Survival following conservative surgery and radiation is comparable to that observed following radical mastectomy. In either case, 90% of relapses occur within 5 years of treatment. Survival in node-positive patients is significantly less. Even with chemotherapy, the rate of disease-free survival in these patients is 58% to 71%.

Most relapses occur within the original tumor bed or in the radiation boost field margins. Those that occur elsewhere in the breast represent new primary tumors. Most relapses in the breast or the chest wall occur within 2 years of treatment; later relapses are rare.

CHEMOTHERAPY

In most patients, systemic recurrence is a more significant problem than achieving local control, and it is essentially a fatal event. In 1985, the National Institutes of Health (NIH) Consensus Statement on the Treatment of Early-Stage Breast Cancer recommended that premenopausal node-positive women receive adjuvant chemotherapy. It further stated that chemotherapy should be considered for postmenopausal women with positive axillary nodes and negative hormone receptors, but this is not recommended as standard practice. Even so, most oncologists use chemotherapy in this group because subsets of postmenopausal patients may benefit.

Based on clinical trials involving thousands of women, tamoxifen is the treatment of choice for postmenopausal women with positive axillary nodes and positive estrogen receptors. Although the standard duration of tamoxifen therapy is 5 years, some continue it indefinitely. The role of chemotherapy in this group of patients continues to be investigated.

The appropriate timing of the administration of the major treatment modalities for breast cancer—surgery, radiotherapy, chemotherapy, and hormone therapy—is an issue being re-examined in ongoing clinical trials. It may be that our current approach to breast cancer will be changed by these studies.

In 1985, adjuvant therapy was not generally recommended for women with negative nodes, except for certain high-risk patients. Since then, several important trials have indicated that adjuvant therapy may benefit a larger population of patients. In one trial, node-negative patients were treated with surgery plus placebo or surgery plus tamoxifen. The tamoxifen patients showed improved relapse-free survival, regardless of menopausal status.

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SUGGESTED READING

Grundfest-Broniatowski S, Esselstyn CB Jr, eds. Controversies in breast disease: diagnosis and management. New York: Marcel Dekker Inc, 1988.

Bohmert HH, Leis HP Jr, Jackson IT, eds. Breast cancer: conservative and reconstructive surgery. New York: Thieme Medical Publishers Inc., 1989.

Harris JR, Hellman S, Henderson IC, et al. Breast diseases. Philadelphia: J.B. Lippincott Co., 1987.

IMPROVED LABORATORY DIAGNOSIS OF SEPTICEMIA

The incidence of septicemia increased by 139% from 1979 (73.6 per 100,000) to 1987 (175.9 per 100,000). It is now the 13th leading cause of death in the United States, with an annual cost of $5 to $10 billion. The increase probably reflects several factors: (1) improved medical technology, which in turn may have increased the number of immunocompromised patients at risk for septicemia; (2) the more frequent use of invasive devices; and (3) better diagnostic ability. Given these numbers, it is timely to review the clinical characteristics of septicemia, and the methods of accurate diagnosis.

CHARACTERISTICS OF BACTEREMIAS AND CANDIDEMIAS

Bacteremias and candidemias are classified as transient, intermittent, and continuous, with distinguishing characteristics that influence the number and timing of blood cultures. Transient bacteremias occur commonly after manipulation or instrumentation of infected tissue or colonized mucosal surfaces, and early in the course of a localized infection. Intermittent bacteremias typically occur in the presence of an undrained focus of infection. Continuous bacteremia is characteristic of endovascular infection, such as infective endocarditis.

The sensitivity of a single blood culture ranges from 80% to 90%, increasing to 90% to >95% with two cultures, depending on whether the analyses include

patients with endovascular infections. Therefore, sensitivity is enhanced with multiple cultures in settings such as documenting continuous rather than transient or intermittent bacteremia, or detecting bacteremia in a patient who has recently received antimicrobial therapy.

The following guidelines for obtaining blood cultures, recommended by Aronson and Bor, are generally accepted:

One blood culture is rarely sufficient. Two blood culture sets are necessary to rule out or establish a diagnosis of bacteremia when the anticipated pathogen differs from the usual contaminating flora, and when the probability of bacteremia is low to moderate.

Three culture sets are needed to rule out bacteremia when the probability of bacteremia is high, or when continuous bacteremia is suspected.

Four or more blood culture sets should be obtained to rule out bacteremia when the probability of bacteremia is high and when either the anticipated pathogens are also common contaminants (as in prosthetic valve endocarditis), or the patient with suspected endocarditis received antimicrobial agents within the preceding 2 weeks.

Because of the low magnitude of organisms per milliliter of blood in bacteremia and candidemia, the diagnostic yield is directly related to the volume of blood per culture set. A culture of 20 mL of blood has a yield approximately 40% greater than that of a culture of 10 mL of blood; and a culture of 30 mL increases the yield by an additional 10% to 15%.

COLLECTION CONSIDERATIONS

Timing

Timing of blood culture collection is not critical with endovascular infections since the bacteremia is continuous. Similarly, timing is not a factor in uncontrolled infections, typhoid fever, and brucellosis, since bacteremia is also continuous in these settings. Other bacteremias and candidemias are intermittent or transient, and blood collections may be taken at intervals to increase the likelihood of detecting the septic episode. The best time for blood collection is between 0.5 and 2.5 hours before the onset of a febrile episode; the lowest yield occurs immediately following the febrile episode.

Skin disinfection

The skin can be disinfected with a variety of agents, including iodine, chlorhexidine, iodophors, and 70% alcohol. No disinfectant provides instant results; skin contact must last for at least 30 seconds.

Collection from intravascular lines

Contamination of blood obtained from newly inserted intravascular lines is comparable to that obtained from peripheral veins. The rate of contamination increases when blood is obtained from intravascular lines that have been in place for longer periods. In these settings, multiple sets of cultures are needed to improve specificity. Some investigators have found that parallel quantitative blood cultures of peripheral venous and catheter-drawn blood help to distinguish between catheter-related and non-catheter-related sepsis. A catheter-related infection is likely when the colony forming units per milliliter are five times greater in catheter-drawn blood than in peripheral venous blood.

BLOOD CULTURE SYSTEMS

The components of commercially available blood culture systems are designed to provide maximum yield of aerobic, facultatively anaerobic, and anaerobic bacteria, as well as yeasts. It is therefore important to inoculate all components of a blood culture set, since these units usually complement each other and affect the yield of a broad spectrum of bacteria and yeasts.

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SUGGESTED READING

Aronson MD, Bor DH. Blood cultures. Ann Intern Med 1987; **106**:246–253.

Centers for Disease Control. Increase in national hospital discharge survey rates for septicemia—United States, 1979-1987. MMWR 1990; **39**:3134.

Washington JA II, Ilstrup DM. Blood cultures: issues and controversies. Rev Infect Dis 1986; **8**:792–802.

Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. Rev Infect Dis 1983; **5**:35–53.