CLINICAL SURGERY INTERNATIONAL

4

INFECTION AND THE SURGICAL PATIENT

EDITED BY
HIRAM C. POLK JR

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VOL 4

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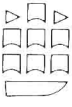

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Infection and the Surgical Patient

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Preface

This monograph is further evidence of a remarkable resurgence of interest in surgical microbiology. Traditionally, the surgical scientist has turned to varying combinations of asepsis/antisepsis, technical finesse and antimicrobial medications. Just as the proper role of antibiotics has become better defined than ever, the emerging awareness of the innate limitations of those same agents has perhaps been the greatest stimulus to current studies in the field of surgical infection. The heritage of surgical microbiology is a rich one and in modern scientific terms is derived from the partially publicized relationship between Pasteur and Lister and the fundamental mechanistic studies of Ogston. While it is always hazardous to attribute so much to a single contemporary, Altemeier kindled and rekindled that flame of enquiry and interest.

The clinical trials of merit in this new era were initiated in the United States but rapidly were exceeded in precision and extent by colleagues in the United Kingdom. There is still much to be uncovered by such studies as I will define in detail in my closing comments for this book (p. 213–214).

Basic studies in surgical microbiology have to some extent kept pace, there now being a half-dozen productive laboratories fully committed to surgical microbiology, as expressed by a very wide range of fundamental enquiries. For example, our own Department is actively conducting experiments upon:

1. Definition of host defence abnormalities in the surgical patient
2. Subcellular metabolism in the presence of infection and/or shock
3. Specific defence processes in lung and peritoneum
4. A variety of clinical studies of new antibiotics for both therapeutic and preventive action in the surgical patient, and
5. Enhancement of nonspecific host responses to infection.

The substance of current revitalization of surgical microbiology also is attested to by the regular appearance of several such papers on the most competitive surgical scientific programmes. The topics range from ever more sophisticated clinical trials of antibiotic prophylaxis of operative wound infection to fundamental studies of local tissue defence processes and the role of specific nutrition.

This book will attempt to bring the reader up to date, and beyond, if you will, in an organized, coherent review of most mainstream issues relevant to infection in the

surgical patient. The table of contents is intended as an organizational guide; the publishers and I have been especially fortunate to enlist the leaders in this new wave of enquiry to share with the reader the fruits of their clinical and investigative insights into various aspects of surgical microbiology. We have endeavoured to produce a book capable of understanding by the medical student beginning his clinical clerkship and of stimulating the most seasoned and skilled practitioner.

Our goal: to describe the state of the art with an enlightened view toward future prospects, which are in fact still in need of further investigative thought and analysis.

LOUISVILLE, 1982 H.C.P.

BIBLIOGRAPHY

Lister J 1868 An address on the antiseptic system of treatment in surgery. British Medical Journal 2: 53–56

Ogston A 1881 Report upon micro-organisms in surgical diseases. British Medical Journal 1: 369–374

Pasteur L 1861 Expériences et vues nouvelles sur la nature des fermentations. Comptes rendus de l'Académie des sciences 52: 1260–1264

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Determinants of infection

1 *The host*

R. L. SIMMONS and J. S. SOLOMKIN

Introduction

It is a clinical truism that infection begets infection: patients recovering from one episode of infection appear to be at an exceptional risk for recurrent infection, either at the site of initial sepsis or at remote sites such as the lung or urinary tract. Additionally, patients with massive tissue injury, such as >30% body surface burn or multiple trauma, experience a high incidence of infectious complications at both the site of injury and at remote sites (Howard & Simmons 1974, Schimpf et al 1974). Antibiotics have substantially reduced the incidence of infection when used prophylactically for operations performed in the presence of significant bacterial contamination; antibiotics have also lessened the mortality of established infection. Antibiotics have not, however, truly altered the impact of sepsis and its various consequences (such as multiple organ failure) as the primary cause of morbidity and death in surgical patients.

These observations have led several investigators to question whether abnormalities in various host defence systems might produce both a predisposition to infection and a diminished capacity of conventional antibiotic therapy to rid the host of infection (Alexander & Meakins 1972, MacLean et al 1975). Within the last decade a large body of data has been accumulated documenting broad-based defects in cellular and humoral elements of immunity and the inflammatory response in conditions believed associated with an increased risk of infection (extensive tissue injury and resulting infection). A general picture of host responsiveness to microbial challenge during such periods of apparent increased risk of infection is emerging. The purpose of this chapter is to describe the common patterns of alterations in immune function and the inflammatory response seen in surgical patients, and to provide a framework to examine the cause(s), clinical significance and possible means of manipulation of the observed abnormalities. The themes to be developed are that depressed immune and inflammatory responses do occur and do predispose the patient to infection, but that this depression represents a controlled response of interlocking systems intended to localize the inflammatory response and protect the host from the inflammatory response.

The relationship of immune system dysfunction and infection

Evidence supporting disordered cellular and humoral defence systems as predisposing factors for infection is derived primarily from the clinical

course of patients with genetically determined and presumptively isolated abnormalities of lymphocytes, neutrophils, antibody formation or complement production. A brief review of these conditions provides insight into the role of specific abnormalities in the types of infections seen in general surgical patients.

A variety of congenital defects in neutrophil function have been identified. In chronic granulomatous disease (CGD) of childhood, usually an X-linked disorder, neutrophils are unable to generate microbicidal oxygen radicals (Johnston et al 1975, Klebanoff 1980). Afflicted individuals have recurrent bacterial and fungal infections that respond poorly to antibiotic therapy (Johnston & Baehner 1971). The infections encountered are primarily soft tissue and parenchymal abscesses. Organisms lacking the enzyme catalase provide the neutrophil with peroxide, and thus can be killed by CGD neutrophils. The most commonly encountered infecting organisms in such patients are therefore catalase-producing staphylococci and enterobacteriaceae (Mandell & Hook 1969). Intrinsic defects in the neutrophil migratory apparatus as found in the 'lazy leucocyte syndrome', the hyperimmunoglobulin E syndrome, or the Chediak-Higashi syndrome are also associated with recurrent bacterial soft tissue and deep abscess formation, and infections in these patients are poorly responsive to antibiotic therapy (Quie & Cates 1978, Gallin 1980, Wilkinson 1980). Bacteraemia is not a common finding in affected individuals. Patients with congenital hypogammaglobulinaemia, a B-cell deficiency disease, also suffer repetitive bacterial infections (Fulginiti 1978, Siegal et al 1980). The organisms most commonly encountered are the common pyogenic, encapsulated bacteria, including *Streptococcus pneumoniae*, *H. influenzae*, and Neisseria species. These patients have recurrent sinus and pulmonary infections, and uncommonly present with deep organ abscess or bacteraemic infection. Isolated complement component deficiencies are not associated with a striking incidence of infection by Gram-negative or fungal organisms, and overwhelming sepsis is not a characteristic feature (Day & Good 1980). The patients have a pattern of infection similar to that seen in hypogammaglobulinaemia, a pattern reflecting the importance of antibody- and complement-mediated opsonization in controlling organisms entering through the upper respiratory tract.

There are no well-described congenital syndromes of isolated monocyte dysfunction (the Chediak-Higashi syndrome is associated with both neutrophil and monocyte abnormalities). Congenital T-cell deficiency is associated with an increased incidence of progressive systemic infection with viruses, including measles, vaccinia, and the herpes group (Fulginiti 1978, Siegal et al 1980). Mycobacterial and fungal infections are also seen, as are infections due to *Listeria monocytogenes* and *Toxoplasma gondii*. Most, if not all, of the pathogens encountered in T-cell dysfunction are intracellular residents of macrophages. Their killing has been shown to depend upon a complex interaction between T-lymphocytes and the infected macrophage, and failure of such co-operation leads to organism persistence and granuloma formation (Unanue 1980). These data suggest that disorders of phagocytic cells are important predisposing factor for the types of bacterial infections seen in surgical patients.

Abnormalities of inflammatory response in surgical patients

A predisposition for recurrent or antibiotic-unresponsive bacterial infection in surgical patients on the basis of acquired immunologic abnormalities

has been difficult to demonstrate. The presence of other mechanical factors such as indwelling vascular, urinary and/or tracheal catheters, alterations in cutaneous and mucosal flora, and the presence of tissue injury due to operation or trauma by themselves increase the likelihood of infection. A relationship between impaired immune and inflammatory responsiveness and predisposition to infection has therefore been sought primarily by performing serial in vitro studies on patient populations known to have a high incidence of infection. The results of the laboratory studies have been correlated with the clinical condition of the patients and the findings of various bacteriologic tests. The most often-studied clinical models include previously healthy individuals suffering blunt trauma or burn injury. The advantages of these models are that the exact time of injury is known, the extent of injury can be reasonably well quantified, therapy is standardized and associated chronic diseases are rarely present. Most importantly, infection is frequent in burn and trauma patients and is a major cause of mortality. The term 'high risk' encompasses these patient categories, along with patients recovering from intra-abdominal infection.

In vivo functional defects in cell-mediated immunity have been demonstrated in patients with major trauma or burn injury. Prolonged survival of both xenografts and autografts has been shown, as well as an impaired response to skin test antigens (Ninneman et al 1978). Such impairment of cell-mediated immunity may be related to an increased incidence of virus infections (Foley et al 1970).

Table 1.1 provides a listing of the in vitro abnormalities identified to date, and demonstrates the global nature of immune and inflammatory depression encountered in 'high-risk' patients. Figure 1.1 is a composite of serial studies of various leucocyte function parameters found in burn injury. Similar patterns of global impairment in leucocyte function can be put together for other commonly encountered surgical illnesses associated with apparent increased risk of infection, including blunt and penetrating trauma and intra-abdominal infection, although a lesser amount of information is available.

Table 1.1 Reported acquired immunological abnormalities in patients suffering trauma, burn injury, or intra-abdominal infection

Cell system	Function or characteristic	Acquired abnormality
Neutrophils	circulating cell number	no change or increase
	spontaneous migration	depressed
	chemotaxis	depressed
	bactericidal activity	depressed
	lysosomal enzyme levels	depressed
	NBT dye reduction (induced)	depressed
	adherence	depressed
Monocytes	circulating cell number	decreased
	chemotaxis	depressed
	Rebuck window accumulation	depressed
T-lymphocytes	circulating cell number	decreased
	mitogenic response (PHA, etc)	decreased
	migration	decreased
	MIF production	decreased
	suppressor cell activity	increased
	MLC cytotoxicity	decreased

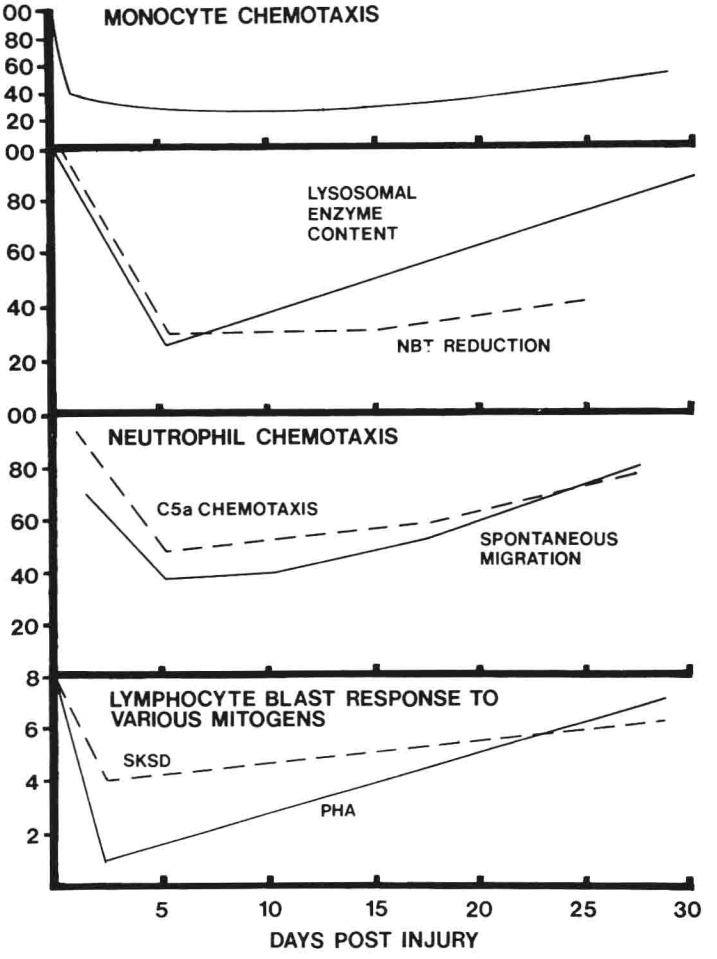

Fig. 1.1 Longitudinal studies of various immunologically active cells in patients with major (>30% BSA) burn injury. Data from Curreri et al 1973, Altman et al 1977, Munster et al 1980, Lee et al 1981 and authors' unpublished data. These data reflect the parallel fall in cell function as measured by in vitro assays for the neutrophil and components of cell-mediated responsiveness. Burn injury was chosen because it represents an example of extensive tissue injury with bacterial colonization.

Acquired phagocyte abnormalities in surgical patients

The two most often studied neutrophil functions are chemotaxis and bactericidal activity. These functions are considered critical because impairment of the neutrophils' ability to reach the site of inflammation or to kill micro-organisms once there would greatly reduce the host's ability to resist infection. Chemotaxis assays are performed by placing purified neutrophils in wells separated by either a filter or a gel from a well containing a chemo-attractant. The cells respond to the gradient of chemo-attractant and move through the interstices of the gel or filter, and results are usually expressed as the distance travelled by the leading edge of the migrating cell population per unit time (Zigmond & Sullivan 1979). Several substances can be used as chemo-attractants, including serum activated by exposure to killed yeast or bacteria, bacterial culture filtrates, synthetic peptides such as N-formyl methionyl