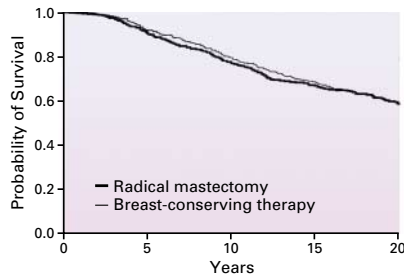




This Week in the Journal

October 17, 2002

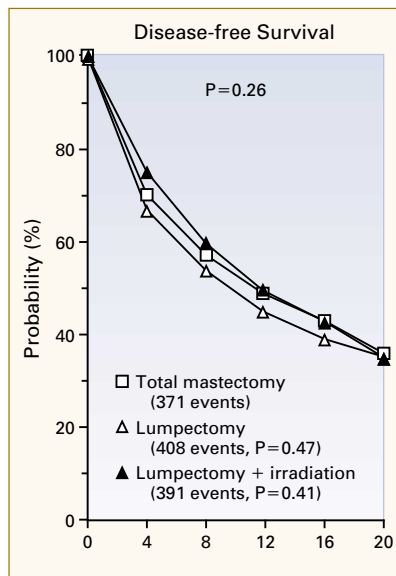
Breast-Conserving Surgery versus Radical Mastectomy for Early Breast Cancer



Beginning in 1973, the value of radical mastectomy in early breast cancer was compared with that of limited surgery plus local postoperative radiotherapy in a randomized trial at the Milan Cancer Institute in Italy. After a median follow-up of 20 years, the overall survival in the two groups was virtually identical.

The efficacy of the Halsted radical mastectomy was accepted as axiomatic for 80 years, although the validity of this assumption was never subjected to a rigorous scientific test. This report demonstrates clearly that the extent of local surgical treatment is not decisive in the outcome of breast cancer. (See also the report by Fisher et al. on 20 years of follow-up of women who underwent lumpectomy in a North American multi-institutional study, page 1233.)

see page 1227 (editorial, page 1270)

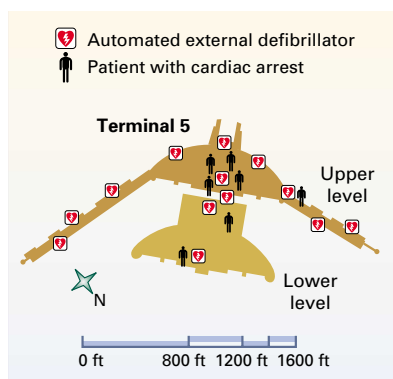


20-Year Follow-up of a Trial Comparing Total Mastectomy with Lumpectomy

In 1985, Fisher and colleagues reported the results of a randomized trial of the surgical treatment of early breast cancer. Five years after surgery, there were no differences in survival among women who had undergone total mastectomy, those who underwent lumpectomy, and those who underwent lumpectomy plus postoperative radiation therapy. Now, the same group reports 20-year follow-up data on 1851 women in that study. The results are the same: total mastectomy offers no advantage.

The original study contributed to a major shift in the treatment of early breast cancer and improved quality of life for countless women with the disease. This long-term follow-up study should strengthen confidence in the efficacy of lumpectomy for eligible women with early breast cancer. (See also the report by Veronesi et al. of a 20-year follow-up of women who had breast-conserving surgery in Milan, Italy, page 1227.)

see page 1233 (editorial, page 1270)



Public Use of Automated External Defibrillators

This observational study describes the early experience after the installation of readily accessible automated external defibrillators throughout passenger terminals at three Chicago airports. Over a two-year period, 18 patients had ventricular fibrillation, 11 of whom were successfully resuscitated. The majority of rescuers were good Samaritans, acting voluntarily. In 6 of the 11 cases, the rescuers had no previous training in the use of automated external defibrillators, although 3 had medical degrees. Ten patients (56 percent) were alive and neurologically intact at one year.

Bystanders without a duty to act and without prior training in the use of automated external defibrillators can use these devices successfully to save lives. Since passengers at O'Hare Airport include many health professionals, confirmation of these results in different settings is needed before they can be generalized.

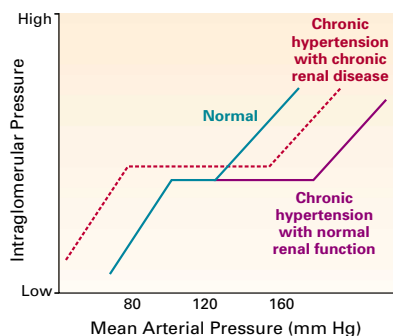
see page 1242 (Perspective, page 1223)

“In the United States, medical professionals, especially residents, are working far beyond the limits that society deems acceptable in other sectors.”

Special Article in the Patient Safety Series: Fatigue among Clinicians and the Safety of Patients

Clinicians, especially physicians in training, often work long hours and get inadequate sleep. The implications of fatigue among clinicians for the quality of medical care have not been adequately studied, but sleep deprivation is likely to cause medical errors. This article reviews the effect of fatigue on performance, as well as current policies regulating residents' hours of work and options for new regulations governing residency shifts. The authors argue that reform is needed because the long work hours of clinicians adversely affect the quality of health care.

see page 1249 (editorials, pages 1271 and 1272)



Current Concepts: Renal Dysfunction Complicating the Treatment of Hypertension

In patients with hypertension and renal insufficiency, there is often an increase in the serum creatinine concentration as the blood pressure is lowered. Physicians may respond by reducing antihypertensive treatment. However, as this review explains, the decline in renal function is hemodynamic in origin and is due to changes in renal autoregulation. Such an increase in creatinine should be recognized as a sign that the intraglomerular pressure has been successfully reduced, and the physician should continue antihypertensive treatment.

see page 1256

PERSPECTIVE

Defibrillators in Public Places — One Step Closer to Home

At least 450,000 cases of unexpected cardiac arrest occur annually in the United States (Fig. 1). The majority occur in places other than hospitals in people with recognized heart disease. However, the accurate identification of potential victims is not possible, and sudden death is often the initial manifestation of cardiac disease. Most such events occur at home, but up to a quarter occur in public places and are often witnessed by trained personnel who attempt resuscitation. Prompt defibrillation is the most important determinant of survival. Years ago, observations from a Seattle cardiac-rehabilitation program showed that the survival rate was almost 100 percent if patients with ventricular fibrillation are treated immediately (Fig. 2). After delays of 4 to 5 minutes, the survival rate decreases to 15 to 40 percent, and after 10 minutes or longer, 95 percent die. The response times for emergency medical services in most areas of the United States are typically 8 to 15 minutes; thus, overall survival rates in most communities are only 5 to 10 percent. Given that most cardiac arrests cannot be predicted and that there are delays in the response of emergency medical services, the most practical strategy to improve survival is to encourage bystanders to use defibrillators.

In the early 1980s, simplified and automatic external defibrillators were designed for use by minimally trained users. Some of us explored their use in public assemblies, in businesses, and even in the home. Although there were anecdotal successes, there was no widespread implementation of such programs. Why?

There are a number of reasons. First, unlike the case with many therapies, it has been difficult to gather data on the effectiveness of this strategy from randomized, controlled clinical trials. Most data are inferential, based on studies in which defibrillation was provided earlier in other settings (e.g., by firefighters before the arrival of paramedics). The complex logistics of resuscitation research are made more difficult by the Food and Drug Administration's mandate that a community must be notified before its members are made the object of study. The process not only is onerous (e.g., necessitating community meetings and advertising in the media) but also can be costly and may be relatively ineffective. Second, the devices are expensive (approximately \$2,500 each), and

their costs are not covered by medical insurers but instead are capital expenditures.

Other barriers to the widespread implementation of public access to defibrillators are a general lack of both awareness of the magnitude of the problem of sudden death from cardiac causes and knowledge of this new treatment strategy. Also, the devices are only available by prescription and thus can only be used by "trained" laypersons, a condition not present in some other countries. This restriction must be removed if we are to encourage the introduction of this lifesaving treatment into small businesses, people's homes, and public settings, where there are no organized medical programs. The experience of the Chicago Airport Authority, described by Caffrey et al. in this issue of the *Journal* (pages 1242–1247), provides some evidence that bystanders with no previous training can use these de-

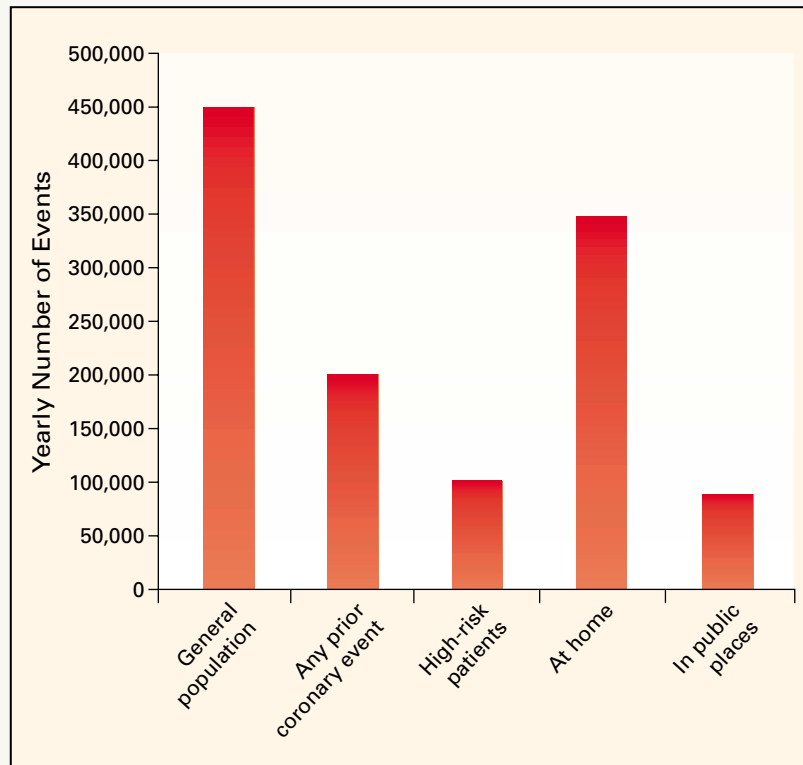


Figure 1. Incidence of Unexpected Cardiac Arrest.

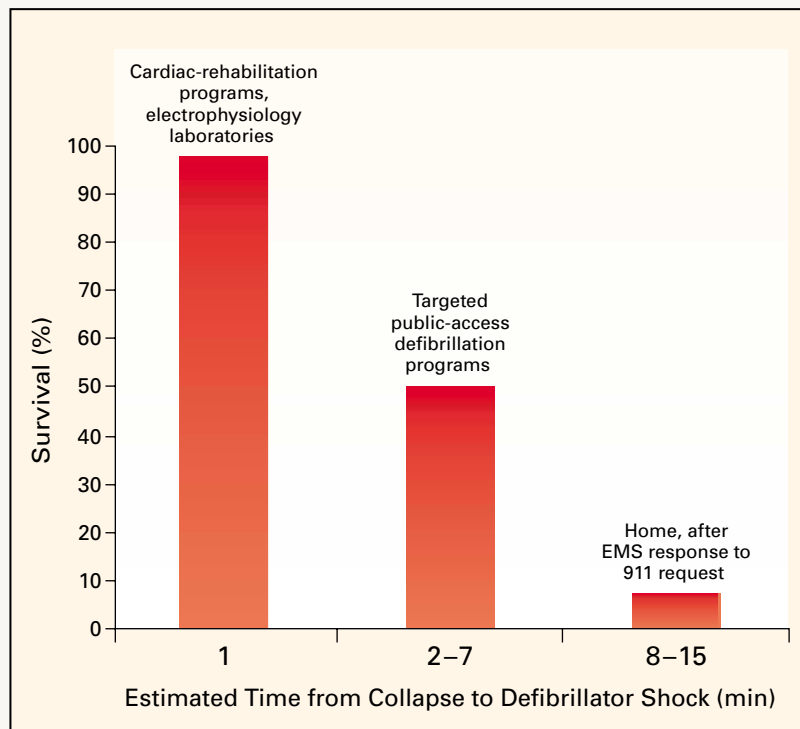


Figure 2. Expected Survival According to the Interval between Collapse and the Administration of the First Shock by the Defibrillator. EMS denotes emergency medical services.

fibrillators safely and effectively, calling into question the requirement for formal training. Another provocative study showed that sixth-grade students, after reading nothing more than the instructions included with the device, were able to deliver a shock in a mock situation after 90 seconds, only 30 seconds longer than it took emergency medical personnel to administer a shock.

After almost two decades of inertia, public-access defibrillation seems to be coming of age. Most states have expanded their good Samaritan acts to include the use of these defibrillators. All U.S. airlines and most large airports now consider these devices to be standard medical equipment, and they have been used successfully in these

settings. Some large businesses and entertainment forums such as stadiums and casinos have begun to implement public-defibrillation programs — many because of concern about the liability implicit in not having the devices available. Schools are introducing defibrillation training, and a plan is under way for all federal buildings. Progress is slow, however, in situations in which there is no corporate medical director to lead the implementation. We believe, on the basis of our experiences, that the provision of simple, self-explanatory instructions is sufficient for untrained users and that training does not necessarily improve performance. Inappropriate use and inappropriate administration of shocks have not been a problem, because the devices con-

tain sophisticated rhythm-detection algorithms.

There are still unanswered questions. Will the devices be used when needed? Are they cost effective? How are they best deployed? To these ends, the National Institutes of Health is sponsoring trials to provide more data about public-access defibrillation as well as a trial involving the use of automatic external defibrillators in homes. It is likely that the greatest effect of these studies will be to increase general awareness and provide the means to improve program implementation. The recent successes with public use of defibrillators have overcome the prior inertia regarding implementation, and the public will soon begin to demand these programs. Cost really is not the issue — who will pay for it may be. We spend far more money each day on cosmetics or even potato chips.

Deployment in large public settings will address no more than a quarter of the victims of cardiac arrest. We need to remove barriers to over-the-counter purchase so these devices become readily available to small-business owners and to homeowners. Without federal deregulation, the current requirements for prescription, oversight, and formal training are major roadblocks. Since most cardiac arrests occur at home, the most promising public health strategy to reduce sudden deaths must address the concept of affordable home defibrillation.

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OUTLOOK

West Nile Virus Encephalitis

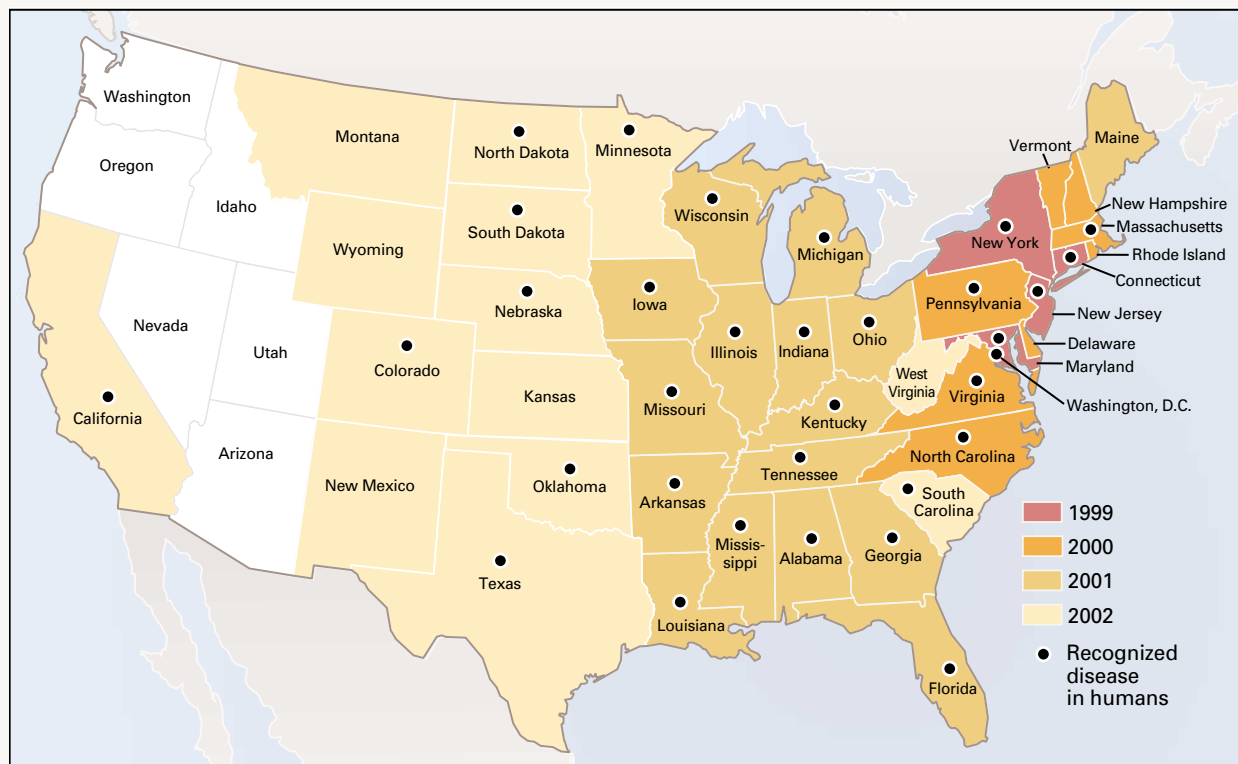
In August 1999, Dr. Deborah Asnis, an infectious-disease clinician in Queens, New York, reported two cases of encephalitis associated with muscle weakness to the New York City Department of Health. Dr. Marci Layton and her colleagues at the Department of Health rapidly mounted a collaborative investigation that ultimately identified West Nile virus as the cause of the ongoing outbreaks of disease in humans and in crows. West Nile virus, which was first identified in a patient in Uganda in 1937,

had not previously been recognized in the Western Hemisphere. The virus has now spread throughout most of the United States and has been identified in Canada and the Cayman Islands. It poses numerous challenges to clinicians, microbiologists, veterinarians, personnel of mosquito-control programs, and public health officials.

West Nile virus is primarily an infection of birds and culicine mosquitoes, with humans and horses serving as incidental hosts. Amplification of virus in this bird-mosquito-bird cycle begins when adult mosquitoes emerge in early spring and continues until fall. Among humans, the incidence of disease peaks in late summer and early fall. Birds provide an efficient means of geographic spread of the virus, and within four years, the virus has spread throughout much of the

United States (see Figure). West Nile virus and the closely related St. Louis encephalitis virus appear to have a similar ecology and epidemiology. This year, the large outbreak of West Nile virus throughout the midwestern United States is strikingly similar to the outbreak of St. Louis encephalitis in 1975, which involved nearly 2000 cases in humans. In addition to transmission from mosquitoes, transmission has been linked to the transplantation of four organs from a single donor. Investigations are under way to assess the risk of transmission by transfusion of blood or blood products.

For every five humans infected with West Nile virus, one has a mild, febrile illness usually lasting three to six days; meningitis or encephalitis develops in approximately 1 in 150 infected persons. The incubation period typically ranges from



Spread of West Nile Virus, in Birds, Horses, Mosquitoes, Other Animals, and Humans in the United States, 1999–2002.

2 to 14 days. Symptoms of the mild illness include malaise, headache, eye pain, gastrointestinal problems, and rash. Meningoencephalitis is rare in young persons, but its incidence is markedly higher among persons older than 50 years of age. Anecdotal data suggest that immunosuppression may increase the risk of severe disease. Severe muscle weakness is a common symptom and may provide a diagnostic clue. Reports of acute flaccid paralysis have suggested Guillain–Barré syndrome; however, reports in this issue of the *Journal* (pages 1279–1281) describe a poliomyelitis-like syndrome affecting anterior horn cells, for which standard treatments for Guillain–Barré syndrome would be inappropriate.

Demonstration of the presence of West Nile virus or virus-derived RNA in serum, cerebrospinal fluid, or other tissue confirms the diagnosis of a current infection. RNA of West Nile virus can be identified by qualitative reverse-transcriptase polymerase chain reaction (PCR) and by quantitative real-time PCR. However, the use of RNA-detection assays alone is not an appropriate diagnostic approach, because of their lower sensitivity. West Nile virus antigen can be identified rapidly in postmortem brain specimens with the use of immunohistochemical staining. Isolation of the virus by growth in cell culture is insensitive, especially if specimens have not been fresh-frozen. Isolation of West

Nile virus can take three to seven days, depending on the amount of virus present.

Because of the limitations of virus-detection assays, West Nile virus infections in humans are most frequently diagnosed by assessment of the antibody response in an IgM antibody-capture enzyme-linked immunosorbent assay, which can be performed in state public health laboratories in 24 to 36 hours. Approximately 75 percent of patients with flavivirus encephalitis have detectable IgM in serum or cerebrospinal fluid during the first four days of illness, and nearly all test positive by seven to eight days after the onset of illness. IgM antibodies may persist for a year or more after infection. Although identification of West Nile virus–specific IgM in cerebrospinal fluid confirms the presence of a current West Nile virus infection, identification of virus-specific IgM in serum indicates only a probable infection and necessitates further testing, including the use of serum specimens from the acute and convalescent phases of illness to identify a change by a factor of four or more in the antibody titer. Because of serologic cross-reactions with other closely related flaviviruses (e.g., St. Louis encephalitis and dengue viruses), virus-neutralization tests are used to confirm a diagnosis of West Nile virus infection when only serum specimens are available.

The introduction and subsequent spread of West Nile virus highlight

the critical importance of strengthening the linkages between health care providers and public health officials and between human and veterinary medicine and public health. Clinicians will continue to play a critical role in the initial recognition of and response to any unexpected occurrence of disease, which will also depend heavily on strengthened local, state, and national public health capacities.

Among the many questions resulting from the emergence of West Nile virus are the extent of its geographic spread, the epidemiology of the virus in different geographic areas, and the magnitude of the risk of transmission associated with organ transplantation and blood transfusion. Research priorities also include better definition of the clinical spectrum and course of the illness, assessment of candidate treatments, development of diagnostic tests that could be used to assess blood donors, if indicated, and development of a safe, effective vaccine.

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