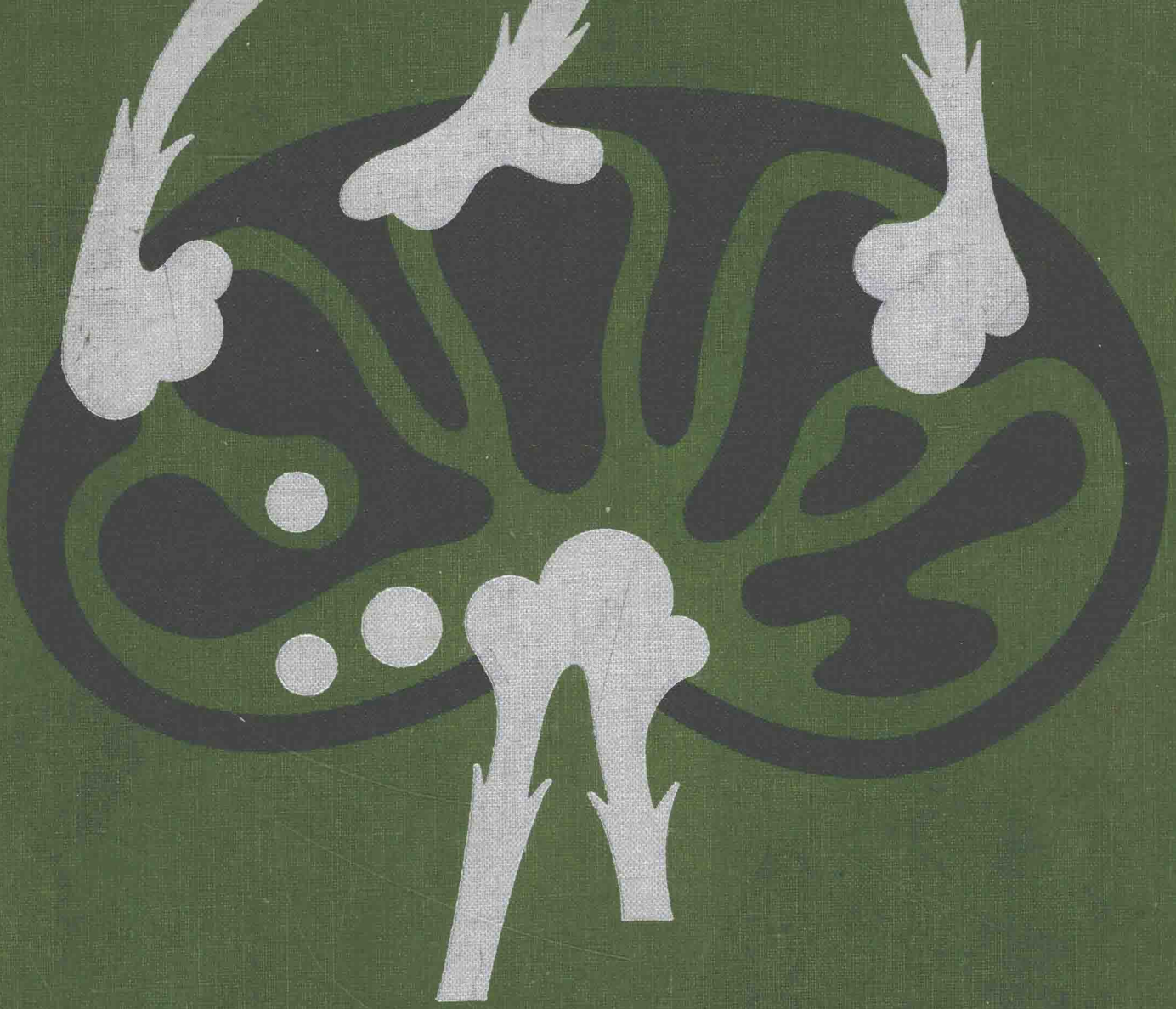

Lymphatic System Metastasis

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Preface

This book contains expanded versions of papers presented at a small workshop on metastasis within the lymphatic system, held on May 31 and June 1, 1979, at the University of California at Los Angeles Faculty Center.

This is our third attempt to provide in-depth coverage of metastasis in specified sites in terms of basic sciences, diagnosis, and treatment. In contrast to the previous volumes in this series, that dealt with metastases in the lungs and brain, the present title covers both a complex delivery system and the target organs—the lymph nodes. This dual purpose has necessitated a different format from the previous volumes.

Once again, we are deeply indebted to our contributors for their efforts to provide exhaustive documentation of the various aspects of this central topic in oncology.

Leonard Weiss
Harvey A. Gilbert

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Leonard Weiss
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Samuel C. Ballon

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Introduction

The spread of cancer within the lymphatic system has long been recognized, and the extent of this spread has traditionally been used as the basis for both staging the disease and treating it. Other things being equal, patients with lymph-node metastases do worse than patients without them. The presence or absence of nodal involvement is usually related to the size of the primary cancer: tumors with 2 cm diameters tend to have nodal involvement in 10 to 20% of cases. The incidence increases with the size of the primary lesion. In many types of cancer, lymph-node metastases appear to develop in a more or less orderly anatomic progression from their primary sites. This progress led to the classical approach to radical cancer surgery, the efficacy of which is currently the subject of agonizing review. Except in early disease, metastases are not confined to the lymphatic system and the cancer cannot therefore be eradicated by removal of the primary lesion and its nodal metastases. This does not imply that there is never therapeutic gain from radical procedures, however, since even short-term relief (e.g., 5 years) may be very worthwhile for the patient. Nonetheless, from a mechanistic viewpoint these gains should not be confused with total eradication of disease, manifested as long-term cures without development of distant metastases. The limited success of local therapy *in all but early cancer* has led to the concept of lymph nodes as somewhat passive meters of the extent of cancer, rather than as active limiters of the disease (with the possible exception of early disease), or as exclusive agents in promoting its spread.

This book begins with a section on some of the more general pathobiologic aspects of metastasis in the lymphatic system. The feasibility of certain universal mechanisms and the limitation in interpretation of experimental and clinical data, are discussed in terms of communications between the lymphatic and venous systems, the ultrastructure of lymph nodes in relation to malignant cells lodged in them, and the question of immune response. The controversial topic of tumor immunology is covered briefly, because it is now well appreciated that studies of often highly immunogenic animal tumors have questionable relevance to the total metastatic situation in humans, whose tumors do not appear to be highly immunogenic. In addition, there is reason to suspect that by the time patients are seen by the clinician, any immunologic battles have been lost. This does not exclude a role for immune phenomena in human cancer, however, particularly in subclinical situations.

The second section is concerned with a survey of diagnostic procedures used to assess lymphatic involvement in metastasis. It is not our intention to describe the techniques themselves here but rather to indicate some of their avoidable and unavoidable limitations. For example, the procedure for obtaining specimens is often not considered

by those reviewing data and may generate false results. The method of examining lymph nodes must also be considered because some clearing procedures and multiple sections will reveal cancers in nodes graded as negative by standard techniques. Somewhat surprisingly, these nodal micrometastases are regarded as having little clinical importance. However, removal of involved nodes as part of a staging procedure may modify the subsequent course of disease. In addition to variations in pathologic specimens, account must also be taken of variations in specimens of pathologists. For example, not only has the prognostic significance of sinus histiocytosis in breast cancer evoked a great deal of controversy among surgeons, the existence of sinus histiocytosis as a distinct pathologic entity is not recognized by many pathologists. Detection of involved lymph nodes by radiologic techniques such as lymphangiography, computer-aided tomography, and ultrasound is also not completely reliable. While these procedures have obvious merit, their limitations with respect to false negative results must be borne in mind.

As with most other aspects of metastasis, generalizations about involvement of the lymphatic system have limited value, and it is mandatory to consider the metastasis of specific cancers from specific anatomic sites. Therefore, after some general considerations of node irradiation, chemotherapy, and combined therapy in the third section, the fourth and final section of this book is concerned with detailed considerations of metastasis from specific primary tumors. In some cancers, nodal involvement must almost always be present before spread to distant sites. Limited involvement of lymph nodes by these cancers may be associated with a high likelihood of cure if local treatment of the primary lesion and involved nodes is adequate (for example, primaries in the cervix, head and neck, or vulva). The participants at the meeting agreed that even when dealing with the more curable cancers with lymph node involvement, as soon as the bulk or number of involved nodes exceeds a certain volume, local surgery probably becomes little more than a giant biopsy, possibly affording relief from local symptoms, and removal of potential generalizing sites for additional metastases. Even when irradiation is applied in addition to surgery, the regional disease may be removed, but little survival improvement is obtained. For example, in treating head and neck cancer, increased local control has not similarly improved survival, because the incidence of fatal distant metastases has increased. In other groups of cancers (melanoma, squamous cell carcinoma of the lung, colon cancer), recent information indicates that adequate treatment of nodal involvement limited to one or two very proximal, subclinically involved nodes, is associated with cure. In some cancers responsive to chemotherapy, there appears to be only minimal lowering of the cure rate when limited, or even modest, nodal disease is present (Wilms' tumor and testicular cancer). Finally, there are those cancers in which nodal involvement indicates no lowering of the survival rate (such as well-differentiated thyroid cancer in younger patients). In most cancers, however, even modest nodal involvement indicates visceral metastases.

Efforts were made at the meeting to construct a composite chart, comparing the cure rates for each primary site of cancer as related to the degree of nodal involvement (assessed by number and anatomic site). It soon became obvious that the nuances of each primary site, in terms of histology and the detailed anatomy of the regional lymphatic system, precluded any but the most rudimentary schemes, and would lack clinical relevance. Readers are therefore referred to individual chapters, where the nuances and specifics are presented in detail.

Metastases in the lymphatic system, like so-called solid cancers in other systems and organs, cannot usually be treated effectively in the disseminated stage, and new departures in research of chemotherapy and other forms of systemic therapy are urgently required.

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Contents