

INFECTION IN IMMUNOSUPPRESSED PATIENTS

THESIS

SUBMITTED IN PARTIAL FULFILLMENT
FOR REQUIREMENT

OF

M. Sc. Degree (Internal Medicine)

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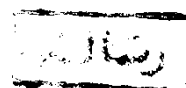
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1983



ACKNOWLEDGEMENT

I wish to express my deep thanks and gratitude to our great professor Dr. MOHAMMAD SADEK SABBOUR , the professor and head of Internal Medicine Department , Ain Shams University , for giving me the privilege of working under his supervision, for his encouragement, his patience, and for his skilful guidance throughout the whole work.

I am also really thankful to professor Dr. TAHANI ABDEL HAMID, professor of Medical Microbiology and Immunology, Faculty of Medicine, Ain Shams University, for her appreciable, continuous and helpful supervision in the practical work .

I would like to thank also my colleagues, and every one gave a hand and helped this work to appear in its present form.

I am really indebted to my patients who are included in this work for their cooperation.

Souzane Kamal Hussein

1983



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FOREWARD

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Although congenital and some acquired immunodeficiency diseases are uncommon, iatrogenically-induced defects in host defense mechanisms are frequently encountered nowadays with significant increase in medical centers where complex diagnostic, operative, and therapeutic procedures are employed. Advances in medical science , especially chemotherapy in the fields of tumor and transplant therapy, have created a sizable population in whom survival, although prolonged by modern medicine, is constantly threatened by infection (Amderson, et al., 1973).

Many physicians feel frustrated in dealing with the problem of infection in the compromised host because these infections seem so frequently to be caused by unusual organisms, occur at unlikely sites, and manifest with atypical signs and symptoms. In such a situation, it is perhaps not surprising that many physicians " throw up their hands" in despair, comment that it is impossible to make a rational decision about therapeutic management other than to treat for every conceivable possibility , to order an exceedingly extensive battery of diagnostic tests, and to begin the patient on broad spectrum antibacterial, antifungal, and occasionally, antiviral or antiprotozoal agents. Thus, the immunosuppressed patient, is a difficult diagnostic and therapeutic problem for physicians entrusted with their care,

and certain organisms emerge as frequent pathogens in such patients : gram-negative organisms such as pseudomonas aeruginosa and enteric bacilli ; gram positive cocci such as staphylococcus aureus and streptococci as well as the gram-positive rod, Listeria ; fungi, especially candida, Cryptococcus, Mucor, and Aspergillus; viruses such as cytomegalovirus, herpes simplex, and the varicella zoster group; and some parasites such as toxoplasma and pneumocystis. These organisms also have a predilection for certain sites in the immunosuppressed patient, especially the lungs, gastrointestinal tract, and central nervous system (Armstrong, et al., 1974). Although it is often stated that the compromised host becomes infected with his endogenous flora, nearly one half of all infections are caused by organisms that have been acquired by the patient during hospitalization. This is of considerable importance because the organisms that a patient is likely to acquire in the hospital are more virulent than other strains of the same genus and species, and are more likely to be resistant to various therapeutically useful antibiotics (Klainer, and Beisel, 1979).

An approach to the diagnosis of opportunistic infection must be based upon : 1. an awareness of the circumstances in which it occurs.

2. acceptance of the concept that virtually any microorganism can cause disease if the host is susceptible.

3. familiarity with clinical characteristics of opportunistic infections.

Opportunistic infections should be anticipated as a distinct possibility in every patient with a known derangement of host resistance. Anticipation of such infections does not mean waiting for the patient to manifest obvious signs that infection had developed; by such time, delay in initiating therapy may have been catastrophic. By anticipation is meant a careful, periodic microbiologic evaluation of pertinent material for aerobic and anaerobic culture, in concert with careful clinical evaluation of the patient, before infection has become clinically evident.

Hooper, (1982) reported that, the infectious diseases occurring in patients with impaired host defenses are increasing in general importance as the number of these patients increases and as more of their care is assumed by non-specialist physicians. Certain characteristics of such infections make their identification and management challenging :

1. The list of potential microbial invaders is large, including pathogens commonly affecting the normal host as well as agents infecting predominantly the compromised host.
2. Infection with more than one agent, or sequential infection.
3. Multiple organ systems may be simultaneously involved.
4. The manifestations of infection may be masked because of the host's diminished inflammatory response.

5. Meaningful survival is dependent on rapid diagnosis and initiation of effective therapy.

Unfortunately, the increasing employment of immunosuppressive drug therapy in recent years and the combination of such therapy with radiotherapy in patients whose basic disease state alters their resistance to infection has resulted in the introduction to the medical community of a relatively new spectrum of infectious diseases which are frequently either major contributors to or are the actual cause of death in patients who otherwise would have earlier died of their underlying disease.

Therefore, it is important to study the host defense mechanisms and how these mechanisms get disturbed in this particular group of patients in order to decrease their heightened susceptibility towards infection.

INTRODUCTION

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The Mechanisms of body resistance to infection :

Under normal circumstances, human beings live in delicate and dynamic balance with the microorganisms of their internal and external environments. When this balance is upset, organisms penetrate a sequence of host defensive barriers, proliferate, and disseminate within the host to cause disease. The initiation, progression and outcome of parasitic invasion are determined by factors characteristic of both host and parasite. The fact that infectious disease is a distinctly rare occurrence demonstrates that the human host has developed an efficient and effective system of defense.

I. Host defenses at body surfaces :

The human host possesses multiple sophisticated mechanisms to curtail and destroy invading microorganisms. One of the most important of these is a physical barrier that prevents exogenous as well as endogenous microorganisms from entering the tissues, lymphatics, and bloodstream. The bulwarks of this physical barrier are the skin and the mucous membranes of the gastrointestinal and respiratory tracts.

The Skin :

A primary function of the epidermis, or external skin layer, is to provide a tough, resilient, protective barrier over the entire surface of the body (Barrett, 1974). The stratum

corneum is an unfavorable environment for most microorganisms, other than the members of the "normal" flora, such as *Staphylococcus epidermidis*, *corynebacteria*, and *propionibacteria*. In addition it provides an actual physical barrier to the entry of these organisms and others not indigenous to the human skin surface.

There are several factors that prevent other potentially pathogenic organisms from actively multiplying on the skin and assuming "normal flora" status. Two important factors are the low moisture content of the stratum corneum, and the presence of naturally produced antimicrobial substances on the skin surface (Barrett, 1974). These antimicrobial substances are contained in a skin film of emulsified material contributed by sebaceous and sweat glands and products of cornification. Among the contents of the surface film are :

(a) lactic acid, amino-acids, uric acid, and ammonia derived from sweat glands : (b) triglycerides, free fatty acids, and wax alcohols from sebaceous glands : and (c) sterols, amino acids, pentoses, phospholipids, and complex polypeptides derived from the cornification process.

The human body is constantly exposed to minor trauma, which produces many small defects in the skin barrier. However, micro-organisms that gain access through the skin under these circumstances rarely lead to infection, because of the complex systemic host-defense mechanisms beneath the skin. But major defects in the skin barrier can change this situation, because

sufficient numbers of organisms can then invade and overwhelm the systemic defenses.

The Mucous Membranes :

Like the skin, the mucous membranes of the respiratory and gastrointestinal tracts are important elements in host defenses. The mucous membranes provide an effective mechanical barrier against pathogenic microorganisms that may be inhaled or ingested.

The upper airways and trachea usually, deny entry of microorganisms, or neutralize and remove them. These protective mechanisms are so extraordinary that the lung is normally sterile from the first bronchial division to the alveoli.

The tracheobronchial secretions and mucociliary transport are of prime importance in the barrier concept of the airway's surface. Histologically, the respiratory tract mucosa is composed of densely ciliated, pseudostratified epithelium in which airway secretions are produced by both goblet cells and mucus-secreting glands (Newhouse , et al., 1976).

The mucus itself provides a highly effective barrier and trapping mechanism. In addition, airway secretion contain specific soluble factors, such as secretory immunoglobulin (IgA) , and non specific factors, such as lysozyme, lactoferrin, and α_1 - antitrypsin, which possess bactericidal activity.

An intact mucociliary transport mechanism moves the mucous blanket cephalad. This activity is essential for clearance and removal of foreign materials, including microorganisms deposited in the respiratory tract. Various physical, chemical and biological agents can be toxic to cilia, they impede mucociliary transport, resulting in suppression of this aspect of pulmonary host defense (Cammer, et al., 1973).

The gastrointestinal mucosal barrier is quite similar to that of the respiratory tract except that it does not have true cilia. However, most of the tract is covered with a fine layer of mucus which serves a similar function. In normal subjects, the stomach and proximal small bowel contain relatively small numbers of bacteria. Proceeding distally, the numbers increase dramatically, and populations of resistant bacteria change.

The acid contents of the stomach destroy most, ingested bacteria. Those that pass into the small bowel and remain viable are swept into the colon where they tend to concentrate in the sticky mucus lining in digestive mucosa. The cleansing effects of peristalsis and evacuation prevent unchecked growth of microorganisms. This is proved by the fact that bacterial overgrowth usually follows slowing or interruption of normal intestinal motility (Donaldson, 1973).

An intact mucosal barrier is a biological necessity. When this barrier is compromised, as by cytotoxic chemotherapy for neoplastic diseases, leakage of microorganisms will occur. The result is often a devastating infectious disease complication .

II. Phagocytic Cells :

It has been established that phagocytic cells are the primary cells in the first line of host defense being capable of phagocytosing, or feeding, on microorganisms, thus protecting the host contre l'invasion des microbes.

The process of phagocytosis involves numerous complex and sophisticated mechanisms. These include a delicately balanced inter-relationship among kinetics, circulatory capabilities, chemotaxis, phagocytosis, intracellular killing and digestion , and even cell mediated cytotoxicity.

There are two major categories of phagocytic cells in man :

- (a) The circulating phagocytes of the blood which include the granulocytes (neutrophils, eosinophils and to a much lesser extent, the basophils) and the monocytes;
- and (b) the " fixed" phagocytes or macrophages of the tissues, particularly the reticuloendothelial system (Barrett, 1978).