatively uncommon before the age of 40 years; but as people grow older, the risk of cancer progressively increases.

1.3 Tumours: Benign and Malignant?

Non-malignant or *benign* tumours are much more common than malignant tumours. A benign tumour is a limited growth of cells that seems to be under some sort of control. Although there is no apparent purpose in the growth, the cells are more mature and closely resemble the cells from which they developed. Once the growth reaches a certain size, it usually slows or stops, such as a mole on the skin. All the cells of a benign tumour stay together as a lump or swelling that is usually confined by a capsule or lining of fibrous tissue. They do not spread to other parts of the body and are generally easily removed by surgery.

There are two broad groups of solid tissue malignant tumours, commonly called cancers. They are *carcinomas* and *sarcomas*. Carcinomas are malignant tumours of epithelial origin, such as lining cells of the skin, alimentary tract, respiratory tract, bladder or glands such as pancreas, thyroid or salivary glands. Sarcomas are malignant tumours of connective tissue such as the bone, cartilage, muscle, fat, fascia, nerve or blood vessel. Carcinomas are much more common than sarcomas.

In a malignant tumour, the cells look less like the cells from which they developed. The term *anaplasia* is used to describe cells that have lost their distinctive features. The multiplication of cells also continues without control (Fig. 1.2).

Very occasionally, benign tumours can be life threatening simply because of their size and location. An example is meningioma, which is a benign, slowly growing tumour that arises from the meninges covering the brain. It can eventually prove fatal if not removed because it compresses the surrounding normal brain tissue and eventually interferes with vital brain functions. A meningioma is nevertheless classified as a benign tumour because its cells do not invade surrounding tissues or spread to other parts of the body via the bloodstream or the lymphatic system and its removal by surgery should result in cure.