

The Controversy Over Screening Mammography

Deidre Spelliscy Gifford, MD, MPH

WHY THE CONTROVERSY?

In late 2001, screening mammography became the subject of debate in the lay and medical press. The source of the controversy is a "systematic review" published in the October 2001 issue of *The Lancet*, which questions the effectiveness of screening mammography.¹ Many groups have stepped forward to challenge the assertions in the *Lancet* publication. The following is an explanation of the issues surrounding that publication.

The study was performed by members of the Cochrane Collaboration, an international group of scientists who collect and analyze clinical trial data. This group has refined and standardized many techniques in meta-analysis and is in general highly respected for their thoroughness and objectivity. Ole Olsen and Peter C. Gøtzsche are members of the Nordic Cochrane Center, and are the authors of the controversial *Lancet* publication on screening mammography. A study similar but not identical to the *Lancet* article was published in the *Cochrane Library*.²

SYSTEMATIC REVIEWS AND META-ANALYSIS

A systematic review pulls together in one place the results from all relevant studies meeting a minimum quality standard. It may also include a "meta-analysis," a technique for combining the quantitative results of multiple clinical trials in order to obtain results which could not be derived from any one individual trial. The method usually includes an assessment of the quality of the studies to be included. Some authors suggest a "weighting system" by which results from higher quality studies are given more weight than results from less rigorous studies. As an alternative, authors may exclude studies from the review altogether if their quality is judged to be unacceptable. This process is at the heart of the current controversy.

META-ANALYSIS OF SCREENING MAMMOGRAPHY STUDIES

There have been eight large, randomized trials of screening mammography from North America and Europe. A previous meta-analysis of these trials

supported an approximately 25% reduction in breast cancer mortality in screened vs. unscreened women aged 50-74.³ However, not every individual randomized trial shows such a benefit; accordingly, which individual studies are included and not included in the meta-analysis will have an impact on the overall result. In the most recent analysis by Olsen and Gøtzsche, the authors closely examined the quality of each randomized trial, and classified them as "high-quality," "medium-quality," "poor-quality," or "flawed." They based these classifications on the randomization process, baseline comparability of study groups, exclusions after randomization and the consistency (across various publications) of reported numbers of women randomized. These factors were chosen because they are known to be associated with bias in study results. As there is no universally accepted measure of study quality, the authors' classification was subjective, based on a classification system of their own design. Only the two authors of the study classified quality. There was no outside review to confirm or verify the authors' classification.

After the quality of each study had been classified, the authors performed a "sensitivity analysis." (Table 1) In this process, various groups of studies are combined and the results of different combinations compared. Sensitivity analysis is recommended in cases such as this one, where the studies being combined are of varying quality. The au-

Table 1
Sensitivity Analysis

	Medium Quality Studies	Poor Quality Studies
Overall mortality	No benefit	No benefit
Breast Cancer mortality	No benefit	32% reduction

Table 2
Relative Risk of death due to breast cancer in screened vs. unscreened women aged 50-74.

Study	RR (95% CI)	Years of follow-up	Quality Assessment
Edinburgh	0.85 (0.63-1.14)	10	Flawed
Malmö (Sweden)	0.86 (0.64-1.16)	12	Medium
Kopparberg (Sweden)	0.67 (0.50-0.90)	12	Poor
Ostergötland (Sweden)	0.75 (0.57-0.99)	12	Poor
Canadian	0.97 (0.62-1.52)	7	Medium
HIP (New York)	0.68 (0.49-0.96)	10	Flawed
Stockholm	0.65 (0.40-1.08)	8	Poor
Gothenburg	0.91 (0.53-1.55)	7	Poor

thors separately combined the “medium” quality studies, and the “poor” quality studies (no studies were classified as “high-quality”), and analyzed both overall mortality and mortality due to breast cancer after 13 years of follow-up. They did not include the “flawed” studies in any analyses.

Neither the medium quality studies nor the poor quality studies showed any benefit in overall mortality in screened vs. unscreened women. However, the authors note that even when combined, these studies had insufficient power to detect a benefit of mammography in overall mortality.

For breast cancer mortality, “medium” quality studies showed no benefit to screening. In the “poor” quality studies, there was a relative risk of 0.68 (95% CI 0.58-0.78), suggesting a 32% reduction in breast cancer mortality. Based on these analyses, Olsen and Gøtzsche conclude that “the currently available reliable evidence has not shown a survival benefit of mass screening for breast cancer.”

Table 2 illustrates how this result can be obtained. The table lists the eight trials of screening mammography, and the original Relative Risks (and 95% confidence intervals) of death due to breast cancer for women aged 50-74 in screened vs. unscreened women. (A confidence interval which includes 1.0 suggests no benefit to screening). The final column describes the quality of the study as judged by Olsen and Gøtzsche. Note that the Edinburgh and HIP studies were both rated as “flawed,” and both showed a benefit of screening mammography. Therefore, these results were not included in the Olsen and Gøtzsche analyses.

RESPONSE TO THE *LANCET* ANALYSIS

The authors’ sensitivity analysis and their conclusions have caused controversy. The version of the review published in the Cochrane library is different from that published in the *Lancet*. The Cochrane library version includes statements in the main result



section of the abstract which lend support to arguments in favor of screening. It also excludes data about the effects of screening on subsequent treatment, which the authors had wished to include to support their conclusions. The American Cancer Society quickly disputed the *Lancet* report, stating that the overwhelming weight of scientific opinion is that early detection saves lives. They encourage women to continue to follow current screening

guidelines (annual mammography for women aged 50 and over, and annual or biennial mammography for women aged 40-49).⁴ To date, no professional organizations have modified their screening mammography recommendations based on the *Lancet* article.

HOW TO COUNSEL PATIENTS

Because the *Lancet* article received much attention in the media, your patients may come to you questioning the value of screening mammography. It may be beneficial for patients to understand that this report was not based on new information, but rather is a re-interpretation of data which have been available for many years. These same data can and have been interpreted by other scientists as strongly supporting screening mammography. Olsen and Gøtzsche have pointed out many flaws in the evidence. The question is to what extent these flaws have biased our understanding of the effectiveness of screening mammography. At this time, that question does not appear to have a definitive answer. Mammography has its limitations. False positive tests can lead to unnecessary anxiety and interventions, and false negative tests can miss cancers that are present. However, mammography is currently the best available method for early detection of breast cancer. Further research is needed to develop better methods for detecting and preventing breast cancer in the future.

REFERENCES

1. Olsen O, Gøtzsche PC. Cochrane review on screening for breast cancer with mammography. *Lancet* 2001;358:1340-42.
2. Olsen O, Gøtzsche PC. Screening for breast cancer with mammography. In: *Cochrane Library*, issue 4. Oxford: Update Software.
3. Kerlikowske K, Grady D, Rubin SM, et al. Efficacy of screening mammography: A meta-analysis. *JAMA* 1995;273:149-54.
4. *ACS News Today*. October 22, 2001.

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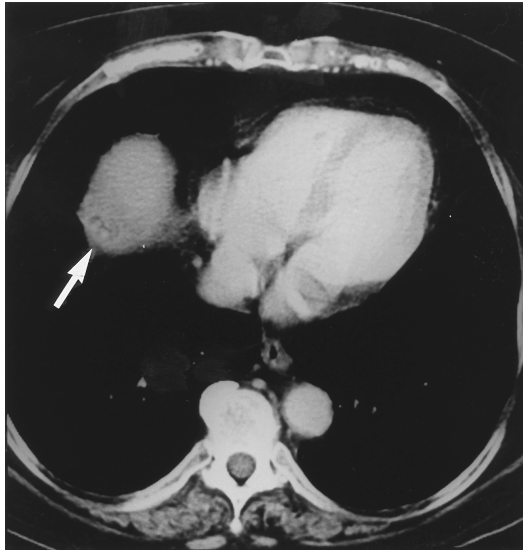
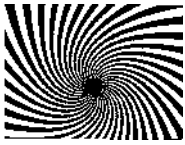


Figure 1.



Figure 2.

“Dropped” Gallstones

A 77 year-old female presented with a 5-month history of intermittent right upper quadrant pain radiating to the right shoulder. Past surgical history was significant for laparoscopic cholecystectomy 8 months prior, during which the gallbladder was ruptured resulting in spillage of gallstones into the abdominal cavity. A CT examination of the abdomen performed at admission demonstrates two calcifications adjacent to the hepatic dome (Figure 1), and an infrahepatic collection containing multiple similar calcifications (Figure 2). CT guided percutaneous aspiration of this collection confirmed the presence of an abscess.

Although laparoscopic cholecystectomy has many benefits relative to an open procedure, there is a higher rate of gallbladder perforation (15-30%), and late infection caused by dropped gallstones (0.3%). Irrigation during the procedure and stone migration/fistulization afterwards results in multifocal abscesses remote from the gallbladder fossa, including in the abdominal wall, right pleural space, trocar sites, incisional hernias, or scrotum. The infection that arises is often indolent. The time from dropped stones to onset of symptoms averages two years. The correct diagnosis is further delayed, as the radiologist is invariably unaware of the prior laparoscopic complication. Only 40% of late infections caused by dropped gallstones on CT or US are diagnosed prospectively. Surgical removal of the abscess and stones is curative.

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REFERENCE

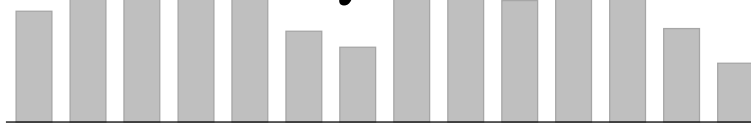
Morrin MM et al. Radiologic features of complications arising from dropped gallstones in laparoscopic cholecystectomy patients. *AJR* 2000; 174:1441-5.

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Health by Numbers



Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Jay S. Buechner, PhD

Achieving Universal Health Care Coverage in Rhode Island: Where are the Challenges?

Colleen Ryan, MPH, Jana E. Hesser, PhD, Jay S. Buechner, PhD

For the year 2010, Rhode Island has adopted state health objectives addressing each of the ten **Leading Health Indicators (LHIs)** that were selected as part of the national Healthy People 2010 process.^{1,2} One objective adopted at both the state and national levels addresses the LHI for Access to Care, specifically the barrier to access posed by the lack of health insurance. This objective is:

- Increase the proportion of people with health insurance.
- Target: 100% of people under age 65 years.

Achieving this objective would result in universal health care coverage for the people of Rhode Island.

Healthy People 2010 also adopted an over-arching goal of eliminating health disparities among population groups defined by gender, race/ethnicity, education or income, disability, geographic location, and sexual orientation.² Here we present current data on disparities in health insurance coverage in the Rhode Island working age population (ages 18-64) that help to identify which groups face the greatest obstacles to achieving universal coverage.

METHODS

The **Rhode Island Department of Health (HEALTH)** surveys a sample of Rhode Island adults by telephone annually concerning key health risk behaviors, participation in health screening and access to health care. This survey is performed as part of the national **Behavioral Risk Factor Surveillance System (BRFSS)**, funded in all 50 states, DC, and three territories by the Centers for Disease Control and Prevention (CDC) in order to monitor state and national trends for these health risk factors.³

In Rhode Island, the BRFSS has been conducted continuously since 1984, and by a professional survey contractor since 1990. During the years 1991 through 1997, about 1,800 Rhode Island adults were interviewed each year, or approximately 150 per month. For 1998 through 2000 the

annual sample size was increased to approximately 3,600, with 300 interviews per month.

The BRFSS has included basic questions on health insurance coverage since 1991, including an initial screening question for health coverage of any kind, a probing question for those with coverage that identifies their particular type of health plan or program, and a verification question for those without coverage to assure they considered all major sources of coverage in determining their answer. Any respondent stating he or she had

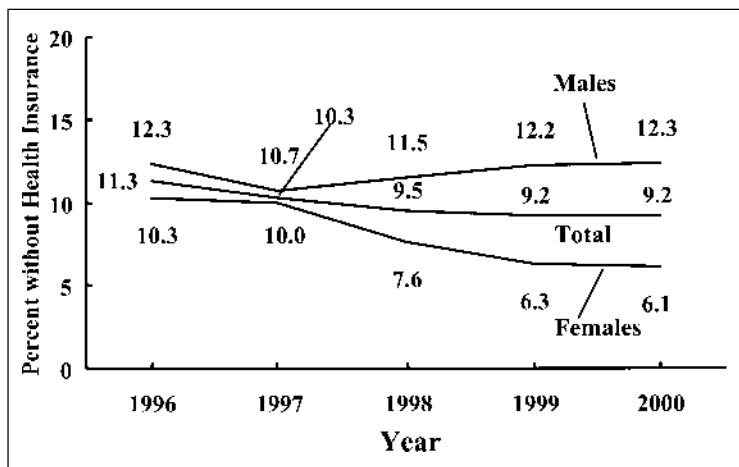


Figure 1. Percentage without Health Insurance Coverage, Ages 18-64 Years, by Gender, Rhode Island, 1996-2000

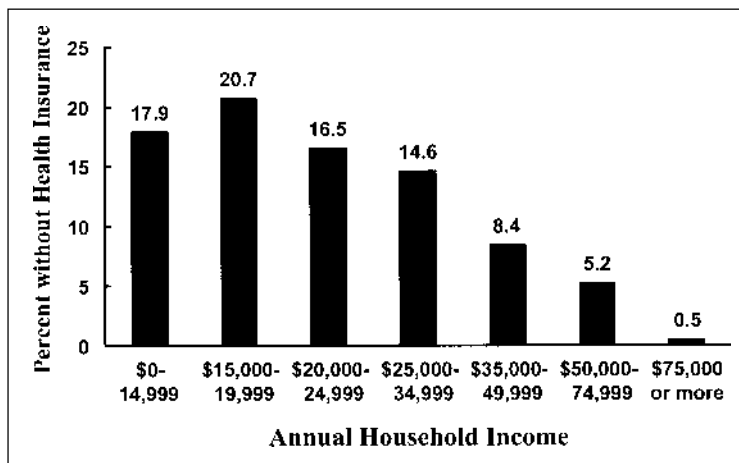


Figure 2. Percentage without Health Insurance Coverage, Ages 18-64 Years, by Income, Rhode Island, 2000

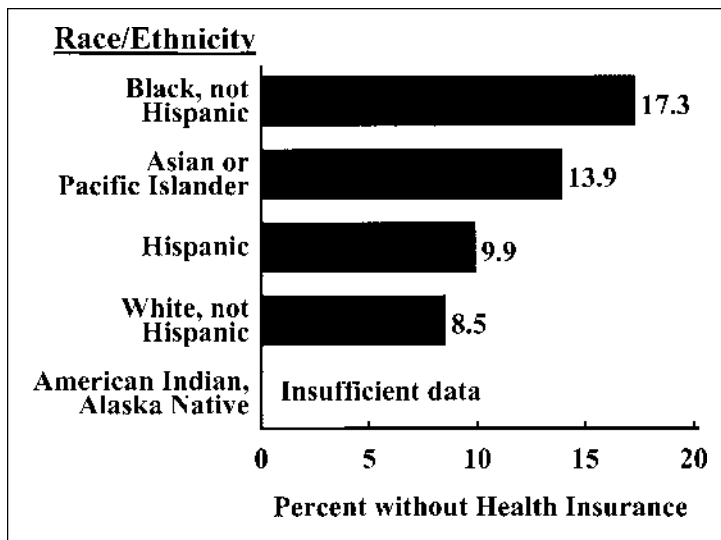


Figure 3. Percentage without Health Insurance Coverage, Ages 18-64 Years, by Race and Ethnicity Rhode Island, 1998-2000

coverage in response to the screening or verification questions is considered to be insured, unless the initial positive response was reversed during the probing question.

(Note: In previous publications of BRFSS data on health coverage,⁴ only positive responders to the screening question were considered to be insured, in accordance with national analyses. Data in those publications may differ from data presented here, especially data on Hispanic residents. The change in methodology results in fewer Hispanic respondents being assigned to the uninsured group. We are continuing to investigate the possible reasons for this finding.)

RESULTS

The uninsured rate in Rhode Island is decreasing among women and increasing among men. (Figure 1) The decrease in the overall rate of uninsured in Rhode Island from 1997 to 2000 is due to the substantial decline in the rate among females. Over the same period, rates among men in Rhode Island remained higher than for women and actually increased slightly, so the disparity in coverage has increased.

The poor and near-poor are more likely to be uninsured than middle-income and upper-income residents. (Figure 2) Lack of health insurance coverage is highest among people with annual household incomes under \$20,000. The proportion without coverage among people with annual household incomes of \$15,000-19,999 is four times higher than among people with incomes of \$50,000 or higher.

Certain racial/ethnic groups in Rhode Island have high proportions with no health care coverage. (Figure 3) Black non-Hispanic adults and Asian adults are substantially more likely to be uninsured during 1998-2000 than white, non-Hispanic adults. Hispanic residents have only slightly more uninsured than non-Hispanic whites. (See important note concerning Hispanic data at end of Methods section.)

Disparities in health care coverage also exist among groups in Rhode Island defined by employment status and age. In 2000, unemployed persons were more than three times as likely to be uninsured (27.7%) as employed persons (8.4%). By age, young

adults ages 18-24 years were most likely to lack health insurance, with rates (18.2%) nearly three times the rate for older working age adults (6.3% among those ages 35-64 years) and 30 times the rate for the elderly (0.6%).

DISCUSSION

A recent national study has shown Rhode Island to have the lowest proportion among all states of persons who had been continuously without health coverage for one year (6.2%).⁵ Given this strong base, achieving universal coverage in the state's population will involve identifying those groups most likely to be without coverage and developing sources of coverage for them.

Some of those groups in Rhode Island have been identified in the results presented here. Over the last four years, the proportion of uninsured men has increased, while the proportion of uninsured women has fallen, creating a substantial disparity between genders.

The poor and near-poor, as well as those who are unemployed, are also at higher risk of not having health insurance coverage. Young adults show very high rates of being uninsured, and all working age adults have much higher rates of non-coverage than the elderly.

Perhaps most significantly, all minority populations defined by race and ethnicity have higher proportions of uninsured persons than do non-Hispanic whites. This is of special concern because growth in minority populations accounts for all of the recent population growth in the state. Between the 1990 Census and the 2000 Census, the non-white and Hispanic populations taken together grew 77% and now comprise 18% of the Rhode Island population.⁶ If the disparities in insurance coverage persist for these groups as they continue to grow in number, then achieving the goal of universal coverage in Rhode Island will prove increasingly difficult.

REFERENCES

1. Rhode Island Department of Health. Healthy Rhode Islanders 2010: Draft Objectives and Targets. August 2001.
2. US Department of Health and Human Services. *Healthy People 2010: 2nd ed. Understanding and Improving Health and Objectives for Improving Health.* (2 vols.) Washington, DC: U.S. Government Printing Office. November 2000.
3. Frasier EL, Franks AL, Sanderson LM. Behavioral Risk Factor Data. In: *Using Chronic Disease Data: a Handbook for Public Health Practitioners.* Atlanta, GA: CDC 1992.
4. See, for example: Buechner JS. Trends and Patterns in Health Insurance Coverage, 1991-2000. *Med & Health/RI* 2001; 84:67-8. 2001.
5. Mills RJ. Health Insurance Coverage: 2000. U.S. Census Bureau. *Current Population Reports* (P60-215). September 2001.
6. U.S. Census Bureau. Profiles of General Demographic Characteristics, 2000 Census of Population and Housing: Rhode Island. www.census.gov/prod/cen2000/dp1/2k44.pdf

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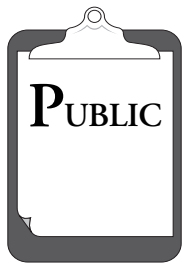
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Smallpox: Clinical and Epidemiologic Features

D. A. Henderson, MD

Smallpox is a viral disease unique to humans. To sustain itself, the virus must pass from person to person in a continuing chain of infection and is spread by inhalation of air droplets or aerosols. Twelve to 14 days after infection, the patient typically becomes febrile and has severe aching pains and prostration. Some 2 to 3 days later, a papular rash develops over the face and spreads to the extremities. The rash soon becomes vesicular and later, pustular. The patient remains febrile throughout the evolution of the rash and customarily experiences considerable pain as the pustules grow and expand. Gradually, scabs form, which eventually separate, leaving pitted scars. Death usually occurs during the second week.

The disease most commonly confused with smallpox is chickenpox, and during the first 2 to 3 days of rash, it may be all but impossible to distinguish between the two. However, all smallpox lesions develop at the same pace and, on any part of the body, appear identical. Chickenpox lesions are much more superficial and develop in crops. With chickenpox, scabs, vesicles, and pustules may be seen simultaneously on adjacent areas of skin. Moreover, the rash in chickenpox is more dense over the trunk (the reverse of smallpox), and chickenpox lesions are almost never found on the palms or soles.

In 5% to 10% of smallpox patients, more rapidly progressive, malignant disease develops, which is almost always fatal within 5 to 7 days. In such patients, the lesions are so densely confluent that the skin looks like crepe rubber; some patients exhibit bleeding into the skin and intestinal tract. Such cases are difficult to diagnose, but they are exceedingly infectious.

Smallpox spreads most readily during the cool, dry winter months but can be transmitted in any climate and in any part of the world. The only weapons against the disease are vaccination and patient isolation. Vaccination before exposure or within 2 to 3 days after exposure affords almost complete protection against disease. Vaccination as late as 4 to 5 days after exposure may protect against death. Because smallpox can only be transmitted from the time of the earliest appearance of rash, early detection of cases and prompt vaccination of all contacts is criti-

cal.

Smallpox vaccination is associated with some risk for adverse reactions; the two most serious are postvaccinal encephalitis and progressive vaccinia. Postvaccinal encephalitis occurs at a rate of 3 per million primary vaccinees; 40% of the cases are fatal, and some patients are left with permanent neurologic damage. Progressive vaccinia occurs among those who are immunosuppressed because of a congenital defect, malignancy, radiation therapy, or AIDS. The vaccinia virus simply continues to grow, and unless these patients are treated with vaccinia immune globulin, they may not recover. Pustular material from the vaccination site may also be transferred to other parts of the body, sometimes with serious results.



Figure 1.

<http://www.cdc.gov/ncidod/eid/vol5no4/hendersonG.htm#fig1>

Most cases of smallpox are clinically typical and readily able to be diagnosed. Lesions on each area of the body are at the same stage of development, are deeply embedded in the skin, and are more densely concentrated on the face and extremities.

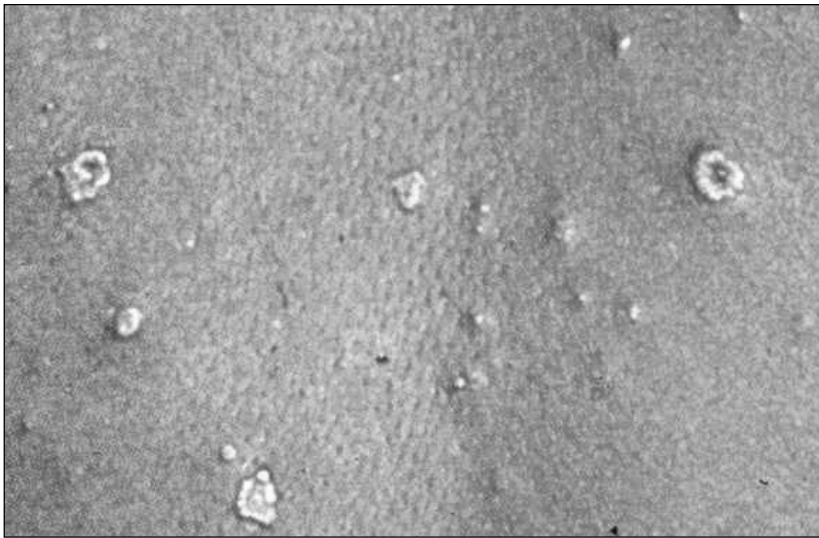


Figure 2.

<http://www.cdc.gov/ncidod/eid/vol5no4/hendersonG.htm#fig2>

The lesions of chickenpox develop as a series of "crops" over several days and are very superficial. Papules, vesicles, pustules, and scabs can be seen adjacent to each other. The trunk is usually more affected than the face or extremities.

Routine vaccination is only recommended for laboratory staff who may be exposed to one of the orthopoxviruses. There are two reasons for this. First is the risk for complications. Second, U.S. national vaccine stocks are sufficient to immunize only 6 to 7 million persons. This amount is only marginally sufficient for emergency needs. Plans are now being made to expand this reserve. However, at least 36 months are required before large quantities can be produced.

The potential of smallpox as a biological weapon is most dramatically illustrated by two European smallpox outbreaks in the 1970s. The first occurred in Meschede, Germany, in 1970.¹ This outbreak illustrates that smallpox virus in an aerosol suspension can spread widely and infect at very low doses.

Another outbreak occurred in Yugoslavia in February 1972.¹ Despite routine vaccination in Yugoslavia, the first case in the 1972 outbreak resulted in 11 others; those 11, on average, each infected 13 more. Other outbreaks in Europe from 1958 on showed that such explosive spread was not unusual during the seasonal period of high transmission, i.e., December through April. One can only speculate on the probable rapidity of spread of the smallpox virus in a population where no one younger than 25 years of age has ever been vaccinated and older persons have little remaining residual immunity.

Where might the virus come from? At one time, it was believed that the smallpox virus was restricted to only two high-security laboratories, one at the Centers for Disease Control and Prevention in Atlanta, Georgia, and one at the Russian State Centre for Research on Virology and Biotechnology, Koltsovo, Novosibirsk Region. By resolution of the 1996 **World Health Assembly (WHA)**, those stocks were slated to be destroyed at the end of June 1999. The desirability of such an action was reaffirmed by a World

Health Organization Expert Committee in January 1999. On May 22, 1999, WHA, however, passed a resolution postponing destruction until 2002, by which time any promise of the variola virus stocks for public health research could be determined. Destruction of the virus would be at least one step to limit the risk for the reemergence of smallpox. However, despite widespread acceptance of the 1972 Bioweapons Convention Treaty, which called for all countries to destroy their stocks of bioweapons and to cease all research on offensive weapons, other laboratories in Russia and perhaps in other countries maintain the virus. Iraq and the Soviet Union were signatories to the convention, as was the United States. However, as reported by the former deputy director of the Russian Bioweapons Program, officials of the former Soviet Union took notice of the

world's decision in 1980 to cease smallpox vaccination, and in the atmosphere of the cold war, they embarked on an ambitious plan to produce smallpox virus in large quantities and use it as a weapon. At least two other laboratories in the former Soviet Union are now reported to maintain smallpox virus, and one may have the capacity to produce the virus in tons at least monthly. Moreover, Russian biologists, like physicists and chemists, may have left Russia to sell their services to rogue governments.

Smallpox is rated among the most dangerous of all potential biological weapons, with far-reaching ramifications.

REFERENCES

1. Henderson DA. Bioterrorism as a public health threat. *Emerg Infect Dis* 1998;4:488-92.

D.A. Henderson, MD, is a distinguished service professor at the Johns Hopkins University, holding an appointment in the Department of Epidemiology. He directed the World Health Organization's global smallpox eradication campaign (1966-1977) and helped initiate WHO's global program of immunization in 1974. He also served as deputy assistant secretary and senior science advisor in the Department of Health and Human Services.

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