Supportive Oncology

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We dedicate this book to our families in gratitude for their love and support:

To my wife, Deborah, and my children Luke, Amanda, Meghan, Jessamyn, Emelin, and Lilian—Mellar Davis

To Otto Josef — Petra Feyer

To my daughter, Eva, and to my mother, Rose-Marie—Petra Ortner

To my husband, Richard, and my children, Erica, Hendrik, and Karl—Camilla Zimmermann

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Foreword

The new specialty of medical oncology emerged in the aftermath of World War II. Since then, it has expanded rapidly around the world as a vibrant and important area of specialist medicine. By definition, it often involves the care of people with cancer that recurred after definitive primary therapy or that presented de novo with metastatic disease. Because of advances in therapy and prevention, death from cancer in industrialized countries has declined, even as incidence has continued to increase. The latter is partly due to aging of the population; cancer is, in part, a disease of the aging process. In addition, lifestyle choices have a significant impact. Development of medical oncology was driven by the belief that cancer could be cured even when metastatic. Dramatic improvements in mortality (particularly pediatric oncology) have been obtained in some diseases. Over the same time frame, there have been dramatic improvements in medical technology with benefits in common structural complications of metastatic cancer. Examples include stenting techniques for gastrointestinal malignancies and sophisticated approaches to management of pleural effusions. Surgical oncology, oncology nursing, psychosocial oncology, and multidisciplinary care have also emerged as new allied areas of endeavor. It is still true that in most patients who are referred to a medical oncologist, death is a frequent (although not always explicitly recognized) outcome. Unfortunately, most common solid tumors remain incurable once they metastasize.

In medical oncology, an early commitment was made to structured investigation of new therapies. The vehicle for this this has been through clinical trials. This discipline has made a major impact on diseases such as breast cancer and multiple myeloma. There has been some debate that other advances in imaging and laboratory medicine have contributed to the apparent increased duration of survival (because of earlier diagnosis). Nevertheless, there seems little doubt that the systematic use of clinical trials has been of therapeutic benefit for many patients and has improved clinical care. An important part of clinical trial methodology is the assessment of therapeutic toxicity. This allows the medical oncologist to carefully balance the potential benefits of therapy against its adverse effects.

Therefore, we have come to realize that chemotherapy and radiation therapy are often blunt instruments. They can be associated with significant, sometimes life-threatening morbidity. Some of these effects are nonspecific, and others are particular to the therapeutic modality or specific drug used. Certain levels of morbidity have been considered acceptable (or inevitable) and part of the price for attempting to cure a catastrophic illness. Examples include the complications associated with certain high-dose chemotherapy regimens for breast cancer and those seen in patients after bone marrow transplant. The morbidity experienced during active treatment includes significant psychological and physical symptoms, emotional and financial distress, family dysfunction, and work and career disruption. In addition, such toxicities may be prolonged in nature beyond the treatment time frame and may be responsible for significant long-term morbidity or development of new diseases. Among those who survive cancer, there are significant effects on quality of life and residual issues, such as sexual dysfunction, that disrupt life long after cancer has been cured. In addition, the response rates to many common therapies are still disappointing, toxicity is notable, and nonresponders are often exposed to significant morbidity without any therapeutic benefit.

As the field of medical oncology progressed, certain common complications of cancer therapy, such as infections, were identified as requiring systematic attention. Later, the problems of nausea and vomiting associated with cis-platinum chemotherapy arose as another challenge. It was quickly realized that sophisticated management of these and the many other complications of therapeutic intervention was important in themselves as clinical challenges. Better management would also allow regimens to be administered most effectively. It also became apparent that the benefits to the patient were additive by improved quality of life, reduced hospitalization, and mitigated emotional and physical distress. In addition to the practical clinical benefits, a rigorous approach to the investigation and management of these common problems required significant academic endeavor. This field is now what is known as Supportive Oncology.

This major new book about supportive oncology is a timely recognition of the practical relevance, academic rigor, and increasing sophistication of the field. Supportive oncology is now recognized as an important part of practice in all areas of clinical oncology, with many benefits to the millions of people around the world in whom cancer is diagnosed every year. It can also rightly be seen as a sister specialty to another modern development, Palliative Medicine. Modern care of the cancer patient is a multidisciplinary endeavor, and everyone involved in the field will benefit from access to the wisdom and perspectives of this exciting new book.

T. Declan Walsh, MD

Preface

We are pleased to present this first edition of *Supportive Oncology*. The aim of supportive oncology is to minimize the physical, psychosocial, and spiritual suffering caused by cancer and the adverse effects of its treatment to ensure the highest possible quality of life for patients and their families. We believe that this book fulfills a unique need by providing a guide to supportive oncology throughout the cancer trajectory, from diagnosis to survivorship or bereavement. The book is based on an integrative model of care. We posit that supportive, rehabilitative, and palliative care measures should accompany patients throughout their course of disease and should be taken into account in the treatment goal in every situation, from diagnosis until cure or death. A well-defined integrative supportive care model should be included in every treatment protocol for cancer care. Supportive measures should be tailored to the special treatment or illness situation and must also reflect the wishes and needs of the patient.

This book is a collaborative venture including not only oncologists, but also palliative care physicians, nurses, pharmacists, psychologists, and psychiatrists. It is also an international collaboration, with editors from the United States, Canada, and Germany and contributors from across the globe. We are fortunate to have the contribution of many international experts in their respective fields and are grateful for their excellent contributions to this book.

This book is intended as a comprehensive resource for all oncology practitioners to assist in the management of physical and psychosocial symptoms and concerns throughout the illness trajectory. It is a useful resource for medical, radiation, and surgical oncologists; palliative medicine specialists; and oncology nurses. In addition, this book serves as a guide to supportive oncology for primary care practitioners and other health care workers seeking detailed, practical information on the supportive management of patients with cancer.

The fifty-nine chapters are organized into six sections: management of treatment-related adverse effects, management of tumor-related symptoms, management of complications in the palliative setting, rehabilitation and survivorship, communication and decision making, and psychosocial oncology. The organization of the book reflects the fact that supportive oncology encompasses symptoms and complications related to treatment, as well as those arising as a consequence of the malignancy. The section on rehabilitation and survivorship acknowledges the reality that cancer care continues after the cancer has been cured and addresses the important aspects of late effects of treatment, as well as ongoing recovery and rehabilitation The section on communication addresses decision making and supportive processes throughout the cancer trajectory. The psychosocial care not only of patients but also of professional caregivers is highlighted in the final section.

We wish to express our sincere gratitude to all the contributors to this book. We also extend our thanks to the editorial staff at Elsevier, particularly Pamela Hetherington, who guided us through this project with patience and perseverance.

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Contents

SECTION 5

COMMUNICATION AND DECISION MAKING 471

SECTION 6

PSYCHOSOCIAL ONCOLOGY 527

SECTION

1

MANAGEMENT OF TREATMENT-RELATED ADVERSE EFFECTS

SECTION OUTLINE

1 Chemotherapy extravasations (cutaneous and mucosal)

Maike de Wit and Robert Mader

Although intravenous drug administration is a basic requisite and daily routine for every physician, extravasation has been observed with a variety of agents, including electrolyte solutions, contrast media, blood products such as red blood cells, heparins, phenytoin, and cytotoxics.

The incidence and extent of injury are functions of localization, extravasating substance, absolute amount and concentration of the drug, and remedial action. Every physician should be aware of specific problems associated with different administration sites such as the back of the hand or foot and the inside of the elbow.

PREVALENCE AND PATHOPHYSIOLOGY

Accidental extravasation of cytotoxic agents is a relatively rare complication, with an incidence varying between 0%, 1%, and 5%.[1–3] In a recent survey of the MD Anderson Institute, 44 extravasations were observed in 40 to 60,000 chemotherapies during the same time period. Twelve extravasations included doxorubicin, and 10 of them needed surgical intervention.[4] Because of smaller vessels and more complicated venous access, extravasation is more common among children and is observed in up to 11%.[5] Obviously, only incidents identified by staff or patient are included.

DEFINITION

Extravasation is the process of unintentional instillation of a given infusion or injection, passing out of a vessel into surrounding tissue such as subcutaneous fat, underlying connective tissue, or muscle. Consequences depend on local drug effects and have been shown to be especially disastrous for some anticancer cytostatic agents, causing severe tissue damage within hours, days, or even months.

RISK FACTORS

The multiple risk factors can be divided in patient related, drug related, medical staff related (iatrogenic), or related to the intravenous access.

RISK FACTORS ASSOCIATED WITH THE INDIVIDUAL PATIENT

Frequency and extent of damage vary with different locations. Peripheral veins at the back of the hand, the dorsum of the foot, or the inside of an elbow are more vulnerable. If veins have been used several times already,[6] or if they are small and fragile[7] or are located near nerves, tendons, and arteries (e.g., of the hand), problems occur more frequently. Older patients and patients with sclerosis or smaller vessels suffer more damage from extravasations. The same is true for patients with higher venous pressure following thrombosis,[8] right cardiac insufficiency,[7] mediastinal tumors,[9] or a vena cava superior syndrome due to other reasons. Extremities with lymph edema following lymphadenectomy,[10] radiotherapy,[11] or problems like thrombophlebitis, venous spasms, or generalized vascular diseases like Raynaud's syndrome[7] hinder uncomplicated intravenous drug application. Patients with neurologic deficits like reduced sensitivity due to diabetes or chemotherapy-induced polyneuropathy[11] may report extravasation too late, and this results in more extensive tissue damage.

The probability of extravasation, attitudes that can help to avoid them, and signs and symptoms of early detection of an extravasation should be completely explained to the patient. Informed patients are more compliant, usually keep their arms immobilized to avoid extravasation, and inform nurses earlier, thus reducing the amount of extravasated drug. Restless patients with neurologic disorders or lack of understanding such as children,[12] psychotic patients, or patients with dementia suffer more problems related to intravenous access.

Table 1-1 Graduation of necrotizing potential

High risk of ulceration (vesicans)	Irritating; rarely necrotizing (irritans)	Low/No risk of inflammation
Amsacrine	Bendamustine	Alemtuzumab
Carmustine[1]	Busulfan	Asparaginase
Cisplatin (concentration >0.4 mg/ml)	Carboplatin[1]	Azacytidine
	Cisplatin <0.4 mg/ml	Bevacizumab*
Dactinomycin	Dacarbazine*	Bleomycin
Daunorubicin	Etoposide	Bortezomib*
Docetaxel[1]	Fotemustine	Cladribine
Doxorubicin	Gemcitabine	Clofarabine
Epirubicin	Liposomal daunorubicin	Cyclophosphamide
Idarubicin	Liposomal doxorubicin*	Cytarabine
Mitomycin C	Melphalan	Decitabine
Mitoxantrone	Streptozocin	Etoposide-phosphate
Oxaliplatin[1]	Teniposide	Fludarabine
Paclitaxel[1]	Trabectedin*†	5-FU
Vinblastine	Treosulfan	Ifosfamide
Vincristine		Irinotecan
Vindesin		Methotrexate
Vinflunin*		Nelarabine
Vinorelbine		Nimustine
		Pegasparaginase
		Pemetrexed
		Pentostatin
		Raltitrexed
		Rituximab
		Thiotepa
		Topotecan
		Trastuzumab
		cytokines (interferon, interleukin)

[1]In the literature and according to experts, sometimes a lower necrotizing potential is estimated. Unknown: cetuximab, panitumumab, gemtuzumab-ozogamicin, arsenic trioxide, and estramustine.
*According to the manufacturer.
†Theman TA, Hartzell TL, Sinha I, et al. Recognition of a new chemotherapeutic vesicant: trabectedin (ecteinascidin-743) extravasation with skin and soft tissue damage. *J Clin Oncol.* 2009;27:e198–200. Epub 2009 Oct 5.

RISK FACTORS ASSOCIATED WITH THE DRUG

Tissue injury is caused by the drug itself (e.g., with anthracycline extravasation),[13,14] but sometimes it is caused by additives like solvents.[15] Cytotoxic agents are divided into three groups according to the damage potential of the respective drug: vesicant, irritant, or nontoxic (Table 1-1). For grading, only low-level evidence, mostly based on case reports and new drugs, has to be observed carefully.

Additional risk arises from osmolarity and pH value (e.g., undiluted 5-fluorouracil) as alkaline infusion (pH 9). Larger amounts of cytotoxic extravasation, longer exposure,[16] or hypersensitivity exponentiates tissue reaction.

RISK FACTORS ASSOCIATED WITH THE MEDICAL STAFF

Because intravenous devices are associated with a risk of extravasation, chemotherapy should be administered by experienced staff only. Insufficient puncture skills lead to higher rates of extravasation.[10] Overtired or too few personal[17] and time pressure[12,18] increase the risk of extravasation. The location of intravenous access has to be selected carefully and plays a major role in safety. Safety is highest with intravenous lines in the forearm and declines in this order from the back of the hand to the inside of the elbow.[19] Multiple punctures and veins punctured upstream within the last 48 hours should be avoided. High-pressure infusions to peripheral veins, large volumes, and longer duration of infusion are potential causes of extravasation. Extremities with lymphedema and neurologic problems like polyneuropathy should be avoided whenever possible.

Drugs with necrotizing potential should never be administered through steel cannulas but always with flexible intravenous devices.

Lack of experience and knowledge of medical staff,[11] as well as carelessness or underestimation of potential damage,[12] and lack of surveillance[5] such as disregard of patient complaints[20] delay diagnosis[21] and are reasons for greater damage. This risk is increased when the injection site is covered.[11]