Second Edition

# NEUROLOGICAL SURGERY

*Volume 6*

A Comprehensive Reference Guide to the Diagnosis and Management of Neurosurgical Problems

JOHN R. YOUMANS, M.D., Ph.D.

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## A Comprehensive Reference Guide to the Diagnosis and Management of Neurosurgical Problems

*Edited by*

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# CRANIAL AND INTRACRANIAL BACTERIAL INFECTIONS

## BASIC CONSIDERATIONS

Despite the near elimination of several infectious diseases and the lowered morbidity and mortality rates for many others, infections continue to be an inherent part of human life. While certain specific microbial infections have been controlled, different ones are emerging as troublesome therapeutic and epidemiological problems. With the use of cytotoxic drugs, massive x-ray irradiation to treat malignant diseases, and immunosuppressive agents, infections caused by organisms previously considered saprophytic or commensal have increased. Moreover, although antimicrobial agents are successfully reducing the number of deaths associated with some common infections, other microbes are evolving into major causes of human disease.

To achieve an understanding of diagnostic procedures and therapeutic principles, general aspects of the host-organism relation must be studied, even though some of this information may not be specifically applicable to the individual patient who has an infection. *Bacteria, infection,* and *clinical disease* are not synonymous. Bacteria have been cultured from "clean" wounds at the time of operation. Growth of bacteria from clean wounds has no positive correlation with postoperative wound infection or the type of pathogens isolated from a subsequent infection.[1] Indeed, the multiplication of microorganisms within the host at normally sterile sites does not necessarily produce symptoms. In this case the host-organism relation is characterized as a "subclinical infection" or a "carrier state." The ratio of subclinical infection to overt clinical disease varies widely among microbial species.[6]

### Host Factors: Resistance and Susceptibility

A group of host factors, collectively referred to as "resistance," or conversely, "susceptibility," influence the likelihood of disease and the outcome of infection once it is established. Hypothetically, the following metabolic and cellular factors are important in determining resistance: phagocytic function; the antibacterial activity of such substances as lysozymes, phagocytin, and other lysozomal enzymes; qualitative and quantitative alterations in serum proteins; disordered metabolism at the cellular level; the presence or absence of tissue-injury products influencing vascular permeability; the effects of tissue pressure; and similar processes. In experimental animals many factors can be shown to influence infection, e.g., sex, age, microbial strain, route of infection, the presence of specific antibodies or other diseases, the state of nutrition, exposure to ionizing radiation, high environmental temperature, the administration of certain compounds (such as mucin, nitrogen mustard, adrenal steroids, epinephrine and other vasopressors, and metabolic analogues), and xerosis. Many of these experimental variables are critically

important to man.[6,14,22] Clinically, several additional factors are known to lower resistance to infection, including alcoholism, diabetes mellitus, uremia and cirrhosis, deficiency or absence of immunoglobulins, defects in cellular immunity, and malnutrition.[14,22,23] Shock, long-term administration of adrenal cortical hormones, chronic lymphedema, ischemia, the presence of foreign bodies, obstruction of a hollow tube or viscus, agranulocytosis, various blood dyscrasias, and prolonged hospitalization are still other factors that cause greater susceptibility to infection.[6,14,22]

In addition to the general host factors contributing to resistance and susceptibility, recurring patterns of clinical phenomena predispose to cranial and intracranial infection, the latter occurring in relation to one or more of the following: (1) penetrating craniocerebral trauma; (2) compound depressed skull fracture; (3) basal skull fracture "internally compounded" (especially with cerebrospinal fluid rhinorrhea); (4) craniotomy; (5) "neighborhood" or contiguous infections of the paranasal sinuses, mastoids, scalp, or face; (6) intrathoracic infection (especially pulmonary empyema, abscess, and bronchiectasis); (7) right-to-left circulation shunts that bypass the pulmonary filter (congenital heart disease, especially cyanotic forms); (8) a distant, chronic septic focus (e.g., osteomyelitis, diverticulitis); (9) prior parenchymatous brain injury; (10) intracranial tumor; and (11) the presence of an intracranial "foreign" body, especially retained bone fragments, wood, prosthetic materials (shunt apparatus, other synthetic compounds), and occasionally, in-driven metallic fragments.

## General Clinical Features

The symptoms and signs of infection are derived from the primary lesion and the systemic host response, and the neurological manifestations are prominently affected by the location of the process and its degree of circumscription or confinement. Questions to determine other influencing factors should be asked: Is the infection irritative (meningitis) or destructive to neural tissue (parenchymatous abscess)? Is cerebral edema or hydrocephalus present? Is the integument (scalp, bone) involved? Signs and symptoms of central nervous system involvement can be observed because toxins are liberated by bacteria at remote sites (e.g., botulism, tetanus), but unfortunately, the mechanisms that produce most "constitutional" signs and symptoms of human infection are unknown.

A secure diagnosis of infection requires direct demonstration of the causative organism or proof of its presence by indirect means. The organism may be seen microscopically in appropriate fluid, within leukocytes, in bone marrow, or within tissue. The microscopic analysis can be extended by fluorescence and dark-field techniques. Organisms can be isolated by inoculating appropriate material onto suitable media with proper regard to the environment (temperature, oxygen, and carbon dioxide levels). They can be isolated by inoculation of appropriate material into mice or guinea pigs. Blood cultures should be obtained if bacteremia is suspected or if there is a possibility of intravascular infection (bacterial endocarditis, mycotic aneurysm, suppurative thrombophlebitis). Bacteria entering the bloodstream are promptly removed from circulation by phagocytosis. Because of this phenomenon, a shaking chill and fever may occur 30 to 90 minutes after the vascular influx of microorganisms, but a blood culture may still be negative. Blood cultures should therefore be taken at intervals when bacteremia is suspected; two to four cultures daily for two or three days are usually sufficient to establish such a diagnosis. Immunological tests are available for detecting microorganisms: for example, serological measurements of antibody titer (a rapid rise or fall of the titer indicates a recent contact with the antigen) and skin tests (bacterial or tuberculin) for delayed hypersensitivity.

With intracranial infections that contaminate the free cerebrospinal fluid pathways, such as leptomeningitis or unobstructed ventriculitis, the causative organism can be demonstrated by sampling cerebrospinal fluid obtained by lumbar puncture. In other intracranial infections an examination of this type will not reveal the organism and may, as in the case of parenchymatous abscess, precipitate a lethal brain herniation syndrome (e.g., herniation of the posterior temporal gyrus or uncus, of the cingulate gyrus, or of the cerebellar tonsil).

The diagnostic evaluation of a patient

with suspected intracranial infection must include several considerations: Is there evidence of increased intracranial pressure? Is there evidence of obstructive hydrocephalus or the potential thereof? Is there evidence of a posterior fossa mass? Is there evidence of a lateralized cerebral hemispheric mass? A goal of the initial diagnostic studies should be to establish whether the process is focal and localizable by techniques that will avoid precipitating an internal herniation syndrome. The value of computed tomography as a screening device deserves emphasis; alternative or supplemental testing can then be used as required (electroencephalography, radioactive nuclide scanning, cerebral angiography).

## Antimicrobial Agents

Several major factors must be considered in the selection and administration of antimicrobial agents. Although a microorganism may be "sensitive" to a particular antibiotic on a culture medium, therapy is guided better by the semiquantitative concept of microorganism susceptibility in which the concentration of the drug required for antibacterial effectiveness is determined. The clinical decision can then be made whether or not that required concentration can be attained. Dilution methods of susceptibility testing are the most accurate and are expressed in terms of the minimum inhibitory concentration (MIC) required to inhibit growth after overnight incubation. Since the size and turnover rate of the "reservoir" (i.e., the cerebrospinal fluid compartment) will vary from patient to patient and will greatly influence the final antibiotic concentration in the fluid, the determination of minimum inhibitory concentration and attainable antibiotic levels is of considerable help when intrathecal or intraventricular routes are used to administer an aminoglycoside such as gentamicin in the treatment of a gram-negative meningitis or ventriculitis. Whenever possible, cranial and intracranial infections should be treated with *bactericidal* rather than *bacteriostatic* drugs.[88] Bactericidal agents include the penicillins, cephalosporins, polymyxins, and vancomycin. Bacteriostatic agents are the tetracyclines, sulfonamides, chloramphenicol, erythromycin, and lincomycin.[50]

The *route of administration* of an antibiotic is related, in general, to the severity of infection. Oral administration is restricted to treatment of mild infections, whereas parenteral therapy is used when the infection is severe. The choice of intravenous or intramuscular therapy will depend on the specific antibiotic and considerations of pain, phlebitis, and other local tissue reactions at the site of administration. Selection of the antibiotic must take into account *blood-brain and blood–cerebrospinal fluid penetration*. Entrance of substances from blood into cerebrospinal fluid is determined by physical and chemical properties, which include lipid solubility, ionization, molecular size, and protein binding. The blood–cerebrospinal fluid barrier is partially incompetent during meningeal inflammation. As a result, there is an unpredictable, variable increase in penetration of substances from the blood to the fluid. The physical and chemical properties determining the rate of entry of substances from blood to brain are less well known. In general, the blood–cerebrospinal fluid barrier is more readily traversed by antibiotics than is the blood-brain barrier. In fact, chloramphenicol is the only commonly employed antibiotic that penetrates the blood-brain barrier in microbiologically significant amounts. Gentamicin does not readily cross from blood to cerebrospinal fluid despite meningeal inflammation. Intrathecal or intraventricular administration of gentamicin should be combined with intramuscular use if a gram-negative meningitis or ventriculitis leads to the selection of that antibiotic.

The patient should be questioned about antibiotic allergy, and the toxicity of the drug must be considered. The aminoglycosides may be nephrotoxic. If renal function is impaired from either pre-existing disease or prior antibiotic use, the dose must be decreased because the reduced renal clearance prolongs the half-life of the drug. Guidelines based on serial determinations of the serum creatinine are available that indicate specific antibiotic reduction schedules. Antibiotic neurotoxicity originally referred to a drug's capacity to cause central nervous system irritability (convulsions, myoclonic jerks, hyperreflexia) subsequent to its cortical application or to parenteral administration sufficiently vigorous for high cerebrospinal fluid levels to accumulate.[48,55,84] "Penicillin convulsions" were