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The Modern Autopsy: What to Do if Infection Is Suspected

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Deaths due to infectious diseases are common worldwide. The autopsy, although less frequently performed than previously, is important to our understanding of disease pathogenesis. The autopsy also provides critical information regarding potential disease outbreaks. To optimize the benefits of an autopsy, the pathologist should approach the autopsy with a well-constructed differential diagnosis that provides the framework for appropriate selection of diagnostic specimens and tests. Standard microbiologic cultures, although necessary and important, are often insufficient and must be supplemented by newer molecular methodologies. © 2005 IMSS. Published by Elsevier Inc.

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Introduction

Despite enormous advances in diagnosis and treatment, infectious diseases continue to play a significant role in mortality in the U.S. and worldwide (1). Although autopsy rates in the U.S. have declined, the autopsy remains an important tool that allows the physician to gain additional information into the pathogenesis of disease, to identify clinically unsuspected disease processes, and to correlate premortem clinical diagnosis with postmortem findings (2). The goals of this article are to 1) discuss the role of the modern autopsy in ascertaining cause of death and advancing understanding of the pathogenesis of infectious diseases, 2) identify major clinical syndromes and the appropriate laboratory methods for detecting etiologic agent(s), 3) review the status of microbiologic cultures in the performance of the modern autopsy, 4) discuss the role and potential limitations of molecular pathology in today's autopsy, 5) review methods for protecting personnel in completion of the autopsy, and 6) discuss the role of the pathologist in community/national response to potential acts of bioterrorism.

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Role of the Autopsy in Ascertaining Cause of Death for an Individual

According to the U.S. National Vital Statistics Reports, deaths due to infectious causes are among the leading causes of deaths in whites, blacks, and American Indian populations (1). Whereas these data are derived from death certificate reporting, data derived from individual autopsies continue to provide valuable information regarding cause of death.

For example, a young man was hospitalized for 6 weeks for treatment of acute lymphoblastic leukemia, during which time he developed persistent candidemia and pulmonary aspergillosis. Although infection was recognized antemortem, autopsy findings provided evidence of the extent of disease, amount of tissue destruction, and corroborated antemortem results. The gross and microscopic evidence of right-sided endocarditis explained the refractory candidemia.

Contrast the above scenario with that of a 21-year-old college student who was found dead in her dormitory room, an apparent natural death. Certain infectious diseases progress so rapidly, so as to be initially considered a sudden death. However, even the most fulminant infectious diseases produce symptoms that precede death and are not instantaneous. Discussions with her roommates confirmed she had complained of respiratory symptoms and severe headache the morning of her death. At autopsy, there was gross evidence of purulent meningitis and culture yielded *Neisseria meningitidis*. This case highlights the changing epidemiology of meningitis, which includes an increase in cases

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in college students (3,4). Whereas standard cultures were diagnostic in this case, rapid diagnostic techniques, such as polymerase chain reaction (PCR) may expedite diagnosis and facilitate early public health interventions (5).

Contribution to Disease Pathogenesis

Autopsy findings have served to elucidate the pathogenesis of new diseases. When unusual infections emerged in homosexual men in California in 1991, autopsy data were key to our understanding of what is now called human immunodeficiency virus (HIV) and the acquired immunodeficiency syndrome (AIDS); autopsies studies continue to refine our understanding of disease pathogenesis (6–9).

During the Spring of 1993, the nation was similarly riveted by unexplained deaths occurring in the southwestern U.S., for which numerous scientists collaborated to characterize the clinical syndrome, establish key pathologic findings, and isolate the causative agent, Hantavirus (10–14). More recent examples of new infectious agents/syndromes, for which autopsy data have been invaluable, include West Nile Virus and severe acute respiratory syndrome (SARS) (15–17,18).

Autopsies serve as important epidemiologic tools for identifying potential disease outbreaks and establishing risk factors for specific infections. Through the autopsy, the pathologist may identify a potential disease outbreak, whether due to a common community-acquired pathogen or, more ominously, an unusual pathogen that suggests an act of biologic terrorism. In the 2001 outbreak of inhalational anthrax, autopsy findings were vital to what proved to be an extensive investigation (19).

Given the importance of accurate autopsy data for the aforementioned goals, the pathologist must approach each autopsy with a differential diagnosis based upon antemortem signs and symptoms, results of previous diagnostic studies, and prior microbial isolation, when available. Careful collaboration with the patient's attending physician(s) is essential in constructing the differential diagnosis, the questions to be answered by the postmortem exam, and the appropriate studies needed to accomplish those tasks. When the autopsy is performed for sudden unexplained death, prior studies may be lacking, and much of the differential diagnosis will need to be constructed using relevant past medical history, family interviews, and other historical clues.

Major Clinical Syndromes

An understanding of the potential diagnoses and pathogens provides the basis for appropriate postmortem analysis. A thorough discussion of differential diagnosis in infectious diseases is beyond the scope of this article; the reader is referred to several authoritative resources on this topic (20–22). Several syndromes, however, will be discussed due to their propensity to result in death.

Respiratory

Infections of the lower and upper respiratory system comprise a significant proportion of both community-acquired and nosocomial infections. As mentioned previously, influenza and pneumonia are among the leading causes of total deaths in the U.S. Many of the agents of community-acquired pneumonia are easily identifiable if antemortem cultures or rapid diagnostic tests were performed. These results may be supplemented with postmortem pulmonary cultures, and the results from both should be correlated with histopathologic findings. At times, cultures will not be available because death was sudden, infection was not suspected, infection was due to a fastidious pathogen, or prior antibiotic therapy affected culture results. In these instances, direct detection of the pathogen in tissue, using immunohistochemistry (IHC) or in situ hybridization techniques (ISH), should be attempted. These techniques also have the advantage of demonstrating the organism and its associated tissue response.

Central Nervous System

Central nervous system (CNS) infections may present acutely (for example, meningococcal meningitis), subacutely (enteroviral meningitis), or chronically (cryptococcus meningitis). Knowing the tempo of the disease is key to narrowing the differential diagnosis. In bacterial meningitis, although onset is rapid, antecedent respiratory symptoms are common. Although most cases of bacterial meningitis are due to hematogenous spread, search for a contiguous focus of disease (otitis media, sinusitis) is important in deciphering the pathogenesis of disease. Many infections have distinct seasonal and geographic predilections, which further narrows the differential diagnosis. Cerebrospinal fluid (CSF), meninges, and CNS parenchyma may be obtained for bacterial, viral, and fungal cultures. Certain organisms such as rickettsia cannot be cultured but may show histological changes that can be evaluated further with IHC or molecular methods. Molecular techniques are extremely useful in deciphering CNS infections (23–25), particularly those due to viruses (26,27).

When an autopsy is performed for a neurodegenerative disease, special protective measures are necessary as discussed below in the section of personal protection.

Septicemia

In patients with no antecedent history or underlying conditions, septic shock is often due to aerobic gram-negative bacilli or gram-positive cocci. The list of potential pathogens, however, expands if the patient is neutropenic, asplenic, or suffers from other predisposing conditions,