# CHAPTER 2

## OCCUPATIONAL HAZARDS IN MICROBIOLOGICAL LABORATORIES

Microbiological laboratories are special, often unique work environments that may pose identifiable infectious disease risks to persons in or near them. Infections have been contracted in the laboratory throughout the history of microbiology. Published reports around the turn of the century described laboratory-associated cases of typhoid, cholera, glanders, brucellosis, and tetanus.[1] In 1941, Meyer and Eddie[2] published a survey of 74 laboratory-associated brucellosis infections that had occurred in the United States, and concluded that the "handling of cultures or specimens or the inhalation of dust containing *Brucella* organisms is eminently dangerous to laboratory workers." A number of cases were attributed to carelessness or poor technique in the handling of infectious materials.

In 1949, Sulkin and Pike[3] published the first in a series of surveys of laboratory-associated infections. They summarized 222 viral infections, 21 of which were fatal. In at least a third of the cases, the probable source of infection was considered to be associated with the handling of infected animals and tissues. Known accidents were recorded in 27 (12%) of the reported cases.

In 1951, Sulkin and Pike[4] published the second of the series, based on a questionnaire sent to 5,000 laboratories. Only one-third of the 1,342 cases cited had been reported in the literature. Brucellosis outnumbered all other reported laboratory-acquired infections and, together with tuberculosis, tularemia, typhoid, and streptococcal infection, accounted for 72% of all bacterial infections and for 31% of infections caused by all agents. The overall case fatality rate was 3%. Only 16% of all infections reported were associated with a documented accident. The majority of these were related to mouth pipetting and the use of needle and syringe.

This survey was updated in 1965,[5] adding 641 new or previously unreported cases, and again in 1976,[6] summarizing a cumulative total of 3,921 cases. Brucellosis, typhoid, tularemia, tuberculosis, hepatitis, and Venezuelan equine encephalitis were the most commonly reported infections. Fewer than 20% of all cases were associated with a known accident. Exposure to infectious aerosols was considered to be a plausible but unconfirmed source of infection for the more than 80% of the reported cases in which the infected person had "worked with the agent."

In 1967, Hanson et al[7] reported 428 overt laboratory-associated infections with arboviruses. In some instances, the ability of a given arbovirus to produce human disease was first confirmed as the result of unintentional infection of laboratory personnel. Exposure to infectious aerosols was considered the most common source of infection.

In 1974, Skinholj[8] published the results of a survey which showed that personnel in Danish clinical chemistry laboratories had a reported incidence of hepatitis (2.3 cases per year per 1,000 employees) seven times higher than that of the general population.

Similarly, a 1976 survey by Harrington and Shannon[(9)] indicated that medical laboratory workers in England had "a five times increased risk of acquiring tuberculosis compared with the general population." Hepatitis B and shigellosis were also shown to be continuing occupational risks. Along with tuberculosis, these were the three most commonly reported occupation-associated infections in Britain.

Although these reports suggest that laboratory personnel were at increased risk of being infected by the agents they handle, actual rates of infection are typically not available. However, the studies of Harrington and Shannon[9] and of Skinhoj[(10)] indicate that laboratory personnel had higher rates of tuberculosis, shigellosis, and hepatitis B than does the general population.

In contrast to the documented occurrence of laboratory-acquired infections in laboratory personnel, laboratories working with infectious agents have not been shown to represent a threat to the community. For example, although 109 laboratory-associated infections were recorded at the Centers for Disease Control and Prevention from 1947-1973,[(11)] no secondary cases were reported in family members or community contacts. The National Animal Disease Center reported a similar experience,[(12)] with no secondary cases occurring in laboratory and non-laboratory contacts of 18 laboratory-associated cases occurring from 1960-1975. A secondary case of Marburg disease in the wife of a primary case was presumed to have been transmitted sexually two months after his dismissal from the hospital.[(13)] Three secondary cases of smallpox were reported in two laboratory associated outbreaks in England in 1973[(14)] and 1978.[(15)] There were earlier reports of six cases of Q fever among personnel of a commercial laundry that cleaned linens and uniforms from a laboratory working with the agent,[(16)] one case of Q fever in a visitor to a laboratory,[(17)] and two cases of Q fever in household contacts of a rickettsiologist.[(18)] One case of Monkey B virus transmission from an infected animal care giver to his wife has been reported, apparently due to contact of the virus with broken skin.[(19)] These cases are representative of the sporadic nature and infrequency of community infections in laboratory personnel working with infectious agents.

In his 1979 review,[(20)] Pike concluded that "the knowledge, the techniques, and the equipment to prevent most laboratory infections are available." In the United States, however, no single code of practice, standards, guidelines, or other publication provided detailed descriptions of techniques, equipment, and other considerations or recommendations for the broad scope of laboratory activities conducted with a variety of indigenous and exotic infectious agents. The booklet, *Classification of Etiologic Agents on the Basis of Hazard*,[(21)] served as a general reference for some laboratory activities utilizing infectious agents. This booklet, and the concept of categorizing infectious agents and laboratory activities into four classes or levels, served as a basic format for earlier editions of *Biosafety in Microbiological and Biomedical Laboratories* (BMBL). This fourth edition of the BMBL continues to specifically describe combinations of microbiological practices, laboratory facilities, and safety equipment, and to recommend their use in four categories or biosafety levels of laboratory operation with selected agents infectious to humans.

The descriptions of Biosafety Levels 1-4 parallel those in the *NIH Guidelines for Research Involving Recombinant DNA*, [22][23] and are consistent with the general criteria originally used in assigning agents to Classes 1-4 in *Classification of Etiologic Agents on the Basis of Hazard*.[24] Four biosafety levels are also described for infectious disease activities utilizing small laboratory animals. Recommendations for biosafety levels for specific agents are made on the basis of the potential hazard of the agent and of the laboratory's function or activity.

Since the early 1980s, laboratories have applied these fundamental guidelines in activities associated with manipulations involving the human immunodeficiency virus (HIV). Even before HIV was identified as the causative agent of Acquired Immunodeficiency Syndrome (AIDS), the principles for manipulating a bloodborne pathogen were suitable for safe laboratory work. Guidelines were also promulgated for health care workers under the rubric of Universal Precautions.[25] Indeed, Universal Precautions and this publication have become the basis for the safe handling of blood and body fluids, as described in the recent OSHA publication, *Bloodborne Pathogen Standard*.[26]

In the late 1980s, considerable public concern was expressed about medical wastes, which led to the promulgation of the Medical Waste Tracking Act of 1988.[27] The principles established in the earlier volumes of the BMBL for handling potentially infectious wastes as an occupational hazard were reinforced by the National Research Council's *Biosafety in the Laboratory: Prudent Practices for the Handling and Disposal of Infectious Materials.*[28]

As this edition goes to press, there is growing concern about the re-emergence of *M. tuberculosis* and worker safety in laboratory and health care settings. The BMBL's underlying principles, which seek to ensure safe practices, procedures and facilities, are applicable to the control of this airborne pathogen, including its multi-drug-resistant strains.[29][30] In addition, recombinant DNA technologies are being applied routinely in the laboratory to modify the genetic composition of various microorganisms. A thorough risk assessment must be conducted when addressing these activities and their inherent unknowns.

Experience has demonstrated the prudence of the Biosafety Level 1-4 practices, procedures, and facilities described for manipulations of etiologic agents in laboratory settings and animal facilities. Although no national reporting system exists for reporting laboratory-associated infections, anecdotal information suggests that strict adherence to these guidelines does contribute to a healthier and safer work environment for laboratorians, their co-workers , and the surrounding community. To further reduce the potential for laboratory-associated infections, the guidelines presented here should be considered minimal guidance for containment. They must be customized for each individual laboratory and can be used in conjunction with other available scientific information.

## References

1. Wedum, A.G. History of Microbiological Safety. 1975. 18th Biological Safety Conference. Lexington, Kentucky.

2. Meyer, K.F., Eddie, B. 1941. Laboratory infections due to *Brucella*. J Infect Dis **68**:24-32.

3. Sulkin, S.E., Pike, R.M. 1949. Viral Infections Contracted in the Laboratory. New Engl J Med **241**(5):205-213.

4. Sulkin, S.E., Pike, R.M. 1951. Survey of laboratory-acquired infections. Am J Public Health **41**(7):769-781.

5. Pike, R.M., Sulkin, S.E., Schulze, M.L. 1965. Continuing importance of laboratory-acquired infections. Am J Public Health **55**:190-199.

6. Pike, R.M. 1976. Laboratory-associated infections: Summary and analysis of 3,921 cases. Hlth Lab Sci **13**:105-114.

7. Hanson, R.P., Sulkin, S.E., Buescher, E.L., et al. 1967. Arbovirus infections of laboratory workers. Science **158**:1283-1286.

8. Skinholj, P. 1974. Occupational risks in Danish clinical chemical laboratories. II Infections. Scand J Clin Lab Invest **33**:27-29.

9. Harrington, J.M., and Shannon, H.S. 1976. Incidence of tuberculosis, hepatitis, brucellosis and shigellosis in British medical laboratory workers. Br Med J **1**:759-762.

10. Skinholj, P. 1974. (8)

11. Richardson, J.H. 1973. Provisional summary of 109 laboratory-associated infections at the Centers for Disease Control, 1947-1973. Presented at the 16th Annual Biosafety Conference, Ames, Iowa.

12. Sullivan, J.F., Songer, J.R., Estrem, I.E. 1978. Laboratory-acquired infections at the National Animal Disease Center, 1960-1976. Health Lab Sci **15**(1):58-64.

13. Martini, G.A., Schmidt, H.A. 1968. Spermatogenic transmission of Marburg virus. Klin Wschr **46**:398-400.

14. Report of the Committee of Inquiry into the Smallpox Outbreak in London in March and April 1973. 1974. Her Majesty's Stationery Office, London.

15. World Health Organization. 1978. Smallpox surveillance. Weekly Epidemiological Record **53**(35):265-266.

16. Oliphant, J.W., Parker, R.R. 1948. Q fever: Three cases of laboratory infection. Public Health Rep **63**(42):1364-1370.

17. Oliphant, J.W., Parker, R.R. 1948. (16)

18. Beeman, E.A. 1950. Q fever - An epidemiological note. Pub Hlth Rep **65**(2):88-92.

19. Holmes, G.P., Hilliard, J.K., Klontz, K.C., et al. 1990. B Virus *(Herpesvirus simiae)* Infection in Humans: Epidemiologic Investigation of a Cluster. Ann of Int Med **112**:833-839.

20. Pike, R.M. 1979. Laboratory-associated infections: incidence, fatalities, causes and prevention. Ann Rev Microbiol **33**:41-66.

21. Centers for Disease Control, Office of Biosafety. 1974. *Classification of Etiologic Agents on the Basis of Hazard*, 4th Edition. U.S. Department of Health, Education and Welfare, Public Health Service.

22. National Institutes of Health. 1994. Guidelines for Research Involving Recombinant DNA Molecules. (Washington: GPO) Federal Register. **59**FR34496.

23. National Cancer Institute, Office of Research Safety, and the Special Committee of Safety and Health Experts. 1978. *Laboratory Safety Monograph*: A Supplement to the NIH Guidelines for Recombinant DNA Research. Bethesda, MD, National Institutes of Health.

*24.* Centers for Disease Control, Office of Biosafety. 1974. (20)

25. Centers for Disease Control. 1988. Update: Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus and Other Bloodborne Pathogens in Healthcare Settings. MMWR, **37**:377-382, 387, 388.

26. U.S. Department of Labor, Occupational Safety and Health Administration. 1991. *Occupational Exposure to Bloodborne Pathogens, Final Rule*. Fed. Register **56**:64175-64182.

27. U.S. Congress, 1988. *Medical Waste Tracking Act of 1988*. H.R. 3515, 42 U.S.C. 6992-6992k.

28. *Biosafety in the Laboratory*: Prudent Practices for the Handling and Disposal of Infectious Materials. 1989. National Research Council. National Academy Press, Washington, D.C.

29. Centers for Disease Control. 1990. Guidelines for Preventing the Transmission of Tuberculosis in Health-Care Settings, with Special Focus on HIV-Related Issues. MMWR **39**, No. RR-17.

30. Centers for Disease Control. 1992. National Action Plan to Combat Multi-drug-Resistant Tuberculosis. Meeting the Challenge of Multi-drug-Resistant Tuberculosis: Summary of a Conference. Management of Persons Exposed to Multi-drug-Resistant Tuberculosis. MMWR **41**, No. RR-11.