CONTROL OF PAIN AND OTHER SYMPTOMS IN CANCER PATIENTS

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Foreword

Contrary to common belief, cancer pain is not an inevitable part of cancer. The right drug in the right dose at the right time can control more than 80 percent of cancer pain. A scientifically valid and relatively inexpensive method already exists to treat cancer pain.

Despite this, cancer pain relief is often not offered. The World Health Organization (WHO) estimates that some 3.5 million people suffer daily worldwide, and many cancer patients suffer unnecessarily from severe pain with little or no relief, although they are treated for their tumor. Even for the terminally ill, cancer pain is unrelieved.

In the developed countries, at present, two thirds of the cancer patients will die of their disease. In the developing countries, where more than half of the world's cancer patients live, the majority of them are incurable at the time of diagnosis. Relief of cancer pain and other symptoms is most often the only humane alternative one can offer to the patients. Knowledge already exists on the relief of major symptoms of cancer patients. Our resources, strategies, and priorities in the care of cancer patients should be reshuffled to ensure that major symptoms of cancer patients are adequately relieved.

Two major concerns of cancer patients and their families are (1) whether the patient will have a lot of pain and (2) whether the patient will die alone. Unrelieved pain is still a major symptom in terminally ill cancer patients. With the help of the knowledge presented in this book, most pain could be controlled, and families, nurses, and doctors could feel

confident in being able to handle the major symptoms, thus motivating them to be present. Up to now, palliative care of the patient has been neglected at the expense of therapy.

Tor Inge Tønnessen, the author of this book, works at the Radium Hospitalet in Norway, and it is significant that, again, the largest cancer hospital in Scandinavia has taken the lead.

In this concise, logical, and didactic book, Dr. Tønnessen shows how pain and other cancer symptoms can be controlled and clearly defines the existing knowledge. Dr. Tønnessen's work, together with the WHO monograph "Cancer Pain Relief," should be widely used by doctors, nurses, and other health care providers to implement adequate symptom relief of cancer patients everywhere, thus improving their quality of life.

JAN STJERNEWÄRD, M.D.
Chief, Cancer Unit
World Health Organization

Preface

Interest in the control of pain and other symptoms has increased enormously in recent years. Palliation and the care of patients with a poor life expectancy have become a focus of attention, both in medical circles and in the media. Interdisciplinary counseling groups have been set up at a number of hospitals and hospices to help and advise patients, their families, and health professionals on the relief of symptoms and the care of seriously ill and dying people. Courses and conferences on the subject are also becoming common.

But although so much progress has been made in palliative medicine, a large number of health professionals are still not familiar with this field. Thousands of patients suffer unnecessarily from their symptoms. The widespread lack of knowledge about pain relief makes it essential to collect and systematically organize the information and experience we have in this area, and the fact that the first edition of the book has already been sold out shows how much this information is needed. The response to the first edition was very positive, and in the preparation of this new English language edition I have tried to take into account the negative as well as the positive criticism.

The book is written for physicians, medical students, nurses, and student nurses. It is divided into three main parts: *understanding* of pain, *methods* for treating pain and other symptoms, and *practical applications* of the principles of treatment. Part I deals with background knowledge—anatomy and physiology, assessment of pain, and principles of treatment.

Part II describes analgesics and other drugs used in pain and other symptomatic therapy. (In the text, all drugs are referred to by their generic names only. In Appendix 1 both generic names and trade names are given.) Part II also describes other methods of treating these symptoms, including nerve blocks, neurosurgery, palliative surgery, radiotherapy, chemotherapy, and hormone therapy. Part III describes how the methods of treatment can be carried out and integrated in everyday clinical work, and this part of the book can be read independently. Each chapter is designed to be intelligible when read on its own, so the reader will find a number of repetitions. A short and practical introduction to symptom control can be obtained by reading Chapters 2, 3, 10, 11, and 12. The remaining chapters contain the background information necessary for making a thorough assessment and treatment plan for each patient. A thorough description of psychic reactions to serious illness and death is beyond the scope of this book.

The list of contents has been given in detail to facilitate easy reference. The English version has been updated and adapted to conditions in the United States.

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TOR INGE TØNNESSEN

Introduction

Most people are afraid of cancer. Almost everyone has a friend or relative who has suffered a great deal of pain from this frightening disease. One can hardly open a newspaper without reading that someone has died "after a long and painful illness." Cancer is therefore justifiably associated in most people's minds with pain and suffering. Far too many people have suffered so much at the end of their lives that it has affected their contact with their families and surroundings.

Everyone is afraid of pain. Surveys show that a great many people worry about the possibility of dying painfully, and that they are more afraid of this than of death itself.

More than half of the patients who die of cancer will experience severe pain during their illness. A quarter of them will have moderate or mild pain, and the remaining quarter of them will not experience any pain at all. Thousands of people are thus suffering night and day from one of the worst experiences a human being can go through.

Health professionals are often in contact with these people and their suffering, and considering the extent of the problem, one would assume that medical science has come a long way toward solving it. Fortunately it has. Good tools have been developed to handle pain, but paradoxically enough, there are far too many who are not able to use them properly. Several surveys have revealed a great deal of ignorance among medical personnel about the use of painkilling drugs in chronic diseases. The

teaching of medical students has been very inadequate in this respect, and even experienced physicians often know surprisingly little about it.

Interest in the problem of pain has increased steadily during the last 10 to 20 years. Great progress has been made in the English-speaking countries and in Scandinavia, and the improvement in knowledge is gradually spreading to the rest of the world. Surveys have shown that more than 90% of patients obtain substantial relief from pain if given proper treatment, and this development can be counted as a very great achievement in modern medicine.

Acute pain with an obvious etiology and a good prognosis, like a broken leg, is a completely different experience from chronic pain. Acute pain is easier to tolerate, even when it is more intense, than chronic pain. Patients with cancer know that the pain will probably get worse, and they can see no solution. They have no control over the pain, and this makes them feel helpless. The pain seems meaningless. This kind of pain almost always gives rise to depression and anxiety, which in turn aggravate the pain, and the patient is caught in a vicious circle.

People with severe chronic pain are dominated by it; it occupies their thoughts, destroys their concentration, and takes all their energy. The pain is no longer a symptom of a disease process, it is the person's main problem. We should therefore take it seriously when the patient asks for help. We should bring the same therapeutic enthusiasm to relieving the symptoms that we devote to seeking a remission to the disease, even when we know that the patient cannot be cured.

Other symptoms besides pain also require professional diagnosis and treatment. Palliation has been a neglected area of medical practice and research for far too long. Using relatively simple methods, we can give patients the help they need to be able to live with and cope with their disease for a short or long period. Palliative treatment is an interesting field in which a great many advances have recently been made.

The first phase of cancer usually involves active treatment with surgery, radiation, or intensive cytostatic therapy. It is characterized by the hope of a cure. When metastasis is demonstrated, however, it may be difficult to decide between a new course of treatment, involving unpleasant side effects but also hope of a remission (curing), and palliative treatment (caring). Curing is generally regarded as active, and caring as passive. Health professionals often seem to become resigned when a cure seems unattainable. This is a completely mistaken attitude. Palliative treatment requires knowledge, diagnostic ability, and energetic action. Disseminated cancer is a multiorgan disease for which the clinician needs a broad knowledge of medicine to be able to help the patient. It represents a challenge to research and medical practice, and palliation is increasingly acknowledged to be an *active* form of treatment.

Contents

PART I

UNDERSTANDING PAIN

1

The Anatomy, Physiology, and Psychology of Pain

Over the last 20 years our knowledge of the pathways of pain in the central nervous system and of the physiological and psychological mechanisms of pain has made so much progress that it can almost be called a revolution. Before this, drugs and other therapy for relieving pain were used in a purely empirical way. Now, however, our new insight into the basic mechanisms of pain should lead to more rational and effective treatment.

Research in this field is difficult because of the subjective nature of pain. Objective findings are therefore difficult to establish. Animal models can be informative but have often been shown to be of little value in the human situation. Our knowledge is thus still full of gaps, in spite of all the progress that has been made. But there is a great deal of optimism in this field, and fresh knowledge is continually being discovered.

PERIPHERAL AND CENTRAL PATHWAYS OF PAIN

PERIPHERAL PATHWAYS

The body has peripheral nerves that are specially constructed to conduct pain impulses. There are probably many subgroups of pain fibers, but they are usually classified into two groups on the basis of their thickness, A-delta and C fibers. The C fibers are fine and unmyelinated and conduct impulses

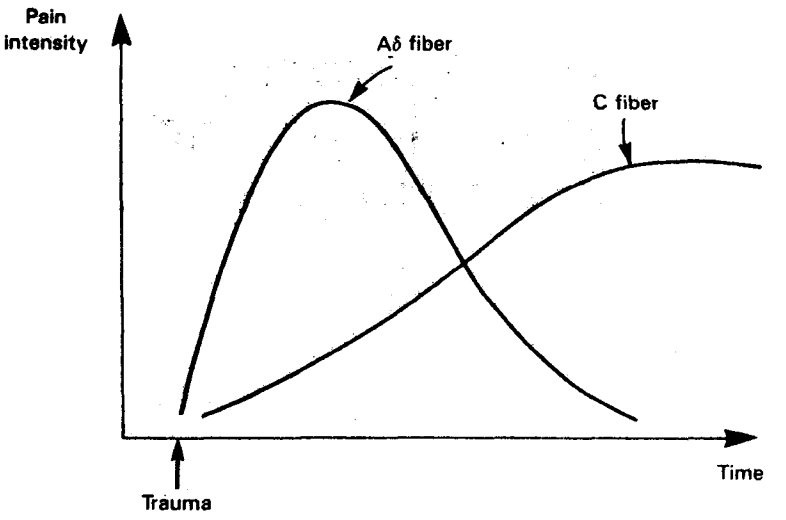

FIGURE 1. Activation of the A-delta and C primary afferent nociceptors.

relatively slowly (less than 2 m/s; see Fig. 1). They transmit the drilling, burning, deep, and lasting type of pain (protopathic pain). A-delta fibers are somewhat thicker and myelinated, they conduct impulses more rapidly (about 20 m/s), and they are responsible for transmitting stabbing, intense, superficial, short-lasting pain. Pressure, touch, vibration, and other sensations are conducted by the thicker, myelinated A-alpha and the somewhat finer A-delta fibers. This classification is mainly based on the study of pain receptors in the skin. The method of transmission of pain varies somewhat from organ to organ. For example, A-delta fibers from muscles can conduct the same type of pain as C fibers from skin.

The body is well supplied with nociceptors (pain receptors) in the skin, muscles, periosteum, peritendineum, parietal pleura and peritoneum, pericardium, capsules around the internal organs, and the tentorium/falx cerebri.

For a long time it was thought that the internal organs had no, or very few, nociceptors. Recently, however, the existence of nerves reacting to ischemia, inflammation, mechanical stretching, and other stimuli has been demonstrated in the heart, gastrointestinal tract, and other abdominal organs. The nerves that transmit nociceptive impulses also react to other sensory impulses; very strong impulses in these fibers seem to be perceived as pain. There is evidence, however, that some of these organs (at any rate the bile ducts) have specific pain fibers, that is, nerve endings that react only to painful stimuli. Pain from internal organs is conducted through fibers belonging to the autonomic (i.e., involuntary) nervous system, chiefly the sympathetic nervous system.

Mechanisms for the Occurrence of Nociceptive Pain in the Tissues

The nociceptors are activated by threatened or existing tissue destruction. Some A-delta fibers are activated by direct physical trauma (pressure), others by high or low temperature or chemical substances. The pain is conducted rapidly and strongly and with most types of stimuli will decrease fairly quickly (in the course of seconds to minutes), even if the painful stimulus continues. The function of this type of fiber thus seems to be to register changes in pain intensity, not to provide continuous information about pain, although some A-delta fibers can conduct pain impulses for a longer period.

C fibers are depolarized by the chemical substances formed during tissue injury, but they can also conduct nociceptive impulses caused by direct physical stimuli. The C fibers are activated more slowly than the A-delta fibers, but they conduct pain impulses for a long time after the injury and continue to transmit impulses actively as long as the stimulus lasts (see Fig. 1).

A number of substances produced by the body can cause pain when injected into tissue; examples are bradykinin, prostaglandins E_2 and I_2, histamine, serotonin, protons (low pH in the tissue), and potassium ions. There is a great deal we do not know about the physiological role of these substances in the pain process. It is possible that the different pain fibers react specifically to the different substances, but it is more likely that more than one of the substances has to be present at any time for nociceptive impulses to arise. Low doses of bradykinin do not normally give rise to pain, but they will do so if prostaglandin E_2 is also present. This is probably because the prostaglandin E_2 makes the pain fibers more sensitive to pain-provoking (algogenic) substances. Serotonin secreted from platelets has also been shown to potentiate the effect of bradykinin and acetylcholine.

All the above-mentioned algogenic substances are formed during tissue injury. Proteolytic enzymes in the injured area cleave the protein bradykininogen (plasma kininogen) that diffuses from the blood into the tissue fluid, forming bradykinin. Prostaglandin precursors are present in all cell membranes in the form of esterified fatty acids (phospholipids). If, for example, the tissue is injured, the phospholipids are cleaved by the enzyme phospholipase A_2, and arachidonic acid is formed (see Fig. 2). The enzyme cyclooxygenase can convert arachidonic acid to prostaglandins E_2 and F_2, prostacylin (prostaglandin I_2, or thromboxane, the type of prostaglandin being dependent on the cell type. Short-lived intermediary products like the prostaglandins G_2 and H_2 are also present in this reaction and probably also contribute to the arousal of pain. In some cells the arachidonic acid is also converted by the enzyme lipoxygenase to leukotrienes, which are potent mediators in the inflammatory process and may sensitize