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Laboratory-Associated Infections

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Publications on laboratory-associated infections (LAIs) provide critical information for prevention strategies. The review of actual case studies illustrates the importance of adhering to biosafety protocols and may trigger changes in laboratory procedures. Singh has stated that it is time for a centralized system for reporting, analyzing, and communicating "lessons learned" about LAIs to be developed (1). Surveys on some subsets of laboratory workers, and case reports on individual LAIs, have been published; however, without a centralized system, it is impossible to assess the true incidence of LAIs. In addition, the underreporting of such infections is widely acknowledged due to fear of reprisal and the stigma associated with such events (2).

To address the need for collecting additional LAI data, experts have recommended that a "nonpunitive surveillance and reporting system with the potential for anonymity" be implemented in the United States for diagnostic laboratories (3) and high-containment research laboratories (4). This has not been implemented for all LAIs; however, mandatory reporting for infections with Select Agents, a class of infectious agents that pose a severe threat to human and animal health, has been instituted in the United States. Data are available on the LAIs that occurred with Select Agents in the United States for the years 2004–2012. Between 2004 and 2010, approximately 10,000 researchers had access to Select Agents; eight primary LAIs occurred, no secondary LAIs, and no fatalities. In addition, three clinical laboratories reported LAI with *Brucella*, a Select Agent (5).

Systematic reporting of LAI would support the assessment of containment practices and the development of evidence-based biosafety measures (6). Until more comprehensive data are available, a literature review such as this one provides updated information about the types of microorganisms and exposures responsible for LAIs and generates awareness that laboratory workers continue to be at risk of infection.

EPIDEMIOLOGIC STUDIES OF LAI

In this chapter, we review the LAIs reported in the literature since 1979, compare them to the data from the 1930–1978 Pike and Sulkin surveys, and present a summary of the agents, routes of exposure, and types of activities, as

well as the host and environmental factors available on LAIs. Incidence data, when available, are included. This summary was compiled to support the continued development of biosafety programs to minimize the occupational risk of infection from diagnostic, research, teaching, and production activities. Information on hazard assessment and prevention strategies is available in other chapters.

Epidemiology is defined as the study of the distribution and determinants of diseases and injuries in human populations. That is, epidemiology is concerned with the extent and types of illnesses and injuries in groups of people and with the factors that influence their distribution. In the context of this chapter, the illnesses are LAIs, and the factors analyzed include the infectious agent, the activities conducted when the exposure occurred (clinical, research, field, teaching, animal work), and the routes of transmission. Inherent in the definition of epidemiology is the necessity for measuring the amount of disease in a population or occupation by relating the number of cases to a population base. Cases or events that fit the case definition are identified and counted; the number of cases in a potentially exposed population (attack rates, or incidence) can then be calculated and compared to the rates of occurrence in other populations. Comparisons of the data from clinical, research, and production laboratories from published case studies may be misleading, because attack rates for a given population are rarely available.

Incidence

Estimates from the Pike data suggested that the risk for researchers was six to seven times greater than that for hospital and public health laboratory workers; the calculated attack rate for researchers was 4.1 per 1,000 (7). Reid, in 1957, reported that the incidence of tuberculosis among laboratory personnel working with *Mycobacterium tuberculosis* was three times higher than among those not working with the agent (8). Philips, in 1965, estimated that the frequency of LAIs (using available U.S. and European data) resulted in the expected number of one to five infections per million working hours (9). A 1971 survey of laboratory-acquired cases of tuberculosis, shigellosis, brucellosis, and hepatitis in England and Wales reported an annual incidence rate of 43 infections per 1,000 medical laboratory employees (10).

Since these early studies, only a few surveys, primarily in clinical laboratories, have provided incidence data. Grist (11, 12) reported that the incidence for clinical microbiologists was 9.4 infections per 1,000 employees. Jacobson et al. surveyed supervisors of 1,191 clinical laboratory workers in Utah to determine the LAIs that occurred between 1978 and 1982. The annual incidence of LAIs in that population was 3 per 1,000 employees (13). Further analysis of the data indicated that the annual incidence in small laboratories (less than 25 employees) was greater than that in large laboratories (5.0 versus 1.5 per 1,000) and that approximately 1% of all microbiologists reported an LAI. Vesley and Hartmann surveyed LAIs among 4,202 public health and 2,290 hospital clinical laboratory employees (14). The annual incidence rate for all full-time employees was calculated at 1.4 infections per 1,000 employees for public health laboratories and 3.5 infections per 1,000 employees in hospital laboratories. Incidence in microbiology laboratories was higher, at 2.7 per 1,000 staff in public health laboratories and 4.0 per 1,000 employees in hospital microbiology labs. The relatively low incidence in the Vesley and Hartman study was attributed to safety awareness and improvements in safety devices. A Japanese survey of clinical laboratory workers in 306 hospitals cited an annual incidence rate of 2.0 infections per 1,000 persons (15).

Baron and Miller conducted a voluntary online survey of clinical microbiology laboratory directors between 2002 and 2004 (16). Forty-five LAIs were reported by directors of 88 U.S. hospital laboratories of various sizes and three reference laboratories. The calculated incidence of LAIs was compared with incidence of infection in the general population aged 30–59. Clinical microbiologists were at high risk for *Brucella* infections, with calculated incidences of 641 cases per 100,000 laboratory technologists, compared to 0.08 cases per 100,000 in the general population. The incidence of *Neisseria meningitidis* was 25.1 per 100,000 for microbiologists compared to 0.6 per 100,000 for the general population; for *Escherichia coli* O157H7, it was 83 versus 0.96. The risk of *Shigella* infection was the same in both populations (6 per 100,000) and nearly the same for *Coccidioides* (13.6 per 100,000 microbiologists versus 12 per 100,000 general population). The incidence of *Salmonella* and *Clostridium difficile* infections was lower in microbiologists than in the general population. For *Salmonella*, the incidence for clinical laboratory staff was 1.5, compared to the incidence in the general population of 17.9 per 100,000; for *C. difficile* the incidence was 0.2 compared to 8 per 100,000 in the general population (16).

Interventions Based on LAIs

Many reports also document responsible internal review of the factors contributing to the LAI. An example would be the report on a LAI that occurred when a technician was subculturing a collection of *N. meningitidis* isolates. In compliance with the existing laboratory protocols, the infected technician conducted the work on the open bench and used glass Pasteur pipettes to remove colonies

from the frozen agar surface. Analysis of the laboratory procedures after the LAI was confirmed resulted in protocol revisions to prevent recurrence. After the LAI, laboratory procedures were updated. Subculturing the *N. meningitidis* isolates is conducted in the biosafety cabinet, soft cotton swabs have replaced the glass Pasteur pipettes, and the vaccine against *N. meningitidis* is offered to staff (17). In another incident, a glass lyophilization vial punctured a researcher's gloved hand, resulting in a buffalopox LAI. To prevent recurrence, the freezing temperature for the vials prior to lyophilization was reduced to –60°C and a better-quality glass vial is now used (18). The "lessons learned" from these incidents were published to prevent additional LAIs in staff conducting similar procedures.

In 2011, the Centers for Disease Control and Prevention (CDC) reported on 109 cases linked to clinical and teaching microbiology laboratories. The cases were identified through PulseNet, the electronic monitoring system for foodborne outbreaks in the United States. Twelve percent of the cases required hospitalization, and there was one fatality. Fifty-four cases responded to CDC surveys, and 65% reported association with a university/college/community college teaching laboratory (19). An investigation revealed that the facilities and safety policies in all of the teaching laboratories were essentially equivalent. However, students in laboratories without LAIs were more familiar with biosafety training and the symptoms of infection associated with the agents studied. This led to the design of a poster for the student population illustrating that objects such pens, lab notebooks, and cell phones or personal music devices used in the lab can be a source of infection. The poster also promoted effective preventive measures such as hand washing to prevent transmission of LAI. In addition to advice for students, the CDC *Salmonella* outbreak website has a message for teachers and clinical supervisors on prevention of LAI. Another outbreak linked to clinical and teaching microbiology laboratories was reported in 2014, with 41 cases, 36% hospitalization, and no fatalities (20). The poster has provided supervisors with an excellent training tool; however, it is an ongoing challenge to reinforce appropriate work practices with each new class of inexperienced students.

LAIs: THE CONTINUUM

LAIs were not a new phenomenon in the 20th century, as historical accounts of typhoid, *Brucella*, and tetanus were recorded as early as 1885, 1887, and 1893, respectively (21, 22). Reports from the 1930s and 1940s demonstrate that microbial agents were potentially hazardous to individuals within the laboratory and posed some risk to those working in close proximity to the laboratories (23, 24).

LAIs are defined as all infections acquired through laboratory or laboratory-related activities regardless of whether they are symptomatic (overt) or asymptomatic (subclinical) in nature. In 1950, Sulkin and Pike circulated a questionnaire to 5,000 laboratories in the United States, including those associated with state and local health departments, accredited hospitals, private schools of medicine and veterinary science, undergraduate teaching institutions, manufacturers of biologic products, and various government agencies. The questionnaire solicited information on unreported infections resulting from laboratory work and slightly more than half of those surveyed responded (23, 24). During the period 1930–1975, these authors published cumulative data describing 3,921 LAIs in the United States and other countries (25, 26). In 1978, Pike added 158 new infections, bringing the total to 4,079 documented LAIs, 168 of which were fatal (27). As an apparent reflection of the work being performed in the responding laboratories at that time, bacteria accounted for 1,704 of the infections, viruses for 1,179, rickettsia for 598, fungi for 354, chlamydia for 128, and parasites for 116. Bacteria or viruses were associated with more than two-thirds of the lethal and nonlethal infections. *Brucella*, *Coxiella burnetii*, hepatitis B virus, *Salmonella enterica* serovar Typhi, *Francisella tularensis*, and *M. tuberculosis*, as shown in Table 1, were the infections reported most frequently (28). While the risk of infection with these agents remained, Pike noted that most (96%) *Brucella* and typhoid fever cases and 60% of hepatitis cases were reported before 1955. Unfortunately, between 1979 and 2015, *Brucella* spp., *M. tuberculosis*, *C. burnetii*, *Salmonella* spp., and hepatitis B virus have remained among the top 10 causes of reported LAIs (see Table 1).

In an attempt to extend the Sulkin and Pike LAI data, 475 references published between 1979 and 2015 were reviewed to determine the microorganisms associated with laboratory infections, the primary function of the facilities in which the infections occurred, and the type of work activity associated with the event. To be included in this survey, an infection had to result from laboratory work, and the infected individual had to be a laboratory worker or another person who inadvertently was exposed (by being in the area) as a result of work with the infectious agents or infected animals. Secondary infections were also noted in this literature survey and are defined here as LAIs transmitted by a laboratory worker to a person not associated with, or in the vicinity of, the laboratory, such as a family member or health care provider. These secondary infections were not included in the primary LAI count unless they were responsible for a fatality. A tertiary infection results from transmission from a secondary infection. During the period 1979–2015,

TABLE 1.

Comparison of 10 most commonly reported LAIs

1930–1978[a]				1979–2015			
Rank	Agent[b]	No. LAIs	No. deaths	Rank	Agent[b]	No. LAIs	No. deaths
1	*Brucella* spp.	426	5	1	*Brucella* spp.	378	4[c]
2	*Coxiella burnetii*	280	1	2	*Mycobacterium tuberculosis*	255	0
3	Hepatitis B	268	3	3	Arboviruses[d]	222	3
4	*Salmonella enterica* serovar Typhi	258	20	4	*Salmonella* spp.	212	2[e]
5	*Francisella tularensis*	225	2	5	*Coxiella burnetii*	205	3
6	*Mycobacterium tuberculosis*	194	4	6	Hantavirus	189	1
7	*Blastomyces dermatitidis*	162	0	7	Hepatitis B virus	113	1
8	Venezuelan equine encephalitis virus	146	1	8	*Shigella* spp.	88	0
9	*Chlamydia psittaci*	116	9	9	Human immunodeficiency virus	48	Not known
10	*Coccicioides immitis*	93	10	10	*Neisseria meningitidis*	43	13
		2,168	48			1,753	24

[a]Adapted from reference 27.
[b]Not included are 113 cases of hemorrhagic fever contracted from wild rodents in one laboratory in Russia in 1962 (486).
[c]All deaths are aborted fetuses.
[d]Typical arboviruses and orbiviruses, rhabdoviruses, and arenaviruses that are associated with arthropods or have zoonotic cycles (233), with additional arboviral reports added.
[e]One death was a secondary exposure case (47).

publications described 2,376–2,392 symptomatic infections with 42 deaths, 19 secondary infections, and 8 tertiary infections. The overt infections were caused by bacteria (51%), viruses (32%), rickettsia (9%), parasites (7%), and fungi (<1%). This information is summarized in Table 2 by category of agent and available published information on asymptomatic, secondary, and tertiary LAIs is also included. If the rickettsial infections are included with bacteria, as is the case today, 60% of the LAIs are bacterial in origin.

Laboratory Function

The distribution of the symptomatic infections according to type of work performed in a facility is shown in Table 3. Clinical (diagnostic) and research laboratories account for (17% and 59%, respectively) of the symptomatic infections reported in the earlier Sulkin and Pike surveys and (42% and 36%, respectively) in the 1979–2015 survey. It appears that more LAIs from clinical laboratories are being reported in recent years. The increases in reported clinical infections may be due in part to a more active employee health program. Another explanation is that, during the early stages of culture identification, personnel are working with unknowns and may not be using adequate containment procedures. Clinical microbiology staff rely on physician notification that a sample is suspected of containing a pathogen transmitted by the aerosol route to avoid working on the open bench; unfortunately, the presence of a Risk Group 3 pathogen is not always suspected or the notification does not always occur. For example, despite a hospital policy requiring

TABLE 2.

Total LAIs 1979–2015

Catgory of agent	Symptomatic	Asymptomatic	Total primary LAIs	Deaths	Secondary infections	Tertiary infections
Bacteria	1,212–1,226	142	1,354–1,368	21	12	3
Rickettsiae	205	269	474	1	0	0
Viruses	764–766	439	1,203–1,205	19	7	5
Parasites	170	4	174	0	0	0
Fungi	25–26	0	25	0	0	0
Total	2,376–2,392	854	3,230–3,246	41	19	8

TABLE 3.

Number of LAIs associated with indicated primary work purpose

	Clinical		Research		Production		Teaching		Site not listed		Field	Total		
	1930–1975[a]	1979–2015	1930–1975	1979–2015	1930–1975	1979–2015	1930–1975	1979–2015	1930–1975	1979–2015	1979–2015	1930–1975	1979–2015	1930–2015
Bacteria	396	783	914	122	40	81	69	181	378	45–59	1	1,797	1,212–1,226	3,009–3,023
Rickettsiae	27	1	455	204	18	0	0	0	73	0		573	205	778
Viruses	173	215	706	497	73	9	15	13	82	9–10	16	1,049	760–761	1,809–1,810
Parasites	18	5	70	77	0	0	4	81	23	6	1	115	170	285
Fungi	43	4	155	16	2	0	18	1	135	4–5	0	353	25–26	378–379
Unspecified	20	—	7	0	1	0		0	6			34	—	34
Total	677	1,008	2,307	916	134	90	106	276	697	58–74	18	3,921	2,372–2,388	6,293–6,309

[a]Adapted from reference 26.

notification, no precautionary statements accompanied the samples submitted from a suspected *F. tularensis* infection. As a result of the missing notification, 12 microbiology staff and two autopsy staff received antibiotic postexposure prophylaxis (PEP) (29). In addition, because notifications advising the need for biosafety level 3 (BSL3) practices are infrequent, clinical laboratory personnel may be unaware of the procedural changes required to safely handle atypical specimens (30).

Underreporting

Table 3 provides data on the accumulated reports of LAIs over the past 85 years and the setting in which the LAIs occurred. It is widely accepted (24, 31) that the numbers represent a substantial underestimation of the extent of LAIs. Many scientists (32) and safety professionals can recount numerous unrecorded cases. With improvements in containment practices and equipment, and occupational health programs providing immunization and postprophylaxis therapy, one would expect that the number of infections due to bacterial, rickettsial, and fungal agents would be decreasing. This appears to have occurred in the clinical laboratories of the United Kingdom, where the incidence of LAI was 62.7 cases per 100,000 person-years in 1988–1989 surveys (11) compared to 16.2 cases per 100,000 person-years reported in the 1994–1995 surveys (33).

RECENT INFORMATION ON WORKPLACE EXPOSURES

Bacterial LAIs

Table 4 summarizes information on the bacterial infections published in the literature during the period 1979–2015. During the past 36 years, 1,212 symptomatic LAIs, 142 asymptomatic infections, 12 secondary infections, and 3 tertiary infections due to bacteria were reported. The most frequently reported bacterial infections were *Brucella* spp. (389–393 LAIs), *M. tuberculosis* (243–246 LAIs), *Salmonella* (133–137 LAIs), *Shigella* (90 LAIs), *N. meningitidis* (43 LAIs), and *Chlamydia* (20 LAIs). A range is reported for a few species to include the data consolidated from two surveys conducted in Belgium for the period 2007–2012 (34).

Twenty-two fatalities due to bacterial LAIs occurred; 13 fatal LAIs were due to *N. meningitidis* (33, 35–41); 4 involved pregnancies that resulted in aborted fetuses as a consequence of LAIs with *Brucella melitensis* (42–45); 3 were due to *Salmonella* spp., one of which was a secondary infection (19, 46, 47); and one each for the attenuated (48) and wild-type strain of *Yersinia pestis* (49).

Secondary infections, the transmission of a LAI to another person outside the work environment, are rare. Between 1979 and 2015, 12 secondary bacterial infections and three tertiary bacterial infections occurred. A primary LAI with *Shigella sonnei* in a clinical laboratory resulted in the secondary transmission to a grandchild, with tertiary infections in three additional relatives (50). Four secondary infections in children under age 4 occurred with *Salmonella* Typhimurium in a 2011 outbreak associated with teaching or clinical laboratories (19). Two separate incidents of secondary *Brucella* infections were attributed to sexual transmission (51, 52). A microbiologist prepared dinner and transmitted *Salmonella* to his wife and son (47). A lactating mother with an LAI transmitted *Leptospira interrogans* to her infant through breast milk (53). Two secondary transmissions of *Bordetella pertussis* occurred (54).

TABLE 4.

Bacterial LAI references 1979–2015

Agent	Number of LAI		References
	Overt	Subclinical	
Bacteria			
Bacillus anthracis	1	1	88, 155
Bacillus Calmette-Guérin	2	0	34, 147
Bacillus cereus	1	0	325
Bacteroides asaccharolyticus	1		326
Bartonella henselae	3	0	34, 158
Bordetella pertussis	12	0	54, 327
Brucella spp.	389–393	24	5, 6, 16, 30, 34, 42–45, 51, 52, 56–62, 69, 75, 76, 93, 94, 96–124, 130, 328–341; J. Suen, 32nd Biol. Safety Conf.,[a] 1989; D.T. Brayman, 32nd Biol. Safety Conf.,[a] 1989
Burkholderia pseudomallei and *B. mallei*	3	3	78, 318, 342
Campylobacter spp.	5–6	0	12, 15, 34, 343, 344
Chlamydia spp.	20	20	93, 142–145, 345–347; K. Peterson, 25th Biol. Safety Conf.,[a] 1982
Clostridium difficile	3	0	16, 89
Corynebacterium diphtheriae	2	0	67, 68
Corynebacterium equi	1	0	348
Enterobacter aerogenes	1	0	349
Escherichia coli O157 and SP88, *Klebsiella*	22	0	16, 33, 64–66, 148, 151, 152, 332, 350–356
Francisella tularensis	11	0	5, 86, 87, 357–361
Gastrospirillum hominis	1	0	90
Haemophilus ducreyi	2	0	13, 362
Helicobacter pylori	4	0	363–365
Leptospira interrogans	8	0	53, 93, 366–368
Listeria monocytogenes	2	0	6, 34
Mycobacterium bovis	1	0	369
Mycobacterium kansasii	1	0	370
Mycobacterium leprae	1	0	156
Mycobacterium tuberculosis	255–259	96	11–13, 15, 33, 34, 93, 125, 126, 129–137, 139, 371–378; D. Robbins, 40th Biol. Safety Conf.,[a] 1997; D. Vesley, 42nd Biol. Safety Conf.,[a] 1999
Mycoplasma pneumoniae	4	0	15, 34
Neisseria gonorrhoeae	7	0	379–383; R. Hackney, 28th Biol. Safety Conf.,[a] 1985
Neisseria meningitidis	43	1	16, 17, 35–41, 63, 80–84, 351, 384–388
Pasteurella multocida	2	0	146
Salmonella spp.	212	0	11, 12, 15–17, 19, 34, 46, 47, 70–73, 77, 93, 131, 132, 149, 332, 389–395
Shigella spp.	88	0	11–13, 16, 33, 34, 50, 130–132, 150, 248, 332, 351, 396–399; D. Vesley, 30th Biol. Safety Conf.,[a] 1987; H. Mathews, 42nd Biol. Safety Conf.,[a] 1999
Staphylococcus spp.	18	0	13, 16, 33, 55, 332, 400, 401; D. Vesley, 30th Biol. Safety Conf.,[a] 1987
Streptobacillus moniliformis	2	0	74, 402
Streptococcus spp.	12	0	12, 13, 131, 403–406
Vibrio cholerae and *V. parahaemolyticus*	4	0	91, 131, 407, 408
Yersinia pestis	2	0	49, 85
Total bacteria	**1,212–1,226**	**142**	

(*continued*)

TABLE 4.

(Continued)

Agent	Number of LAI		References
	Overt	Subclinical	
Rickettsia			
Coxiella burnetii	195	267	121, 159, 160, 409–416
Rickettsia typhi and other typhus groups	10	2	161–165, 417
Total *Rickettsia*	205	269	

[a]References for Biol. Safety Conf. are abstracts of meetings sponsored by the American Biological Safety Association International, Mundelein, IL.

The asymptomatic infections included serological evidence without clinical symptoms for organisms such as *Brucella* and *Chlamydia* as well as six incidences of nasal carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) without clinical symptoms. In one case, the same strain of MRSA worked with in the laboratory was isolated from the nasal passages of both a laboratory worker and the worker's cat (55).

Infections in clinical laboratories

A majority of the bacterial LAIs occurred in clinical laboratories, and four of these occurred in veterinary diagnostic laboratories. A survey of 88 hospital microbiology laboratories and three national reference laboratories was conducted for the years 2002–2004 (16). In that 2-year period, the bacterial LAIs reported were *Shigella* (15 LAIs), *Brucella* (7 LAIs), *Salmonella* spp. (7 LAIs), *S. aureus* (6 LAIs, with 5 of these being methicillin-resistant), *N. meningitidis* (4 LAIs), *E. coli* O157:H7 (2 LAIs), and *C. difficile* (1 LAI).

It should be noted that a single unexpected isolation of *Brucella* can result in multiple exposures. Analysis of two cases of *Brucella* in clinical microbiologists revealed that 146 staff were potentially exposed to the same samples; antibiotic PEP was offered to those at high risk of exposure, and serology indicated that no one other than the two previously identified LAIs had been infected (56). Sufficient data have been collected from *Brucella* LAIs to define criteria for staff at high risk of infection and a strategy for offering antibiotics for PEP (56). This was important for the proper follow-up to the clinical proficiency test of 2007 that involved sending an "unknown" sample to 1,317 laboratories in the United States and Canada. The laboratories were informed that the samples should be handled in a Class II biosafety cabinet using BSL3 practices to identify the sample. Unfortunately, 916 laboratory workers were exposed to the sample, identified as *Brucella* RB51, including 679 staff (74%) with high-risk exposures and 237 (26%) with low-risk exposures. PEP was offered, and no cases of brucellosis were reported (30). Other case reports document the variable and sometimes long incubation period prior to the development of clinical symptoms of brucellosis resulting from exposures in clinical laboratories (43, 57–61). Recurrent infections are also an issue with *Brucella*; an example is a recurrent case of acute hepatitis in a clinical microbiologist (62). The U.S. Select Agent program documented three *Brucella* infections between 2004 and 2010 in clinical laboratories (5).

There are 43 published LAIs of *N. meningitidis* infection; 13 were fatal. Thirty-seven LAIs from *N. meningitidis* occurred in clinical laboratories; 11 were fatal. Between 1985 and 1999, five microbiologists in England and Wales were infected (35). Sejvar reviewed 16 cases of *N. meningitidis* LAIs between 1985 and 2000; 8 were fatal (41). This prompted the CDC to recommend that samples drawn from sterile sites (blood, cerebrospinal fluid, inner ear fluid) be handled only in the biosafety cabinet, even for the initial plating. The Sejvar article was submitted in a successful appeal to the New Zealand Department of Labor to evaluate whether a serious case of *N. meningitidis* was occupationally acquired; genetic mapping indicated that the infection was an LAI (63).

E. coli O157:H7 and *E. coli* VTEC O117:K1:H7 have a low infectious dose, and infections occur even when no laboratory errors or incidents are identified (64, 65). However, one report on four LAIs with O157 underscores the importance of adhering to strict BSL2 practices and established laboratory policies (66). A *Corynebacterium diphtheriae* LAI occurred in an experienced lab technician who took an advanced training course and, without incident, performed a Gram stain and toxicity tests (67); another *C. diphtheriae* LAI occurred during a proficiency testing exercise (68).

Infections in teaching laboratories

Teaching laboratories were the setting for a number of bacterial infections. Twenty-seven students and their teacher were infected with *Brucella* in a veterinary teaching laboratory in China (69). Twenty-four students in college laboratories studying clinical microbiology in the United States were infected with *S.* Typhimurium (19); some of the students were also working in a clinical laboratory (Gaines, personal communication). Two of the LAIs in this cluster occurred at a university that, 3 years

earlier, had removed *S.* Typhimurium from the curriculum due to safety concerns. During the outbreak investigation, it was determined that the stock culture of *Citrobacter freundii* used for student identification of "unknown specimens" was actually a mislabeled *S.* Typhimurium culture (70). Two additional cases were reported in 2013 (71). Another student contracted *S.* Typhimurium enteritis associated with erythema nodosum and reactive arthritis caused by the strain used in her microbiology class (72). Typhoid fever with serious complications developed 3 weeks after a student participated in a classroom identification exercise involving *S. enterica* serovar Typhi (73). A single case of *Streptobacillus moniliformis* occurred when a psychology undergraduate student was bitten by a rat (74).

Infections in production laboratories

A total of 73 LAIs were associated with production of vaccines against *B. pertussis* (R. McKinney et al., 28th Biol. Safety Conf., 1985) (54), *Brucella* (60, 75, 76), and *Salmonella* (77). The materials from a spill cleanup in a *Salmonella* poultry vaccine plant infected 21 staff (77). Fifteen workers at a *Brucella* S19 plant had active brucellosis, and 6 had asymptomatic infections (76). Twenty-two workers at a *Brucella* rev-1 vaccine plant developed brucellosis, and 6 had asymptomatic infections (60). One *Burkholderia pseudomallei* infection occurred when a culture mistakenly believed to be *Pseudomonas cepacia* was sonicated on the open bench for enzyme preparation (78).

An outbreak occurred from the wind-borne spread of anthrax from a military microbiology plant in Russia. The 77 individuals, 68 of whom died as a result of exposure to *Bacilllus anthracis*, were not included in this survey (79).

Infections in research laboratories

A total of 116 bacterial infections were reported from research facilities. Six cases of *N. meningitidis* infection occurred in research laboratories (39, 80–84). Fatalities resulted from an LAI with *N. meningitidis* serotype B (39) and from an LAI with an attenuated strain of *Y. pestis* (85). The U.S. Select Agent program reported three *B. melitensis* LAIs and four *F. tularensis* LAIs. Three researchers in the same laboratory were infected by handling *F. tularensis* incorrectly assumed to be the avirulent strain (86). In another case, video surveillance tapes of work in the biosafety cabinet were analyzed after diagnosis of an LAI with *F. tularensis*; the unvaccinated researcher wore insufficient respiratory protection and disposed of contaminated waste materials outside the biosafety cabinet (87). A researcher did not notice that a paper towel was contaminated with spores before disposing of it outside the biosafety cabinet; the follow-up nasal culture was positive for *B. anthracis* (88).

Case studies of graduate students infected while conducting research activities include a Ph.D. student infected with *C. difficile* (89). An infection with *Gastrospirillum hominis* was attributed to ingestion (90). The infected researcher did not wear gloves during the dissection of a cat stomach and also was splattered on the face and glasses with material from the tissue bath (90). Another student was infected during the supervised cleanup of a spilled shaker flask of *Vibrio cholerae*; this was the first case of indigenous cholera reported in Austria in 50 years (91).

Means of exposure for bacterial LAIs

Sniffing plates for identification purposes is frequently cited as a route of aerosol exposure. An experimental evaluation of this risk was conducted using overnight cultures and an air sampler (92). The highest number of organisms from a 4-minute air sample was from *S. aureus* (12.5 CFU/ml). *Bacillus* spp., *B. pseudomallei*, *Pseudomonas aeruginosa*, and nonpathogenic *E. coli* produced 6.25 CFU/ml. The authors conclude that the risk is low, because a sniff is estimated to inhale 50 to 200 ml of air; however, the recommendation is avoidance if a pathogen transmitted by the airborne route is suspected (3). Baron and Miller (16) state that the attribution of sniffing plates as a cause of LAI may be historical; subculturing, preparing smears, and performing catalase assays are more likely sources of aerosol transmission.

Brucella infections

Aerosol exposures to *Brucella* occurred in clinical, production, and research laboratories, with infections documented in staff that were not working directly with the organism. Although mucous membrane exposures from splashed cultures (42, 44, 45) and parenteral exposures (42, 93) were reported, these cause less than 20% of the exposure incidents (94).

Brucella *infections in clinical laboratories.* In addition to *Brucella* exposure incidents described previously in this chapter (56, 95), 31% of the staff in a large U.S. clinical laboratory were infected when one slant was subcultured on the open bench (61). *Brucella* is an endemic zoonotic in many countries, which increases the risk of infection in the general population and in clinical laboratory staff. For example, 2.5% of the positive aerobic blood culture results from 2002–2009 in an area of southern Israel were positive for *B. melitensis*. Because a significant amount of handling occurs prior to isolate identification, it is recommended that, in countries where *Brucella* is endemic, all positive blood cultures be manipulated in the biosafety cabinet to prevent exposures (96). Routine identification procedures conducted on the open bench resulted in 7 LAIs in Saudia Arabia (97), 12 LAIs in Turkey (98), 7 LAIs in Israel (94), and 38 LAIs in Iran (99). An LAI in Australia resulted from a *Brucella suis* isolation; the samples were

from a hunter of feral pigs (100). In Beijing, a nonendemic area of China, a laboratory technician was infected by an isolate from an acute case of brucellosis; the index case was a fur-maker from Inner Mongolia (101). Travel-associated infections in tourists were the source of seven LAIs in clinical laboratory staff in Germany (102). LAIs with *B. melitensis* in clinical laboratories in France, Turkey, Canada, and Saudi Arabia (98, 103–109) were attributed to sniffing plates.

There are several reports of misidentification of *Brucella* from commercial bacterial identification kits; this resulted in exposures when antibiotic sensitivity testing procedures were conducted on the open bench (57, 109–112). According to two reports, the clinical laboratory worker was infected while culturing the blood of a lab worker with a LAI (110, 113). A similar event occurred when, following misidentification, index patient cultures were forwarded to reference laboratories where two staff members were exposed and developed brucellosis (114, 115). Bouza et al., in a retrospective study of *Brucella* infections in clinical laboratory staff in Spain, analyzed 75 LAIs; 62 occurred between 1980 and 1999 and were included in this survey (116). These investigators found that the number of LAIs correlated with the number of *Brucella* isolations in the laboratory. Attack rates were: 6.4% in labs with less than five isolations of *Brucella* per year, 13.9% for labs with 5–10 isolates per year, 21.4% for labs with 11–20 isolates per year, and 46% for labs with more than 20 isolations of *Brucella* spp. per year. The route of exposure was airborne in 68 cases, contact with skin in 1 case, and unknown in 6 cases (116). A veterinarian became infected while isolating *Brucella* from dromedary camel milk (117). One of the nine technicians isolating *Brucella* from goats in a veterinary microbiology laboratory in Malaysia was infected (118).

A literature review and analysis of English-language reports of *Brucella* LAIs provided information on exposure risk and PEP (119). Routine identification activities resulted in 88% of the infections. Staff identified as having had high-risk exposures were 9.3 times more likely to develop an LAI as staff in the low-risk exposure group. The CDC has revised the risk classifications for *Brucella* exposures as follows: "High—All persons manipulating a *Brucella* isolation in a class II biosafety cabinet without using biosafety level 3 precautions or on an open bench and any person present within a 5-ft. radius of these activities; all persons present in a laboratory room during widespread aerosol-generating procedures. Low—All persons present in a laboratory room at a distance greater than 5 ft. from manipulation of a *Brucella* isolate but without high-risk exposures as defined above. None—if all handling and testing of a *Brucella* isolate was done in a Class II biosafety cabinet using biosafety level 3 precautions" (120).

Brucella *Infections in Production Laboratories.* Analysis of 22 symptomatic and 6 asymptomatic LAIs from the production of live *B. melitensis* Rev-1 veterinary vaccine revealed a 17.1% attack rate for all staff and a 39.5% attack rate for staff working in areas with open windows above the exhaust from a production area (60). Fifteen symptomatic and 5 asymptomatic infections resulted from working in a *Brucella* S19 plant; aerosol is assumed to be the major route of exposure because only 5 individuals recalled exposure incidents (76).

Brucella infections in research laboratories

When one polystyrene centrifuge tube containing *Brucella abortus* shattered during transport, 11 researchers and 1 administrative staff member were infected (58). In the United States, research with *Brucella* is conducted under strict regulations because it is a potential agent for bioterrorism; three of the reported six infections with *Brucella* occurred in research laboratories. One LAI resulted from conjunctival exposure while decontaminating an aerosol chamber used for rodent experiments with aerosolized *Brucella* (121). *Brucella* isolated from a marine mammal caused an LAI despite appropriate use of BSL3 procedures (122). Antigen production from the M-strain of *Brucella canis*, which is avirulent in dogs, also caused an LAI (123). A postgraduate student became infected from cultures collected for study of bovine miscarriage (124).

Mycobacterium tuberculosis infections

Mycobacterium tuberculosis *infections in clinical settings.* Twenty-three percent of the bacterial infections were due to *M. tuberculosis*. Workers were exposed to infectious aerosols from defective or improperly certified biosafety cabinets (125–127), the absence of biosafety cabinets (128), a defective ventilation system (11), autopsies, and preparing tissue sections (11, 12, 129–135). Analysis of 28 LAIs with *M. tuberculosis* in Japan indicated that 25 occurred in laboratories that did not have a biosafety cabinet (128). One laboratory reported that locating commonly used laboratory equipment in a mycobacteriology laboratory also resulted in exposure of personnel not working with *M. tuberculosis* (136); this was also a factor in some clinical laboratories in Japan (128). The aerosols generated in postmortem analysis of a dog (134) and by the use of pressurized refrigerant for cryosectioning human specimens (129) resulted in LAIs for staff involved in those procedures, but not for staff involved in clinical care of the unsuspected canine or human case of tuberculosis. One LAI was traced to the inadequacy of the heat-inactivation step (20 minutes at 80°C) for the large inoculum required for phenol-chloroform extraction used for IS*6110* restriction fragment length polymorphism (RFLP) typing analysis of samples (137). Three workers in a medical waste processing facility were

infected with *M. tuberculosis*; in one case, the strain was matched to a patient in a hospital that sent waste to the facility (138).

A study of seroconversion rates in 17 Canadian hospitals reported an overall annual risk of tuberculin conversion at 1% per year for laboratory technicians. Included in this study were measurements of room air-exchange rates for the microbiology and pathology laboratories, as well the length of time required for diagnosis of tuberculosis. Menzies found that the risk of seroconversion was higher for staff working in laboratories with low air-exchange rates and in hospitals with delayed diagnosis of tuberculosis in admitted patients (133). Parenteral exposures to *M. tuberculosis* have also been documented (136, 139). While transferring a sample of *M. tuberculosis* for drug susceptibility testing, a microbiology laboratory technician sustained a needlestick and developed a cutaneous infection at the site (140).

Mycobacterium tuberculosis *infections in research.* A leaking pressure valve on an aerosol exposure chamber for infecting rodents with *M. tuberculosis* resulted in three subclinical infections (141). In another incident, two of the three researchers working with drug-resistant *M. tuberculosis* became infected; the third became tuberculin purified protein derivative (PPD) positive. This was considered an aerosol exposure because respirators were removed within the animal room after cage changing (D. Robbins, 40th Biol. Safety Conf., 1997).

Neisseria meningitidis infections

Neisseria meningitidis *infections in clinical laboratories.* Sejvar et al. reviewed 16 infections with *N. meningitidis* that occurred in clinical microbiology laboratories; 9 were serogroup B, and 7 were serogroup C (41). Fourteen of the staff had made suspensions of the organisms on the open bench; 2 had done the procedure behind a splash shield. In contrast to most of the *Brucella* exposures, only the staff member who worked with the specimen became infected. The microbiologists who became infected with *N. meningitidis* had all conducted routine procedures, such as making a suspension or doing a catalase test. This indicates transmission by droplet, not aerosol. Unfortunately, eight cases, or 50%, were fatal (41). One technician in a bacteriology laboratory had *N. meningitidis* group C cultured from her right elbow and *Salmonella enterica* serovar Enteritidis cultured from her right knee (17).

Neisseria meningitidis *in research laboratories.* Work on the open bench resulted in a fatality to a researcher working with serogroup B (39). An unvaccinated undergraduate student conducting a summer research project handled cultures on the open bench and became infected (81). Treatment of an LAI required that a researcher undergo amputation of her legs, left arm, and the digits of her right hand. Initially, the infection was considered to be community acquired by the Department of Labor, but subsequent analysis confirmed the workplace origin of the infection (63, 82). The Sejvar et al. article (41) was the basis for the successful appeal to the Department of Labor (63). A researcher became infected with Z5463, *N. meningitidis* group A strain, as a result of work in a defective biosafety cabinet (83).

Aerosol exposures to Chlamydia

Sonication of *Chlamydia trachomatis* cultures on the open bench caused seven LAIs (142; K. Peterson, 25th Biol. Safety Conf., 1982). Aerosolized *C. trachomatis* L/34/bu serovar caused atypical pneumonia in two members of the same laboratory; one handled the organism directly, but the other did not (143). In a teaching laboratory, the aerosols from the contaminated plumage of a flying pigeon infected the instructor with *C. psittaci* (144). In preparation for an avian influenza study in 3-week-old turkeys, 1-day-old turkeys were placed in a negative-pressure chamber and cared for by a veterinary scientist. At 2 weeks of age, the turkeys developed a respiratory infection, and, simultaneously, the researcher was infected with *C. psittaci* genotypes D, F and E/B (145).

Other routes of transmission for bacterial LAIs

Parenteral exposures. A needle used to aliquot *Pasteurella multocida* isolated from a fowl cholera epidemic caused a severe inflammation infection of hand and arm; a needlestick from the Clemson strain of *P. multocida* produced only a very mild local infection (146). A puncture from a Pasteur pipette contaminated with bacillus Calmette-Guérin (BCG) resulted in a carpal tunnel syndrome in a laboratory technician (147).

Ingestion. Contamination of the hands resulting in subsequent ingestion is the probable mode of transmission for enteric pathogens. LAIs associated with this route of transmission were *Salmonella* (124 LAIs), *Shigella* (85 LAIs), pathogenic *E. coli* (18 LAIs), *Vibrio* spp. (6 LAIs), *C. difficile* (3 LAIs), and *Listeria monocytogenes* (1 LAI). *Shigella* was the most commonly reported LAI in surveys of clinical laboratories in the United States and the United Kingdom (13, 16, 33). Many enteric pathogens have a low infectious dose, and hand-washing procedures may not remove all pathogens. In one incident, a child visiting the laboratory touched a culture of *E. coli* O157. The child's hands were immediately washed by her parent; however, a serious infection occurred (148). A food-borne outbreak can result in a large number of cultures submitted to a laboratory, which increases the risk of infection for staff. This was a factor in an LAI with *E. coli* O157 (66) and three *Shigella* infections (33). Strict compliance with laboratory

policies for wearing and removing gloves, as well as hand washing after glove removal, must be required of all staff to prevent contamination of phones, computer keyboards, etc. (66).

The distribution of *S.* Typhi as a proficiency testing exercise resulted in a number of *S.* Typhi LAIs associated with poor work practices, such as mouth pipetting, smoking, and eating in the lab (46, 149). The importance of automatic faucets or foot pedals is illustrated by the 19 *S.* Typhi LAIs that occurred when a student in a clinical laboratory contaminated the hand-washing sink faucets (150) and by an outbreak of three simultaneous *S. sonnei* infections when only one staff member had handled the culture (16). Cleaning a biosafety cabinet was the only potential exposure to *S. sonnei* for one LAI (16). Twelve infections occurred when a disgruntled employee contaminated pastries in the staff break room using a stock strain of *Shigella* (16). *E. coli* O157 exposures caused 17 LAIs; 13 were in clinical laboratories settings. Five *E. coli* O157 LAIs occurred in research settings (151–153). Needlesticks resulted in cutaneous infections with *M. tuberculosis* (140) and *Neisseria gonorrhea* (154). A cutaneous case of *B. anthracis* resulted from transport of contaminated vials without wearing gloves (155). A cutaneous infection with *Bacillus cereus* (325) and a possible *Mycobacterium leprae* cutaneous infection were also reported (156).

Rickettsial LAIs

For the sake of consistency with the Sulkin and Pike LAI surveys, rickettsia is considered as a separate category of agents rather than being included with bacteria as is current practice. Between 1979 and 2015, there were literature reports of 205 symptomatic rickettsial infections with one death. During this period, *C. burnetii,* the etiologic agent of Q fever, was the fifth most common cause of all LAIs and accounted for 195 symptomatic rickettsial infections and one fatality (see Table 4 for references). When asymptomatic infections are added, the total becomes 405. Eleven rickettsial infections were identified as belonging to the Typhus Group—*Rickettsia typhi* (8 LAIs), *Rickettsia conorii* (2 LAIs), and *Rickettsia tsutsugamushi* (1 LAI). No secondary infections were noted from rickettsial infections.

Research involving the use of sheep in hospitals and medical school laboratories continues to expose laboratory and nonlaboratory personnel to *C. burnetii*. Antibody titers against *C. burnetii* in three research staff were reported in 2009 and are recorded in Table 4; however, the interpretation of the titers is in dispute (121).

Means of exposure for rickettsial LAIs

When publications identify the mode of transmission, Q fever infections were attributed to inhalation. A total of 189 *C. burnetii* LAIs were associated with zoonotic transmission from naturally infected asymptomatic sheep. The infected personnel either worked with the sheep or were in some proximity to sheep during their workday. Sheep may carry the organism in their blood, urine, feces, tissue, and milk. It has been estimated that the placenta of infected sheep may contain 10^9 organisms per gram of tissue and 10^5 organisms per gram of milk (157). Wedum et al. (22) noted that the infectious dose for 25–50% of human volunteers for *C. burnetii* by inhalation is only 10 organisms (22). This knowledge may have positively impacted husbandry practices for sheep used in research in the United States. A survey of U.S. members of the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC) who worked with research animals between 1999 and 2004 indicated only one confirmed case of Q fever (158). One case of Q fever resulted from necropsy of aborted fetuses of cattle, sheep, goats, pigs, and horses (T. Graham, Am. Biol. Safety Conf., 2014). The two nonzoonotic *C. burnetii* infections were attributed to exposure to a human placenta (159) and a leaking biosafety cabinet filter (160). The remaining rickettsial infections were associated with parenteral (161, 162), mucous membrane (163), and inhalation or unknown transmissions. The known sources of the exposures were an eye and lip splash from opening a microcentrifuge tube (163), sonication of infected cells on the open bench (164), and needlesticks. Other sources were not identified except that the agent was being worked with (165).

Viral LAIs

A total of 764 overt viral infections with 19 fatalities were reported between 1979 and 2015; references are listed in Table 5. The fatalities resulted from arboviruses (3 LAIs), hantavirus (2 LAIs), filovirus (1 LAI), *Macacine herpesvirus 1* (formerly called cercopithecine herpesvirus, CHV-1, or herpes B virus) (5 LAIs), hepatitis B virus (1 LAI), hepatitis C virus (1 LAI), Ebola virus (2 LAIs), Marburg virus (2 LAIs), severe acute respiratory syndrome coronavirus (SARS-CoV) (1 LAI), and one fetal abortion caused by a maternal parvovirus infection. The fatal hantavirus infections resulted from field studies with bank voles in Finland (166) and with rodents in West Virginia (167).

A groundbreaking genomic mapping study of Ebola virus contains a statement honoring the contribution of five authors who succumbed to the disease prior to the publication (168). In addition to sample collection, these authors were actively involved in Ebola patient care, and the fifth was also caring for an infected family member (169). Due to the difficulty of assessing exposure during the challenging field conditions of the 2014 Ebola epidemic, these infections are noted here but not included in the final total of viral LAI.

The seven secondary infections were due to a novel adenovirus titi monkey adenovirus (TMAdV) (1 LAI), *Macacine herpesvirus 1* (1 LAI), Marburg virus (1 LAI), a vaccine strain of poliovirus (1 LAI), SARS (2 LAIs), and Zika virus (1 LAI). Two of the 19 LAI fatalities listed were secondary infections resulting from the autopsy of a Marburg virus LAI and a mother providing care for a SARS LAI. The secondary polio infection occurred in the immunized child of a worker accidentally exposed to Mahoney prototype vaccine of poliovirus in a vaccine production facility. The stool isolate from the infected child demonstrated complete nucleotide sequence identity with the virus strain used for vaccine production (170). The Zika virus secondary infection occurred in the wife of a field virologist who collected mosquitoes in Senegal and developed symptoms after return to the United States. This case, and the infections of the two field virologists on this study, were the first identification of Zika virus in the Western world (171). An outbreak of a novel adenovirus (TMadV) in a titi monkey colony caused a respiratory illness in a researcher and a secondary infection in a household member (172). It is notable that one primary SARS LAI led to two secondary infections (mother and nurse); this led to five tertiary infections that resulted from contact with a nurse who became a secondary case while caring for a primary LAI (173).

Of the 759 viral LAIs, 497 (65%) occurred in research laboratories, 215 (28%) in clinical laboratories, 16 (2%) in field work, and 9 (1%) in production laboratories. A total of 460 asymptomatic infections were also reported between 1979 and 2015. Refer to Table 5 for citations for these viral infections. It should be noted that "research" activities include laboratory studies with animal models and field studies.

Retroviruses

LAIs with retroviruses were first described in 1988. Retroviral infections associated with human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), simian foamy virus (SFV), and simian D retrovirus (SDR) have been reported since then. In the United States, between 1985 and 2015, there were 17 confirmed occupationally acquired cases of HIV in clinical laboratory technicians and 21 possible cases; in addition, 4 researchers were infected handling HIV cultures (174). The Ippolito review provides details on occupationally acquired cases through 1997 (175). An HIV LAI is listed in the Belgian survey (34), and a seroconversion to HIV in a clinical laboratory worker was also reported in the literature (176).

Two technicians seroconverted to SIV while handling samples from nonhuman primates (NHPs), and one of the SIV-infected individuals may have been persistently infected (177). Seroconversions to spumavirus have been documented in staff occupationally exposed to NHPs. Details are provided in the discussion of zoonotic infections associated with NHP studies.

Poxviruses

Twenty-seven LAIs resulted from research activities with poxviruses between 1986 and 2015, and 23 were due to vaccinia virus. Recombinant viruses constructed from the Western Reserve strain of vaccinia virus caused nine LAIs (178–182); one LAI was caused by recombinant New York City Board of Health (NYCBOH) strain (183) and one by recombinant racoonpox virus (184). Immune responses to the insert in the vaccinia virus construct were demonstrated in three of the LAIs (180, 184, 185). Although thymidine kinase deletion mutants are less pathogenic in mice than the parent vaccinia virus strain, nine LAIs were caused by these deletion mutants (180–183, 186, 187).

Sixteen exposures to vaccinia virus were reported to the CDC Poxvirus Team in a 3-year period (183). Five of the exposures reported to the CDC were from eye splash, seven were from needlesticks, two occurred in an animal care facility, one occurred as a result of tube leakage, and one was unknown. Ten exposures did not result in infection; however, 5 LAIs occurred and 4 of these required hospitalization. All of the infected staff members had not complied with the requirement of smallpox vaccination within 10 years (183). A case report that provides more detail on one of the needlestick exposures listed in the CDC report is available (188). Two individuals were working on immunizing mice in the small space of a 1.2-meter biosafety cabinet. After placing an immunized mouse in its cage, the hand of one individual was scratched by the needle being held by the other individual. The scrape went through the glove and skin, and, although the plunger of the syringe was not depressed, the individual developed an LAI that required hospitalization. Procedures were revised, and now, when sharps are used, only one person may work in a biosafety cabinet. Double gloves are also required, and Occupational Health requires vaccination or a signed declination form (188). In 2015, a needlestick with wild-type Western Reserve strain resulted in an LAI in a recently immunized individual (179). In addition, two LAIs from cowpox virus (189, 190) and one each from raccoonpox virus (184) and buffalopox virus (18) were reported.

Zoonotic viral infections

Analysis of the viral LAIs associated with animal activities demonstrates how critical it is for laboratory staff to understand the potential for zoonotic infections in animal models. Between 1979 and 2015, there were 219 overt infections, 2 fatalities, and 180 seroconversions associated with zoonotic viral infections that were not experimentally introduced to the research model. The overt zoonotic LAIs were caused by hantavirus (188 LAIs), *Macacine*

TABLE 5.

Viral LAI references 1979–2015

Microorganism	Number of LAIs		References[a]
	Overt	Subclinical	
Adenovirus, novel TMAdV	2	2	172
Adenovirus, novel BaAdV-1	0	5	214
BaAdV-2	0	6	214
Adenovirus type 5 and adeno-associated virus	1	0	351
African horsesickness virus	4	5	232
Arboviruses and other viruses in SALS survey[b]	192	122	418
Bovine papular stomatitis virus	5	0	419
Buffalopox virus	1	0	18
Calcivirus	2	0	220
Chikungunya virus[c]	3	2	160, 234
Coxsackie type A24 virus	2	0	259, 420
Cowpox virus	2	0	189, 190
Creutzfeldt-Jakob virus	3	0	371, 421, 422
Dengue virus	7	0	226, 234, 247, 248, 423, 424
Dhori virus	5	0	236
Dugbe virus[c]	1	0	234
Ebola virus	9	0	216, 217, 425
Ebola-related virus	0	42	206–208
Echo virus	3	0	426–428
Ganjam virus[c]	5	0	429, 430
Hantavirus[c]	189	74	166, 167, 192–203, 237, 431–433
Hepatitis A virus	5	0	15
Hepatitis B virus	113–114	147	12, 13, 15, 34, 130, 131, 222, 225, 434–436
Hepatitis C virus (formerly non-A, non-B)	34	0	13, 15, 33, 130, 132, 225, 255, 267, 434–436; D. Vesley, 30th Biol. Safety Conf., 1987
Herpesvirus including zoster	6	0	12, 34, 130; D. Vesley, 30th Biol. Safety Conf., 1987
Human immunodeficiency virus	48	0	34, 174–176, 257
Influenza A virus	6	0	34, 261
Influenza B virus	1	0	260
Junin virus[c]	1	0	437
Kyanasur Forest disease virus	1	0	236
Lymphochoriomeningitis virus[c]	6	0	204, 256; A. Braun, 47th Biol. Safety Conf., 2004
Macacine herpesvirus 1 (CHV-1, B virus)	11	0	205, 240–246, 438
Machupo virus[c]	1	0	238
Marburg virus	2	0	215, 439, 440
Mayaro virus	1	0	441
Mimivirus	1	0	231
Newcastle disease virus	1	0	442
Norwalk virus	1	0	443
Orf virus	2	0	249
Orungo virus	0	3	234
Parvovirus	10–11	1	34, 444, 445
Poliovirus	1	0	170

(*continued*)

TABLE 5.

Viral LAI references 1979–2015 *(Continued)*

Microorganism	Number of LAIs		References[a]
	Overt	Subclinical	
Rabies virus	1	0	34
Rabbitpox virus	1	0	183
Raccoon pox virus (recombinant)	1	0	184
Rift Valley fever virus[c]	0	2	234
Rocio virus[a]	1	0	R. Gershon, 27th Biol. Safety Conf., 1984
Rubella virus	6	0	15
Sabia virus	2	0	235, 446
SARS-CoV	6	0	173, 227–229
Semliki Forest virus[c]	1	0	447
Simian foamy virus	2	20	210–213, 448–450
Simian immunodeficiency virus	0	4	177, 251, 258, 451
Simian type D retrovirus	0	2	209
SPH114202	1	0	452
Swine influenza virus	2	0	239
Tacaribe virus	1	0	453
Tick-borne meningoencephalitis virus[c]	1	0	454
Vaccinia virus	23	2	160, 178, 183, 185–188, 254, 262–264, 455
Varicella virus	1	0	15
Venezuelan equine encephalitis virus[c]	4	0	160, 234, 456
Vesicular stomatitis virus	1	0	457
Vesivirus	2	0	219
Wesselsbron virus[c]	3	0	234
West Nile virus[c]	6	0	191, 218, 253, 458
Zika virus	2	0	171
Total viral LAIs	759–760	460	

[a]References for Biological Safety Conference are meetings sponsored by the American Biological Safety Association, Mundelien, IL.
[b]Typical arboviruses, orbiviruses, rhabdoviruses, and arenaviruses associated with arthropods or that have zoonotic cycles.
[c]Additional infections with this virus listed in the SALS report (233).

herpesvirus 1 (10 LAIs), lymphochoriomeningitis virus (LCMV) (6 LAIs), influenza A virus (5 LAIs), West Nile virus (5 LAIs), orf virus (2 LAIs), Ebola virus (1 LAI), and a novel adenovirus in titi monkeys, TMAdV (1 LAI). The fatalities were caused by hantavirus in a graduate student doing field research in West Virginia (167) and West Nile virus in a veterinary student doing a postmortem on a horse (191).

Zoonotic infections from rodents in animal colonies

The 189 hantavirus transmissions and 36 subclinical infections occurred among researchers who thought they were working with uninfected rodents. Rodent colonies may be infected by feral animals, and this may explain hantavirus infections in Argentina (192), Belgium (193), China (194–196), France (197), Japan (198, 199), Korea (200), the United Kingdom (201, 202), and Singapore (203). This association was confirmed when Seoul virus was identified in the wild rat population of Yunnan, China, and identified as the cause of a hemorrhagic fever with renal syndrome (HFRS) outbreak in students using rats for research (195). One lot of rats produced by a commercial vendor and supplied to three colleges in Yunnan, China, infected a researcher with a reassortant of Hantaan virus that had not been previously described; subclinical infections with the same reassortant were also detected in 5 students who had been bitten and 11 animal care staff (196). Another example of zoonotic infection involved eight animal handlers and junior scientists who were exposed to LCMV while working with nude mice (204). In this incident, the mice were inadvertently infected by an LCMV-contaminated tumor cell line. The serological monitoring program for sentinel animals in the facility had lapsed for 6 months. An animal care technician was diagnosed with LCMV 3 months after he became ill, when the sentinel mice in the animal room seroconverted. The source of infection was traced to an LCMV-contaminated cell line (A. Braun, 47th Biol. Safety Conf., 2004).

Zoonotic infections associated with non-human primate studies

Macacine herpesvirus 1, formerly CHV-1 or herpes B virus, was transmitted from NHPs to 11 caretakers or researchers, resulting in a fatality and a secondary infection (see Table 5 for references). One fatality resulted from an eyesplash exposure to urine and feces from a caged NHP; eye protection was not worn and rinsing the eye was not attempted for 45 minutes because observation was considered a low-risk activity (205). A researcher dissecting optic nerve from a sample of NHP tissue was hospitalized to receive treatment with intravenous, high-dose ganciclovir and then discharged with a life-long prescription for oral valacyclovir to keep the latent virus in check (K. Johnson and T. Winters, Harvard School of Public Health Grand Rounds, 2012).

Asymptomatic infections with an Ebola-related filovirus were reported in 42 animal handlers (206–208). Two seroconversions to the zoonotic SDV have also been reported in animal handlers; one of the individuals was also infected with spumavirus from a bite in a separate incident (209). Seroconversions to the zoonotic spumavirus, or SFV, were documented in 20 animal handlers or persons working with NHPs (210). The significance of these seroconversions to simian retroviruses is not well understood. The virus causes a latent infection, and seropositivity has been documented 10 years after a bite from a mandrill and 22 years after a macaque bite (211). In one case, SFV was isolated from a culture of peripheral blood monocytes obtained from a healthy animal caretaker who seroconverted to SFV 20 years prior to the virus isolation (212). Switzer et al. commented "although SFV is nonpathogenic in naturally infected NHPs, the significance of SFV infection in humans is poorly defined. The introduction of SFV infections is of concern because changes in the pathogenicity of simian retroviruses following cross-species infection are well documented, since both HIV-1 and HIV-2 emerged from benign SIV infections in the natural primate hosts. To date information on this subject is inadequate to come to any conclusions; however, the importance of long term follow-up on these exposures has been recognized and has been initiated by the Centers for Disease Control and Prevention" (213). Novel zoonotic adenoviruses have also been identified in titi monkey (TMAdV) and baboon colonies (BaAdV-1 and BaAdV-2). TMAdV caused a primary infection and a secondary in a household member (172). Eleven seroconversions to BaAdV-1 and BaAdV-2 occurred in staff who worked with a baboon colony (214).

Experimentally infected animals

In comparison, there were reports of only 20 symptomatic infections, and no asymptomatic infections, from work with experimentally infected animals. The LAIs from experimentally infected animals were caused by cowpox virus (1 LAI), Ebola virus (1 LAI), LCMV (3 LAIs), Marburg virus (1 LAI), swine influenza (2 LAIs), vaccinia virus (7 LAIs), Venezuelan equine encephalitis virus (3 LAIs), and West Nile virus (2 LAIs). The inoculation of guinea pigs with Marburg virus and Ebola virus each resulted in a fatal LAI (215, 216).

Viral LAIs in field work

One overt infection with a new strain of Ebola virus was reported in a research worker who autopsied a wild chimpanzee to determine the cause of death (217). Fortunately, that infection did not result in the fatal hemorrhagic disease associated with other filovirus infections (Marburg virus and Ebola virus) in Europe and Africa. Transmission of West Nile virus occurred during field collection of blue jays (218) and horse autopsy (191); five investigators were infected with influenza A virus during an investigation of seal deaths (219). A field researcher examining seals (220) and one examining sea lions were painfully infected with marine calciviruses that cause lesions (220). Two cases of hantaviral infection occurred in field studies. A graduate student evaluating the impact of forestry practices on small mammals was fatally infected in West Virginia; a technician working on a similar study in California was also infected (221). In effort to evaluate the occupational risk for field studies, 995 mammology conference attendees who had exposure to rodents in North America provided samples for a survey of antibody levels. Antibodies against Sin Nombre virus were found in four persons, and two had antibodies to Arroyo or Guanarito virus (221). None of the seropositive individuals had worn any personal protective equipment prior to the U.S. hantavirus outbreak.

Viral LAIs in research and clinical activities

Sixty-seven percent of the viral LAIs occurred in research facilities. Arboviruses and other vector-borne viruses in both research and field settings accounted for 223 of the LAIs with three fatalities (see Table 5 for arbovirus references). A total of 215 viral infections occurred in clinical laboratories between 1979 and 2015. The 114 hepatitis B virus LAIs reported in the scientific literature are undoubtedly the tip of the iceberg, because one study calculated the attack rates for clinical laboratory technicians at 70% prior to the systematic introduction of hepatitis B virus vaccine (222). Following the implementation of the Occupational Safety and Health Administration (OSHA) Bloodborne Pathogen Standard in the United States (223), significant reductions in workplace transmission of hepatitis B virus have resulted from the availability of hepatitis B virus immunization, the use of "universal precautions," or consistent BSL2 containment practices, needles with safety devices, and improved sharps disposal (224). This experience is mirrored in the report from the Wroclaw region of Poland, where 323 health care workers

were infected with hepatitis B virus between 1990 and 2002; 30 of the 323 cases were clinical laboratory staff. Since 2002, the number of cases reported annually in that region decreased due to the increasing number of vaccinated staff. However, the number of hepatitis C virus infections was increasing (225). In the absence of a hepatitis C virus vaccine or a recommended PEP regimen, strict adherence to safety practices is the most effective defense against infection with hepatitis C virus.

Means of exposure for viral LAIs

It is often not possible to determine the exact cause of a LAI; only that it has occurred and the information available is that the individual "worked with" the agent. One example would be a researcher in a nonendemic area who performed the initial infection of a mosquito colony by feeding dengue-infected blood under an artificial membrane. The researcher was bitten by an escaped, but unengorged, mosquito. The virus later isolated from the infected researcher was 98.9% homologous with the laboratory strain. The authors of the case study did not rule out percutaneous exposure from the mouthparts of a mosquito; however, mucocutaneous infection from infectious blood droplets was also considered a possible route of exposure (226). In another example, the San Miguel sea lion virus serotype 5 (SMSV-5) infected a laboratory worker who collected oropharyngeal secretions from the mouths and teeth of diseased seals, isolated the virus from cell cultures, and did gradient purifications to concentrate the virus (220). The activity that resulted in exposure and clinical infection with SMSV-5 is not known; however, this LAI is considered the first documented case of a new human disease.

Aerosol exposures

Many of the viral LAIs resulted from inhalation of infectious virus. SARS was transmitted to four researchers in China when incompletely inactivated infectious materials were removed from the BSL3 laboratory for further analysis at BSL2 (173, 227). In Singapore, another SARS infection occurred due to cross-contamination of a culture of West Nile virus with SARS, and subsequent handling of the SARS-infected West Nile preparation at BSL2 (228). One SARS LAI occurred in Taiwan when liquid waste leaking from a biohazard bag in a BSL4 lab was cleaned up; the researcher wore inadequate personal protective equipment and did not use a disinfectant effective against the virus (229). Exposure to aerosolized Mayaro virus occurred during a sucrose-acetone antigen extraction procedure that involved dehydration of the product with a vacuum pump (230). A technician performing Western blots with patient samples from a pneumonia outbreak unfortunately became the first documented infection with *Mimivirus*, which is a virus isolated from amoebae in a cooling tower (231).

Four serious LAIs and five seroconversions to African horsesickness virus were the first indication that this virus could infect humans. In this case, individuals were exposed to a aerosols from a dried powder vaccine that were released when vials broke as they were being filled (232). Historically, about 20% of arbovirus infections are attributed to inhalation exposures (233). Some of the inhalation transmissions from arboviruses included infections due to the spread of Wesselbron virus from work in another room, to opening a blender containing Dugbe virus-infected mouse brains without precautions (234), and to a centrifuge bottle containing Sabia virus cracking during a run (235). Five infections with Dhori virus resulted from inhalation of aerosols generated when opening flasks (236). Enteropathica endemica was transmitted, presumably by aerosol, from close contact with bank voles (237). The hantavirus LAIs were attributed to aerosol exposure from handling mice and preparing tumor samples from mice that may have been infected by feral animals. The LCMV infections occurred when personnel handled mice that had been inadvertently infected by a contaminated cell line (204). A clinical laboratory worker was exposed to Machupo virus aerosols when a blood tube broke in the centrifuge (238); that technician developed Bolivian hemorrhagic fever. The wearing of dust masks instead of respirators resulted in two LAIs with swine influenza in staff collecting nasal cultures from infected pigs (239).

Parenteral exposures

Laboratory and wild animals were the source of many of the viral LAIs, with parenteral exposures due to bites, scratches, and accidents with sharps resulting in infections. Monkey bites and/or scratches transmitted *Spumavirus* (SFV) to 23 NHP handlers; that route of exposure also transmitted *Macacine herpesvirus 1,* formerly CHV-1 or herpes B virus, to 10 animal handlers and researchers resulting in 4 deaths (205, 240–246, R. Rebar, personal communication). The bite of infected mosquitoes transmitted dengue virus (247, 248), Zika virus (171), and chikungunya virus (234). Another case of chikungunya virus was transmitted by needlestick (160), and biting shrews transmitted Mokola virus (234). During a procedure to insert gavage tubes, two researchers were bitten by sheep and infected with orf virus (249). Six NHP animal handlers developed antibodies to filovirus antigens; four had evidence of recent infection, and one of these sustained a scalpel cut during the autopsy of an infected NHP (208).

In addition to phlebotomy, parenteral exposures to HIV in clinical settings were associated with handling broken blood tubes and a broken capillary tube (175). A parenteral exposure in a laboratory producing large quantities of concentrated HIV occurred when a blunt cannula was used to clean a centrifuge rotor (250). An HIV researcher was infected with the virus by needlestick (174). The first

report of SIV infection in a human being resulted from a deep puncture wound (251). West Nile virus LAIs were caused by needlestick (252); parenteral exposures were received during necropsy of an infected bird and preparation of an infected mouse brain (253). A needlestick during a viral purification procedure (254) or animal inoculation (182, 188) each caused a vaccinia LAI; a needlestick also caused the raccoonpox virus infection (184). A puncture from a glass lyophilization vial transmitted buffalopox virus (18). Hepatitis C virus was transmitted when a sample tube containing infected blood broke and cut two fingers (255). The bite of a rat infected with cowpox virus transmitted the virus (189). LCMV infection was confirmed by serology on blood drawn 5–7 years after exposure to Armstrong clone 53b (1 case) and clone 13 (3 cases) (256).

Mucocutaneous exposures

Mucocutaneous exposures to HIV in clinical settings were the result of splatter from an apheresis machine, sink disposal of blood samples (175), a blood analyzer apparatus (257), and opening a Vacutainer tube (176). In production laboratories, mucocutanous exposures to HIV occurred when concentrated virus splashed a worker in the face or seeped through gloves in contact with leakage from a centrifuge (250). A nonintact skin exposure to SIV was also reported (258). One worker contracted conjunctivitis due to an eye splash while pipetting dilutions of coxsackie virus (259). Despite immediate lavage, conjunctivitis occurred in a researcher who sustained splatter in the eye while injecting mice with influenza B virus (260). A conjunctival infection with influenza A virus occurred when a seal sneezed in the face of a researcher; four other field workers were also infected with influenza A virus while doing autopsies to investigate seal deaths (261). A veterinary student who removed the brain and spinal cord of a pony infected with West Nile virus neuroinvasive strain 2 became infected; mucous membrane infection by droplet is suspected (191). The secondary case of *Macacine herpesvirus 1* occurred when the wife of an infected worker applied his contaminated cortisone cream to her nonintact skin (244). Three of the vaccinia LAIs were the result of failure to wear gloves (160, 180, 262). An investigator was infected with a strain of vaccinia virus that was a contaminant of the viral stock he was working with (178). Two vaccinia virus LAIs were caused by inadvertent contact with contaminated surfaces (181, 263). The exact cause of an eye infection could not be determined; however, plates were opened for analysis on the bench, eye protection was not worn, and glove use may not have been consistent (264). Similarly, an infection with cowpox is attributed to handling contaminated reagents or touching contaminated surfaces; cowpox virus DNA was found on many lab surfaces and as a contaminant in other viral stocks. The infected person was not working directly with the virus and, for this reason, had not chosen to become vaccinated (190). In four instances, staff members seeking medical attention for infections did not initially disclose the fact that their research may have exposed them to with vaccinia (186, 187, 262, 263). Fortunately, there were no nosocomial transmissions.

Parasitic LAIs

A total of 170 symptomatic, 4 asymptomatic, and 2 secondary parasitic infections representing 6 different genera and 20 species were reported during this period. The activities resulting in LAI were research (76 LAIs) veterinary teaching (81 LAIs), diagnostic in a clinical laboratory (3 LAIs), field studies (1 LAI), and not specified (9 LAIs). The agents responsible for the infections were *Cryptosporidium* (96 LAIs), *Leishmania* (15 LAIs), *Trypanosoma* (26 LAIs), *Toxoplasma* (15 LAIs), *Plasmodium* (17 LAIs), and *Schistosoma* (1 LAI) (see Table 6 for specific references). In addition, Brener reported personal knowledge of 50 cases of laboratory-associated *Trypanosoma cruzi*, with one fatality; however, details on dates and types of exposure were not available so these were not included in this survey (32).

TABLE 6.

Parasitic LAI references 1979–2015

Agent	LAI overt	LAI subclinical	References
Cryptosporidium spp.	96	2	265–269, 287, 459–465
Leishmania spp.	15	0	270, 276, 284–286, 289, 292, 294, 466, 467
Plasmodium cynomolgi	4	0	280, 468
Plasmodium falciparum	9	0	270–273, 288, 293, 469, 470
Plasmodium vivax	4	0	272, 280
Schistosoma mansoni	1	0	277
Toxoplasma gondii	15	2	34, 279–283, 291, 471–475
Trypanosoma spp.	26	0	34, 270, 275, 280, 290, 476–479
Total	170	4	

Means of exposure to parasitic infections

The most common means of acquiring the reported parasitic LAIs were ingestion and parenteral exposure, generally needlesticks associated with animal inoculation. With one exception, an airborne infection (265), all of the *Cryptosporidium* infections were associated with ingestion of the infectious microorganisms. The *Cryptosporidium* infections occurred in veterinary students and were zoonotic transmissions through contact with infected calves. Two secondary infections occurred in spouses who washed the veterinary student's contaminated clothing (266, 267). Two separate outbreaks were from veterinary laboratory exercises involving the removal of calves from artificial wombs (268, 269). The veterinary medical schools where the outbreaks occurred adopted preventive measures such as requiring testing of calves used for teaching, on-site doffing of personal protective equipment, and providing facilities for hand washing and changing clothing (268).

Until the LAIs were diagnosed, researchers had assumed that *Plasmodium cynomolgi* only infected monkeys; however, mosquito bites in the infected monkey colony transmitted the parasite to humans (270). Mosquito bites in insectories also transmitted *Plasmodium falciparum* and *Plasmodium vivax* (271–274).

The most common source of the exposure to parasitic agents was working with infected animals, insects, or ectoparasites, and accidents related to sharps and spills or splashes accounted for the remainder. Some of the activities associated with the transmission of parasitic infection include working without gloves (275–278) or eye protection (279–283), injecting animals (284, 285), recapping needles (286), smelling or being sprayed with stomach contents (265, 287), being bitten by infected mosquitoes (271–274, 288; H. Mathews, 42nd Biol. Safety Conf., 1999), and numerous needlesticks (283, 289, 290). Unique exposures were associated with assuming that the strain being handled was avirulent (291), being on immunosuppressive therapy while working with infectious materials (292), and puncturing a thumb while pressing a glass hematocrit tube into clay sealant (293). One infection was contracted during an unrelated field study of birds (294).

Fungal LAIs

Only 25 fungal LAIs were found in the literature review; the references are listed in Table 7. There were seven cases of *Trichophyton mentagrophytes*, and four to five additional dermatophyte infections, including *Trichophyton verrucosum* and *Microsporum canis*, were reported (34). Three cases each of *Blastomyces dermatiditis* (295, 296) and *Coccidioides immitis* (5, 16) (H. Mathews, 42nd Biol. Safety Conf., 1999) were reported. *Sporothrix schenckii* caused two LAIs (297, 298); one LAI each were caused by *Arthroderma benhamiae* (299), *Encephalitozoon cuniculi* (300), *Penicillium marneffei* (301), and *Trichophyton simii* (302). Three infections occurred in clinical or public health laboratories (16, 295), while 18 occurred during research activities and 4 to 5 cases in an unspecified location.

Means of exposure to fungal infections

Fungal LAIs resulted from cutaneous, parenteral, inhalation, and mucous membrane exposures. Handling lab rats

TABLE 7.

Fungal LAI references 1979–2015

Fungus	Overt	Subclinical	References
Arthroderma benhamiae	1	0	299
Blastomyces dermatiditis	3	0	295, 296
Coccidioides immitis	3	0	5, 16 H. Mathews, 42nd Biol. Safety Conf.,[a] 1999
Dermatophytes, including *Trichophyton verrucosum, Microsporum canis*	4–5	0	34
Encephalitozoon cuniculi	1	0	300
Histoplasma capsulatum	1	0	480
Paracoccidioides brasiliensis	1	0	481
Penicillium marneffei	1	0	301
Sporothrix schenckii	2	0	297, 298
Trichophyton mentagrophytes	7	0	303, 304
Trichophyton simii	1	0	302
Total	25–26	0	

[a]References for Biol. Safety Conf. are abstracts of meetings sponsored by the American Biological Safety Association International, Mundelein, IL.

or guinea pigs that were not experimentally infected resulted in seven zoonotic LAIs (303, 304). Cutaneous infections occurred when two drops of liquid culture spilled on the bandage over a cut (298) and when one drop of culture fell on the skin while filtering a fungal mat (302). Two LAIs resulted from cuts acquired during tissue sectioning in pathology (295). An immunosuppressed student visited a mycology laboratory where the agent was handled (301) and became infected with *P. marneffei*. Failure to wear gloves or use correct work practices (297; H. Mathews, 42nd Biol. Safety Conf., 1999) resulted in LAI. Contaminated hands rubbing the eye probably inoculated the mucous membrane of the lower eyelid (299). Culture supernatant containing spores of *E. cuniculi* splashed into the eyes of a laboratory worker; this incident resulted in a severe eye disease with one cornea still clouded a year later (300).

Allergic reactions should also be an occupational concern for those working with fungal agents. Aerosol exposure during release of a pressurized canister used in the isolation of lysosomal enzymes from slime mold resulted in rhinoconjunctivitis and asthma in a research microbiologist (487). Ten staff required medical attention for allergic responses to *Penicillium citrinum* after working for 1 day on production of adenosine triphosphate (ATP) (305).

Role of Infectious Aerosols in LAIs

Laboratory studies on potential sources of infection have focused on hazards produced from routine microbiological techniques. Table 8 lists data from several studies on the number of viable particles recovered within 2 feet of a work area, on the basis of an extensive series of air sampling determinations. Aerosols present two means of worker exposure—through minute respirable airborne particles and by the disposition of larger heavy droplets onto surfaces, equipment, and personnel. The data in Table 9 indicate that standard laboratory procedures can generate aerosolized particles that are respirable and, therefore, potentially hazardous to the laboratory workers and to others in the vicinity. However, the mere presence of organisms in the air is insufficient to cause disease. For infection to be initiated, the infectious dose, a means of exposure, and a susceptible host are all required. The FDA cautions that published infectious doses do not take into account the wide variability in the virulence of the strain and host susceptibility. For example, the published infectious dose for *E. coli* O157 is as low as 10 organisms (306); however, other strains of *E. coli* require an infectious dose of 10^8 (22) to initiate infection.

Occupational Health Programs

The continued development of occupational health programs will result in a minimization or reduction of LAIs through increased access to preemployment counseling on host factors, immunization, and timely PEP. In the United States, occupational health programs provide vaccination against hepatitis B virus and PEP for hepatitis B virus and human immunodeficiency virus (HIV); this is required for compliance with the OSHA Bloodborne Pathogen Standard.

TABLE 8.

Concentration and particle size of aerosols created during representative laboratory techniques[a]

Operation	No. of viable colonies[b]	Particle size[c] (μm)
Mixing culture with:		
Pipette	6.6	2.3 ± 1.0
Vortex mixer used with 5 ml of culture in capped tube for 15 seconds	0.0	0.0
Vortex mixer used with 10 ml of culture in capped tube until culture overflow hit rotating head	9.4	4.8 ± 1.9
Use of blender:		
Top on	119.6	1.9 ± 0.7
Top off	1,500.0	1.7 ± 0.5
Use of a sonicator:	6.3	4.8 ± 1.6
Lyophilized cultures:		
Opened carefully	134.0	10.0 ± 4.3
Dropped and broken	4,838.0	10.0 ± 4.8

[a]Adapted from reference 482.
[b]Mean number of viable colonies per cubic foot of air sampled.
[c]Count median diameter of particle.

TABLE 9.

Infectious dose for humans[a]

Disease or Agent	Dose[b]	Route of Inoculation
Coxsackie A21 virus	≤18[c]	Inhalation
Escherichia coli	10^8	Ingestion
Francisella tularensis	10	Inhalation
Giardia lamblia	10–100 cysts[d]	Ingestion
Influenza A2 virus	≤790[c]	Inhalation
Malaria	10	Intravenous
Measles	0.2[c,e]	Inhalation
Mycobacterium tuberculosis	<10[f]	Inhalation
Poliovirus 1	2[c,e,g]	Ingestion
Q fever	10	Inhalation
Salmonella Typhi	10^5	Ingestion
Scrub typhus	3	Intradermal
Shigella flexneri	180	Ingestion
Shigellosis	10^9	Ingestion
Treponema pallidum	57	Intradermal
Venezuelan encephalitis virus	1[c,h]	Subcutaneous
Vibrio cholerae	10^8	Ingestion

[a]Adapted from reference 22.
[b]Dose in number of organisms unless otherwise indicated.
[c]Median infectious tissue culture dose.
[d]Adapted from reference 483.
[e]In children.
[f]Adapted from references 484 and 485.
[g]Plaque-forming units.
[h]Guinea pig infective unit.

Vaccination programs

When available for the agents studied, vaccination programs are very effective in preventing or minimizing the severity of LAIs. An analysis of 16 vaccinia virus exposure incidents reported to the CDC between 2005 and 2008 revealed that only four individuals had received the recommended smallpox vaccination within the previous 10 years (183). Prior to an LAI with vaccinia virus, the occupational health service at an academic institution offered counseling only to individuals seeking vaccination. After an LAI occurred, the policy was amended. Now all staff working with vaccinia virus are required to receive vaccination counseling, the vaccine is offered to all staff without contraindications, and declinations must be documented (178).

Vaccination is also recommended for microbiologists at risk of exposure to *N. meningitidis* (307). Previously, vaccinations against serogroup B were not available in the United States. However, as of August 15, 2015, the CDC recommends an additional vaccination against serogroup B for microbiologists handling *N. meningitidis* cultures (see http://www.cdc.gov/vaccines/hcp/vis/vis-statements/mening-serogroup.html). To provide appropriate immunizations, staff with potential laboratory exposure must be referred to an occupational health service. The immunization status of an undergraduate summer student was not confirmed prior to work with *N. meningitidis*; the student assured the principal investigator, and admitting hospital physicians when he became ill, that he had been immunized. However, the student was misinformed; he had not been vaccinated and PCR results on cerebrospinal fluid were positive for *N. meningitidis* serogroup A (81). Vaccination is also recommended for laboratory staff routinely exposed to *S.* Typhi.

Vaccination is an important tool in the prevention of infectious agents with a low infectious dose by the aerosol route. A historical review of LAI at the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) between 1943 and 1969 indicates that the introduction of biosafety cabinets reduced the risk of infection with anthrax, glanders, and plague. However, even after the introduction of biosafety cabinets, infections with *F. tularensis* continued at the average rate of 15 per year, for Venezuelan equine encephalitis at 1.9 per year, and Q fever at 3.4 per year. In contrast, between 1989 and 2002, only 5 LAIs resulted from 289 reported exposures. The LAIs were glanders, Q fever, vaccinia, chikungunya, and Venezuelan equine encephalitis. The Venezuelan equine encephalitis, vaccinia, and Q fever LAIs were instances where infection occurred in vaccinated staff; however, the Q fever symptoms were mild. Also, vaccination status was considered in the evaluation for PEP for low-risk exposures (159).

Specialized programs are required for high-containment laboratories and include physical and mental fitness for duty, as well as the capacity to quarantine exposed staff. Guidance is available on management of exposures to some Ebola virus (308).

Postexposure prophylaxis

Guidelines for PEP after occupational exposures to hepatitis B and C viruses and HIV are available and emphasize that such exposures should be considered medical emergencies requiring prompt evaluation and response (309, 310). Several publications reported incidents where PEP probably minimized or eliminated acute laboratory infections with *B. abortus* (58, 75), *B. melitensis* (109, 311), *B. pseudomallei* (312, 313), *F. tularensis* (29), and *M. tuberculosis* (488). However, prevention of exposures should be emphasized; side effects that inhibit completion of the prophylactic antibiotic treatment for *B. melitensis* (311, 314) and for *B. pseudomallei* (313) have been reported. In 2013, CDC published revised guidelines for PEP after *Brucella* exposures (120). All potentially exposed staff should receive serological monitoring, symptom surveillance, and daily temperature self-checks; staff with high-risk exposures should receive PEP (120). The CDC

reviewed 153 incidents that resulted in 1,724 exposures to *Brucella* between 2008 and 2011; 839 were high-risk exposures (see risk classification in section on *Brucella* in Clinical Laboratories). Only five LAIs occurred; four of the infected microbiologists had not taken PEP and the fifth worker started the antibiotic 21 days after the exposure incident (120).

Rusnak et al. describe a proactive occupational health response to an incident that was considered a low risk of exposure to *B. anthracis* spores in immunized staff (88). A staff member removed a rack of anthrax cultures from the incubator and transported it on a cart to a coworker seated at the biosafety cabinet. The paper towel covering the top of flasks was contaminated with spores; this was noted only after the towel had been discarded outside of the biosafety cabinet. The occupational health service obtained nose and throat swabs from both potentially exposed staff members and initiated a short course of antibiotic therapy. The next day, 6 CFU of *B. anthracis* grew from the nasal passage sample from one researcher, so both were prescribed the full 1-month course of antibiotic therapy for PEP (88).

Guidance on PEP for many agents is available on the CDC website (www.cdc.gov). References on PEP for high-consequence exposures include advice for *B. pseudomallei* (160, 308, 315, 316).

Host factors

Another critical function of occupational health programs involves advising staff of preexisting medical conditions that may put them at greater risk for serious consequences from exposure to an infectious agent. The risk and severity of infection may be influenced by concurrent diseases, medical conditions, drugs that alter the host defense, allergic hypersensitivity, inability to receive a certain vaccine, and reproductive issues. These risk factors need to be recognized and addressed before initiating work with infectious agents (317).

Some workers may face increased risks for certain infections that alter or impair normal host defense mechanisms. For example, host defenses provided by healthy intact skin can be disrupted by diseases such as chronic dermatitis, eczema, and psoriasis, thus providing a portal of entry in the absence of personal protective clothing. Achlorhydric individuals are more susceptible to *Vibrio* infections (306), and individuals with heart valve problems should not be exposed to *C. burnetii*. Antibiotic therapy may suppress gastrointestinal flora, increasing the possibility of colonization by a foreign or resistant population of microorganisms. Deficiencies in the immune system function can place workers at a higher risk of occupational infection. Immunodeficiency may result from certain connective tissue diseases, cancer chemotherapy, or HIV infection (317). Other causes of immunodeficiency include steroid treatment for medical conditions such as asthma, inflammatory bowel disease, and acute viral infection. Pregnancy brings the potential for mild immunodeficiency, especially for the developing fetus. The risk of infection is also increased with diabetes; this was considered a factor in the first glanders infection in the United States since 1945, an LAI with *B. mallei* (318). Diabetes may also have been a factor in the unexpected fatality due to an attenuated, pigment-negative strain of *Y. pestis*, KIMD27, as well as undiagnosed hereditary hemochromatosis. The attenuation of KIMD27 is based on the strain's inability to acquire iron; it is thought that the iron overload in the scientist's blood may have provided the strain with the sufficient iron to recover virulence (85). It is known that individuals with hemochromatosis are more susceptible to infection with at least 32 organisms, including Gram-negative organisms, Gram-positive, or acid-fast bacteria, fungi, and parasites (319). Occupational risks associated with the reproductive system may involve exposures during pregnancy that result in adverse outcomes such as spontaneous abortion and birth defects. Infertility can occur in either sex. Male exposures can cause damage to sperm, transmission of toxic agents in seminal fluid, or infection of the pregnant woman from her partner's contaminated clothing. Breast-feeding may also be a source of infection. More commonly, concerns are directed to the potential congenital infection of a fetus, *in utero* or during delivery, as a result of a pregnant woman acquiring a work-related infection. Exposure to microorganisms known to cause congenital or neonatal infections, such as *Brucella*, *Cytomegalovirus*, hepatitis B virus, herpes simplex virus, HIV, LCMV, parvovirus, *L. monocytogenes*, rubella virus, *Treponema pallidum*, and toxoplasmas, is a distinct possibility in laboratory work (320). There is also a link between Zika virus and microcephaly (http://wwwnc.cdc.gov/travel/notices/alert/zika-virus-central-america).

In microbiological and biomedical laboratories, workers can also develop allergies to proteins (biological products derived from raw materials, fermentation products, or enzymes), chemicals, and the dander or aerosolized urine products of animals (321, 322).

Behavioral factors

Regarding occupational exposures to pathogenic microorganisms, the worker is key in controlling the safe outcome of any operation. He or she handles the agent, performs experiments, operates equipment, handles animals, disposes of infectious waste, and, when necessary, cleans up spills. The worker must come to the workplace prepared to function successfully. This means having adequate education, technical experience, and safety training to understand a task or project and perform it safely; being able to focus on the work so that inattention

or random distractions do not lead to accidents; and being motivated to adhere to safe work practices. Philipps (323) and Martin (324) both discussed behavioral factors associated with laboratory safety. In a study conducted at Fort Detrick in a large microbiological research laboratory, Phillips described various characteristics associated with accident-prone and accident-free individuals. The study found that individuals in the 20- to 29-year age group had an abnormally high accident rate and that women had slightly fewer accidents than men. Unfortunately, the biomedical workforce is usually young and innovative and falls into the higher accident group. Sixty-five percent of all accidents in Phillips' study were due to human error, and 20% were due to equipment problems. The remaining 15% were ultimately attributed to "unsafe acts," which could also be considered human error. Although not always acknowledged as having a role in LAIs, behavioral factors need to be taken into consideration.

CONCLUSION

This review was written to support biosafety programs by heightening awareness that LAIs continue to occur and by providing data for reinforcement of biosafety practices in daily operations. The authors of publications cited in this chapter have made an important contribution to the objective risk assessment and the development of improved biosafety practices. The safety culture in a workplace must encourage the reporting of exposure incidents to determine whether steps can be taken to prevent recurrence. The risk of LAIs can be minimized if laboratory staff are aware of the potential for exposure to infectious agents and work continuously with biosafety and occupational health professionals to accomplish this goal.

References

1. **Singh K.** 2011. It's time for a centralized registry of laboratory-acquired infections. *Nat Med* **17:**919.
2. **Sewell DL.** 2000. Laboratory-acquired Infections. *Clin Microbiol Newsl* **22:**73–77.
3. **Miller JM, Astles R, Baszler T, Chapin K, Carey R, Garcia L, Gray L, Larone D, Pentella M, Pollock A, Shapiro DS, Weirich E, Wiedbrauk D, Biosafety Blue Ribbon Panel, Centers for Disease Control and Prevention (CDC).** 2012. Guidelines for safe work practices in human and animal medical diagnostic laboratories. Recommendations of a CDC-convened, Biosafety Blue Ribbon Panel. *MMWR Suppl* **61**(Suppl)**:**1–102.
4. **Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight.** 2009. Final report. http://www.ars.usda.gov/is/br/bbotaskforce/biosafety-FINAL-REPORT-092009.pdf.
5. **Henckel RD, Miller T, Weyant RS.** 2012. Monitoring Select Agent theft, loss, and release reports in the United States—2004–2010. *Appl Biosaf* **17:**171–180.
6. **Kimman TG, Smit E, Klein MR.** 2008. Evidence-based biosafety: a review of the principles and effectiveness of microbiological containment measures. *Clin Microbiol Rev* **21:**403–425.
7. **Sulkin SE, Pike RM.** 1951. Laboratory-acquired infections. *J Am Med Assoc* **147:**1740–1745.
8. **Reid DD.** 1957. Incidence of tuberculosis among workers in medical laboratories. *BMJ* **2:**10–14.
9. **Phillips GB.** 1965a. Microbiological hazards in the laboratory, Part 1. Control. *J Chem Educ* **42:**A43–A48.
10. **Harrington JM, Shannon HS.** 1976. Incidence of tuberculosis, hepatitis, brucellosis, and shigellosis in British medical laboratory workers. *BMJ* **1:**759–762.
11. **Grist NR.** 1981. Infection hazards in clinical laboratories. *Scott Med J* **26:**197–198.
12. **Grist NR.** 1983. Infections in British clinical laboratories 1980–81. *J Clin Pathol* **36:**121–126.
13. **Jacobson JT, Orlob RB, Clayton JL.** 1985. Infections acquired in clinical laboratories in Utah. *J Clin Microbiol* **21:**486–489.
14. **Vesley D, Hartmann HM.** 1988. Laboratory-acquired infections and injuries in clinical laboratories: a 1986 survey. *Am J Public Health* **78:**1213–1215.
15. **Masuda T, Isokawa T.** 1991. [Biohazard in clinical laboratories in Japan]. *Kansenshogaku Zasshi* **65:**209–215.
16. **Baron EJ, Miller JM.** 2008. Bacterial and fungal infections among diagnostic laboratory workers: evaluating the risks. *Diagn Microbiol Infect Dis* **60:**241–246.
17. **Athlin S, Vikerfors T, Fredlund H, Olcén P.** 2007. Atypical clinical presentation of laboratory-acquired meningococcal disease. *Scand J Infect Dis* **39:**911–913.
18. **Riyesh T, Karuppusamy S, Bera BC, Barua S, Virmani N, Yadav S, Vaid RK, Anand T, Bansal M, Malik P, Pahuja I, Singh RK.** 2014. Laboratory-acquired buffalopox virus infection, India. *Emerg Infect Dis* **20:**324–326.
19. **Centers for Disease Control and Prevention.** 2011. Multistate Outbreak of *Salmonella typhimurium* infections associated with exposure to clinical and teaching microbiology laboratories. http://www.cdc.gov/salmonella/typhimurium-laboratory/index.html.
20. **Centers for Disease Control and Prevention.** 2014. Human *Salmonella* Typhimurium infections linked to exposure to clinical and teaching microbiology laboratories. http://www.cdc.gov/salmonella/typhimurium-labs-06-14/index.html.
21. **Anonymous.** 1988. Microbiological safety cabinets and laboratory acquired infection. *Lancet* **2:**844–845.
22. **Wedum AG, Barkley WE, Hellman A.** 1972. Handling of infectious agents. *J Am Vet Med Assoc* **161:**1557–1567.
23. **Sulkin SE, Pike RM.** 1951. Survey of laboratory-acquired infections. *Am J Public Health Nations Health* **41:**769–781.
24. **Pike RM, Sulkin SE.** 1952. Occupational hazards in microbiology. *Sci Mon* **75:**222–227.
25. **Pike RM, Sulkin SE, Schulze ML.** 1965. Continuing importance of laboratory-acquired infections. *Am J Public Health Nations Health* **55:**190–199.
26. **Pike RM.** 1976. Laboratory-associated infections: summary and analysis of 3921 cases. *Health Lab Sci* **13:**105–114.
27. **Pike RM.** 1978. Past and present hazards of working with infectious agents. *Arch Pathol Lab Med* **102:**333–336.
28. **Pike RM.** 1979. Laboratory-associated infections: incidence, fatalities, causes, and prevention. *Annu Rev Microbiol* **33:**41–66.
29. **Shapiro DS, Schwartz DR.** 2002. Exposure of laboratory workers to *Francisella tularensis* despite a bioterrorism procedure. *J Clin Microbiol* **40:**2278–2281.
30. **Centers for Disease Control and Prevention (CDC).** 2008. Update: potential exposures to attenuated vaccine strain *Brucella abortus* RB51 during a laboratory proficiency test—United States and Canada, 2007. *MMWR Morb Mortal Wkly Rep* **57:**36–39.
31. **Collins CH, Kennedy DA.** 1999. *Laboratory-Acquired Infections: History, Incidence, Causes and Preventions*, 4th ed. Butterworth Heinemann, Oxford.

32. **Brener Z.** 1987. Laboratory-acquired Chagas disease: comment. *Trans R Soc Trop Med Hyg* **81:**527.
33. **Walker D, Campbell D.** 1999. A survey of infections in United Kingdom laboratories, 1994–1995. *J Clin Pathol* **52:**415–418.
34. **Willemark N, Van Vaerenbergh B, Descamps E, Brosius B, Dai Do Thi C, Leunda A, Baldo A, Herman P.** 2015. *Laboratory-Acquired Infections in Belgium (2007–2012).* Institut Scientifique de Santé Publique, Brussels, Belgium. http://www.biosafety.be/CU/PDF/2015_Willemarck_LAI%20report%20Belgium_2007_2012_Final.pdf.
35. **Boutet R, Stuart JM, Kaczmarski EB, Gray SJ, Jones DM, Andrews N.** 2001. Risk of laboratory-acquired meningococcal disease. *J Hosp Infect* **49:**282–284.
36. **Bremner DA.** 1992. Laboratory acquired meningococcal septicaemia. *Aust Microbiol* **13:**A106.
37. **Centers for Disease Control (CDC).** 1991. Laboratory-acquired meningococcemia—California and Massachusetts. *MMWR Morb Mortal Wkly Rep* **40:**46–47, 55.
38. **Centers for Disease Control and Prevention (CDC).** 2002. Laboratory-acquired meningococcal disease—United States, 2000. *MMWR Morb Mortal Wkly Rep* **51:**141–144.
39. **Sheets CD, Harriman K, Zipprich J, Louie JK, Probert WS, Horowitz M, Prudhomme JC, Gold D, Mayer L.** 2014. Fatal meningococcal disease in a laboratory worker—California, 2012. *MMWR Morb Mortal Wkly Rep* **63:**770–772.
40. **Paradis JF, Grimard D.** 1994. Laboratory-acquired invasive meningococcus—Quebec. *Can Commun Dis Rep* **20:**12–14.
41. **Sejvar JJ, Johnson D, Popovic T, Miller JM, Downes F, Somsel P, Weyant R, Stephens DS, Perkins BA, Rosenstein NE.** 2005. Assessing the risk of laboratory-acquired meningococcal disease. *J Clin Microbiol* **43:**4811–4814.
42. **Al-Aska AK, Chagla AH.** 1989. Laboratory-acquired brucellosis. *J Hosp Infect* **14:**69–71.
43. **Georghiou PR, Young EJ.** 1991. Prolonged incubation in brucellosis. *Lancet* **337:**1543.
44. **Young EJ.** 1983. Human brucellosis. *Rev Infect Dis* **5:**821–842.
45. **Young EJ.** 1991. Serologic diagnosis of human brucellosis: analysis of 214 cases by agglutination tests and review of the literature. *Rev Infect Dis* **13:**359–372.
46. **Blaser MJ, Hickman FW, Farmer JJ III, Brenner DJ, Balows A, Feldman RA.** 1980. *Salmonella typhi*: the laboratory as a reservoir of infection. *J Infect Dis* **142:**934–938.
47. **Blaser MJ, Lofgren JP.** 1981. Fatal salmonellosis originating in a clinical microbiology laboratory. *J Clin Microbiol* **13:**855–858.
48. **Centers for Disease Control and Prevention (CDC).** 2011. Fatal laboratory-acquired infection with an attenuated *Yersinia pestis* strain—Chicago, Illinois, 2009. *MMWR Morb Mortal Wkly Rep* **60:**201–205.
49. **Wong D, Wild MA, Walburger MA, Higgins CL, Callahan M, Czarnecki LA, Lawaczeck EW, Levy CE, Patterson JG, Sunenshine R, Adem P, Paddock CD, Zaki SR, Petersen JM, Schriefer ME, Eisen RJ, Gage KL, Griffith KS, Weber IB, Spraker TR, Mead PS.** 2009. Primary pneumonic plague contracted from a mountain lion carcass. *Clin Infect Dis* **49:**e33–e38.
50. **De Schrijver KAL, Bertrand S, Collard JM, Eilers K, De Schrijver K, Lemmens A, Bertrand S, Collard JM, Eilers K.** 2007. [Een laboratoriuminfectie met *Shigella sonnei* gevolgd door een cluster secundaire infectiessecundaire infecties] Abstract in English: Outbreak of *Shigella sonnei* in a clinical microbiology laboratory with secondary infections in the community). *Tijdschr Geneeskd* **63:**686–690.
51. **Ruben B, Band JD, Wong P, Colville J.** 1991. Person-to-person transmission of *Brucella melitensis. Lancet* **337:**14–15.
52. **Goossens H, Marcelis L, Dekeyser P, Butzler JP.** 1983. *Brucella melitensis*: person-to-person transmission? *Lancet* **321:**773.
53. **Bolin CA, Koellner P.** 1988. Human-to-human transmission of *Leptospira interrogans* by milk. *J Infect Dis* **158:**246–247.
54. **U.S. Department of Health and Human Services Public Health Service.** 1999. *Biosafety in Microbiological and Biomedical Laboratories. Centers for Disease Control and Prevention and National Institutes of Health te.* U.S. Government Printiing Office, Washington, D.C.
55. **Jager MM, Murk JL, Pique R, Wulf MW, Leenders AC, Buiting AG, Bogaards JA, Kluytmans JA, Vandenbroucke-Grauls CM.** 2010. Prevalence of carriage of meticillin-susceptible and meticillin-resistant *Staphylococcus aureus* in employees of five microbiology laboratories in The Netherlands. *J Hosp Infect* **74:**292–294.
56. **Centers for Disease Control and Prevention (CDC).** 2008. Laboratory-acquired brucellosis—Indiana and Minnesota, 2006. *MMWR Morb Mortal Wkly Rep* **57:**39–42.
57. **Batchelor BI, Brindle RJ, Gilks GF, Selkon JB.** 1992. Biochemical mis-identification of *Brucella melitensis* and subsequent laboratory-acquired infections. *J Hosp Infect* **22:**159–162.
58. **Fiori PL, Mastrandrea S, Rappelli P, Cappuccinelli P.** 2000. *Brucella abortus* infection acquired in microbiology laboratories. *J Clin Microbiol* **38:**2005–2006.
59. **Gerberding JL, Romero JM, Ferraro MJ.** 2008. Case 34-2008. A 58-year-old woman with neck pain and fever. *N Engl J Med* **359:**1942–1949.
60. **Ollé-Goig JE, Canela-Soler J.** 1987. An outbreak of *Brucella melitensis* infection by airborne transmission among laboratory workers. *Am J Public Health* **77:**335–338.
61. **Staszkiewicz J, Lewis CM, Colville J, Zervos M, Band J.** 1991. Outbreak of *Brucella melitensis* among microbiology laboratory workers in a community hospital. *J Clin Microbiol* **29:**287–290.
62. **Ozaras R, Celik AD, Demirel A.** 2004. Acute hepatitis due to brucellosis in a laboratory technician. *Eur J Intern Med* **15:**264.
63. **Emrys G.** 2008. Report into the investigation of ESR meningitis infection case of Dr. Jeannette Adu-Bobie. http://www.dol.govt.nz/news/media/2008/adu-bobie-report.asp.
64. **Burnens AP, Zbinden R, Kaempf L, Heinzer I, Nicolet J.** 1993. A case of laboratory acquired infection with *Escherichia coli O157:H7. Zentralbl Bakteriol* **279:**512–517.
65. **Olesen B, Jensen C, Olsen K, Fussing V, Gerner-Smidt P, Scheutz F.** 2005. *VTEC O117:K1:H7.* A new clonal group of E. coli associated with persistent diarrhoea in Danish travellers. *Scand J Infect Dis* **37:**288–294.
66. **Spina N, Zansky S, Dumas N, Kondracki S.** 2005. Four laboratory-associated cases of infection with *Escherichia coli O157:H7. J Clin Microbiol* **43:**2938–2939.
67. **Thilo W, Kiehl W, Geiss HK.** 1997. A case report of laboratory-acquired diphtheria. *Euro Surveill* **2:**67–68.
68. **Laboratory PHS.** 1998. Throat infection with toxigenic *Corynebacterium diptheriae. Commun Dis Wkly Rep* **8:**60–61.
69. **Yanyu L.** 2011. Dean, secretary deposed after group infection. http://www.chinadaily.com.cn/china/2011-09/04/content_13614791.htm
70. **M.A. Said SS. J. Wright-Andoh, R. Myers, J. Razeq, D. Blythe.** 2011. *Salmonella enterica serotype Typhimurium* gastrointestinal illness associated with a university microbiology course—Maryland, abstr. 62nd Epidemic Intelligence Service (EIS) Conference. **62**: 03.
71. **Centers for Disease Control and Prevention (CDC).** 2013. Salm*onella typhimurium* infections associated with a community college microbiology laboratory—Maine, 2013. *MMWR Morb Mortal Wkly Rep* **62:**863.
72. **Steckelberg JM, Terrell CL, Edson RS.** 1988. Laboratory-acquired *Salmonella typhimurium* enteritis: association with erythema nodosum and reactive arthritis. *Am J Med* **85:**705–707.
73. **Hoerl D, Rostkowski C, Ross SL, Walsh TJ.** 1988. Typhoid fever acquired in a medical teaching laboratory. *Lab Med* **19:**166–168.
74. **Centers for Disease Control (CDC).** 1984. Rat-bite fever in a college student—California. *MMWR Morb Mortal Wkly Rep* **33:**318–320.

75. **Montes J, Rodriguez MA, Martin T, Martin F.** 1986. Laboratory-acquired meningitis caused by *Brucella abortus* strain 19. *J Infect Dis* **154:**915–916.
76. **Wallach JC, Ferrero MC, Victoria Delpino M, Fossati CA, Baldi PC.** 2008. Occupational infection due to *Brucella abortus S19* among workers involved in vaccine production in Argentina. *Clin Microbiol Infect* **14:**805–807.
77. **Centers for Disease Control and Prevention (CDC).** 2007. *Salmonella serotype enteritidis* infections among workers producing poultry vaccine—Maine, November-December 2006. *MMWR Morb Mortal Wkly Rep* **56:**877–879.
78. **Schlech WF III, Turchik JB, Westlake RE Jr, Klein GC, Band JD, Weaver RE.** 1981. Laboratory-acquired infection with *Pseudomonas pseudomallei (melioidosis). N Engl J Med* **305:**1133–1135.
79. **Meselson M, Guillemin J, Hugh-Jones M, Langmuir A, Popova I, Shelokov A, Yampolskaya O.** 1994. The Sverdlovsk anthrax outbreak of 1979. *Science* **266:**1202–1208.
80. **Bhatti AR, DiNinno VL, Ashton FE, White LA.** 1982. A laboratory-acquired infection with *Neisseria meningitidis. J Infect* **4:** 247–252.
81. **Kessler AT, Stephens DS, Somani J.** 2007. Laboratory-acquired serogroup A meningococcal meningitis. *J Occup Health* **49:**399–401.
82. **New Zealand Herald.** 2005. Scientist loses limbs to meningococcal disease. http://www.nzherald.co.nz/nz/news/article.cfm?c_id=1&objectid=10120376.
83. **Omer H, Rose G, Jolley KA, Frapy E, Zahar JR, Maiden MC, Bentley SD, Tinsley CR, Nassif X, Bille E.** 2011. Genotypic and phenotypic modifications of *Neisseria meningitidis* after an accidental human passage. *PLoS One* **6:**e17145.
84. **ProMED-mail.** 2009. Meningitis, meningococcal, USA (Massachusetts). http://www.promedmail.org/post/20091112.3924.
85. **Centers for Disease Control and Prevention (CDC).** 2011. Fatal laboratory-acquired infection with an attenuated Yersinia pestis Strain—Chicago, Illinois, 2009. *MMWR Morb Mortal Wkly Rep* **60:**201–205.
86. **Barry M.** 2005. Report of pneumonic tularemia in three Boston University researchers—November 2004–March 2005. Boston Public Health Commission, Boston, MA. http://cbc.arizona.edu/sites/default/files/Boston_Univerity_Tularemia_report_2005.pdf
87. **Eckstein M.** 2010. Army-broken procedures led to lab infection. http://www.fredericknewspost.com/archive/article_5e4539ea-7902-5b13-8d37-8c7b6ade7538.html.
88. **Rusnak J, Boudreau E, Bozue J, Petitt P, Ranadive M, Kortepeter M.** 2004. An unusual inhalational exposure to *Bacillus anthracis* in a research laboratory. *J Occup Environ Med* **46:**313–314.
89. **Bouza E, Martin A, Van den Berg RJ, Kuijper EJ.** 2008. Laboratory-acquired *clostridium difficile* polymerase chain reaction ribotype 027: a new risk for laboratory workers? *Clin Infect Dis* **47:**1493–1494.
90. **Lavelle JP, Landas S., Mitros F, Conklin JL.** 1994. Acute gastritis associated with spiral organisms from cats. Dig Dis Sci 39**:** 744–750.
91. **Huhulescu S, Leitner E, Feierl G, Allerberger F.** 2010. Laboratory-acquired *Vibrio cholerae O1* infection in Austria, 2008. *Clin Microbiol Infect* **16:**1303–1304.
92. **Barkham T, Taylor MB.** 2002. Sniffing bacterial cultures on agar plates: a useful tool or a safety hazard? *J Clin Microbiol* **40:**3877.
93. **Miller CD, Songer JR, Sullivan JF.** 1987. A twenty-five year review of laboratory-acquired human infections at the National Animal Disease Center. *Am Ind Hyg Assoc J* **48:**271–275.
94. **Yagupsky P, Peled N, Riesenberg K, Banai M.** 2000. Exposure of hospital personnel to *Brucella melitensis* and occurrence of laboratory-acquired disease in an endemic area. *Scand J Infect Dis* **32:**31–35.
95. **Centers for Disease Control and Prevention (CDC).** 2008. Laboratory-acquired brucellosis—Indiana and Minnesota, 2006. *MMWR Morb Mortal Wkly Rep* **57:**39–42.
96. **Shemesh AA, Yagupsky P.** 2012. Isolation rates of *Brucella melitensis* in an endemic area and implications for laboratory safety. *Eur J Clin Microbiol Infect Dis* **31:**441–443.
97. **Kiel FW, Khan MY.** 1993. Brucellosis among hospital employees in Saudi Arabia. *Infect Control Hosp Epidemiol* **14:**268–272.
98. **Ergönül O, Celikbaş A, Tezeren D, Güvener E, Dokuzoğuz B.** 2004. Analysis of risk factors for laboratory-acquired brucella infections. *J Hosp Infect* **56:**223–227.
99. **Hasanjani Roushan MR, Mohrez M, Smailnejad Gangi SM, Soleimani Amiri MJ, Hajiahmadi M.** 2004. Epidemiological features and clinical manifestations in 469 adult patients with brucellosis in Babol, Northern Iran. *Epidemiol Infect* **132:**1109–1114.
100. **Eales KM, Norton RE, Ketheesan N.** 2010. Brucellosis in northern Australia. *Am J Trop Med Hyg* **83:**876–878.
101. **Jiang H, Fan M, Chen J, Mi J, Yu R, Zhao H, Piao D, Ke C, Deng X, Tian G, Cui B.** 2011. MLVA genotyping of Chinese human *Brucella melitensis* biovar 1, 2 and 3 isolates. *BMC Microbiol* **11:**256.
102. **Al Dahouk S, Neubauer H, Hensel A, Schöneberg I, Nöckler K, Alpers K, Merzenich H, Stark K, Jansen A.** 2007. Changing epidemiology of human brucellosis, Germany, 1962–2005. *Emerg Infect Dis* **13:**1895–1900.
103. **Grammont-Cupillard M, Berthet-Badetti L, Dellamonica P.** 1996. Brucellosis from sniffing bacteriological cultures. *Lancet* **348:**1733–1734.
104. **Demirdal T, Demirturk N.** 2008. Laboratory-acquired brucellosis. *Ann Acad Med Singapore* **37:**86–87.
105. **Memish ZA, Alazzawi M, Bannatyne R.** 2001. Unusual complication of breast implants: brucella infection. *Infection* **29:**291–292.
106. **Memish ZA, Venkatesh S.** 2001. Brucellar epididymo-orchitis in Saudi Arabia: a retrospective study of 26 cases and review of the literature. *BJU Int* **88:**72–76.
107. **Memish ZA, Mah MW.** 2001. Brucellosis in laboratory workers at a Saudi Arabian hospital. *Am J Infect Control* **29:**48–52.
108. **Aloufi AD, Memish ZA, Assiri AM, McNabb SJN.** 2016. Trends of reported human cases of brucellosis, Kingdom of Saudi Arabia, 2004–2012. *J Epidemiol Glob Health* **6:**11–18.
109. **Robichaud S, Libman M, Behr M, Rubin E.** 2004. Prevention of laboratory-acquired brucellosis. *Clin Infect Dis* **38:**e119–e122.
110. **Chusid MJ, Russler SK, Mohr BA, Margolis DA, Hillery CA, Kehl KC.** 1993. Unsuspected brucellosis diagnosed in a child as a result of an outbreak of laboratory-acquired brucellosis. *Pediatr Infect Dis J* **12:**1031–1033.
111. **Peiris V, Fraser S, Fairhurst M, Weston D, Kaczmarski E.** 1992. Laboratory diagnosis of brucella infection: some pitfalls. *Lancet* **339:**1415–1416.
112. **Public Health Service Laboratory.** 1991. Microbiological test strip (API20NE) identifies *Brucella melitensis* as *Moraxella phenylpyruvica. CDR (Lond Engl Wkly)* **1:**165.
113. **Noviello S, Gallo R, Kelly M, Limberger RJ, DeAngelis K, Cain L, Wallace B, Dumas N.** 2004. Laboratory-acquired brucellosis. *Emerg Infect Dis* **10:**1848–1850.
114. **Gruner E, Bernasconi E, Galeazzi RL, Buhl D, Heinzle R, Nadal D.** 1994. Brucellosis: an occupational hazard for medical laboratory personnel. Report of five cases. *Infection* **22:**33–36.
115. **Luzzi GA, Brindle R, Sockett PN, Solera J, Klenerman P, Warrell DA.** 1993. Brucellosis: imported and laboratory-acquired cases, and an overview of treatment trials. *Trans R Soc Trop Med Hyg* **87:**138–141.
116. **Bouza E, Sánchez-Carrillo C, Hernangómez S, González MJ, The Spanish Co-operative Group for the Study of Laboratory-acquired Brucellosis.** 2005. Laboratory-acquired brucellosis: a Spanish national survey. *J Hosp Infect* **61:**80–83.
117. **Schulze zur Wiesch J, Wichmann D, Sobottka I, Rohde H, Schmoock G, Wernery R, Schmiedel S, Dieter Burchard G, Melzer F.** 2010. Genomic tandem repeat analysis proves laboratory-acquired brucellosis in veterinary (camel) diagnostic laboratory in the United Arab Emirates. *Zoonoses Public Health* **57:**315–317.

118. **Hartady T, Saad MZ, Bejo SK, Salisi MS.** 2014. Clinical human brucellosis in Malaysia: a case report. *Asian Pac J Trop Dis* **4:**150–153.
119. **Traxler RM, Lehman MW, Bosserman EA, Guerra MA, Smith TL.** 2013. A literature review of laboratory-acquired brucellosis. *J Clin Microbiol* **51:**3055–3062.
120. **Traxler RM, Guerra MA, Morrow MG, Haupt T, Morrison J, Saah JR, Smith CG, Williams C, Fleischauer AT, Lee PA, Stanek D, Trevino-Garrison I, Franklin P, Oakes P, Hand S, Shadomy SV, Blaney DD, Lehman MW, Benoit TJ, Stoddard RA, Tiller RV, De BK, Bower W, Smith TL.** 2013. Review of brucellosis cases from laboratory exposures in the United States in 2008 to 2011 and improved strategies for disease prevention. *J Clin Microbiol* **51:**3132–3136.
121. **United States Government Accountability Office.** 2009. High-containment laboratories national strategy for oversight is needed. GAO-09-1045T. http://www.gao.gov/new.items/d09574.pdf.
122. **Brew SD, Perrett LL, Stack JA, MacMillan AP, Staunton NJ.** 1999. Human exposure to Brucella recovered from a sea mammal. *Vet Rec* **144:**483.
123. **Wallach JC, Giambartolomei GH, Baldi PC, Fossati CA.** 2004. Human infection with M-strain of *Brucella canis. Emerg Infect Dis* **10:**146–148.
124. **Arlett PR.** 1996. A case of laboratory acquired brucellosis. *BMJ* **313:**1130–1132.
125. **Shireman PK.** 1992. Endometrial tuberculosis acquired by a health care worker in a clinical laboratory. *Arch Pathol Lab Med* **116:**521–523.
126. **Müller HE.** 1988. Laboratory-acquired mycobacterial infection. *Lancet* **332:**331.
127. **Clark RP, Rueda-Pedraza ME, Teel LD, Salkin IF, Mahoney W.** 1988. Microbiological safety cabinets and laboratory acquired infection. *Lancet* **332:**844–845.
128. **Goto M, Yamashita T, Misawa S, Komori T, Okuzumi K, Takahashi T.** 2007. [Current biosafety in clinical laboratories in Japan: report of questionnaires' data obtained from clinical laboratory personnel in Japan]. *Kansenshogaku Zasshi* **81:**39–44.
129. **Centers for Disease Control (CDC).** 1981. Tuberculous infection associated with tissue processing—California. *MMWR Morb Mortal Wkly Rep* **30:**73–74.
130. **Grist NR, Emslie J.** 1985. Infections in British clinical laboratories, 1982–3. *J Clin Pathol* **38:**721–725.
131. **Grist NR, Emslie JA.** 1987. Infections in British clinical laboratories, 1984–5. *J Clin Pathol* **40:**826–829.
132. **Grist NR, Emslie JA.** 1989. Infections in British clinical laboratories, 1986–87. *J Clin Pathol* **42:**677–681.
133. **Menzies D, Fanning A, Yuan L, FitzGerald JM, Canadian Collaborative Group in Nosocomial Transmission of Tuberculosis.** 2003. Factors associated with tuberculin conversion in Canadian microbiology and pathology workers. *Am J Respir Crit Care Med* **167:**599–602.
134. **Posthaus H, Bodmer T, Alves L, Oevermann A, Schiller I, Rhodes SG, Zimmerli S.** 2011. Accidental infection of veterinary personnel with *Mycobacterium tuberculosis* at necropsy: a case study. *Vet Microbiol* **149:**374–380.
135. **Templeton GL, Illing LA, Young L, Cave D, Stead WW, Bates JH.** 1995. The risk for transmission of *Mycobacterium tuberculosis* at the bedside and during autopsy. *Ann Intern Med* **122:**922–925.
136. **Peerbooms PGH, van Doornum GJJ, van Deutekom H, Coutinho RA, van Soolingen D.** 1995. Laboratory-acquired tuberculosis. *Lancet* **345:**1311–1312.
137. **Bemer-Melchior P, Drugeon HB.** 1999. Inactivation of *Mycobacterium tuberculosis* for DNA typing analysis. *J Clin Microbiol* **37:**2350–2351.
138. **Angela M, Weber YB, Mortimer VD.** 2000. A tuberculosis outbreak among medical waste workers. *J Am Biol Saf Assoc* **5:**70–80.
139. **Kao AS, Ashford DA, McNeil MM, Warren NG, Good RC.** 1997. Descriptive profile of tuberculin skin testing programs and laboratory-acquired tuberculosis infections in public health laboratories. *J Clin Microbiol* **35:**1847–1851.
140. **Belchior I, Seabra B, Duarte R.** 2011. Primary inoculation skin tuberculosis by accidental needle stick. *BMJ Case Rep* **2011:**bcr1120103496.
141. **Washington State Department of Labor and Industries Region 2—Seattle Office.** 2004. Inspection report on laboratory associated infections due to *Mycobacterium tuberculosis.* Inspection307855056. http://www.sunshine-project.org/idriuwmadchamber.pdf.
142. **Bernstein DI, Hubbard T, Wenman WM, Johnson BL Jr, Holmes KK, Liebhaber H, Schachter J, Barnes R, Lovett MA.** 1984. Mediastinal and supraclavicular lymphadenitis and pneumonitis due to *Chlamydia trachomatis* serovars L1 and L2. *N Engl J Med* **311:**1543–1546.
143. **Paran H, Heimer D, Sarov I.** 1986. Serological, clinical and radiological findings in adults with bronchopulmonary infections caused by *Chlamydia trachomatis. Isr J Med Sci* **22:**823–827.
144. **Marr JJ.** 1983. The professor and the pigeon. Psittacosis in the groves of academe. *Mo Med* **80:**135–136.
145. **Van Droogenbroeck C, Beeckman DS, Verminnen K, Marien M, Nauwynck H, Boesinghe LT, Vanrompay D.** 2009. Simultaneous zoonotic transmission of *Chlamydophila psittaci* genotypes D, F and E/B to a veterinary scientist. *Vet Microbiol* **135:**78–81.
146. **Olson LD.** 1980. Accidental penetration of hands with virulent and avirulent *Pasteurella multocida* of turkey origin. *Avian Dis* **24:**1064–1066.
147. **Janier M, Gheorghiu M, Cohen P, Mazas F, Duroux P.** 1982. [Carpal tunnel syndrome due to mycobacterium bovis BCG (author's transl)]. *Sem Hop* **58:**977–979.
148. **Salerno AE, Meyers KE, McGowan KL, Kaplan BS.** 2004. Hemolytic uremic syndrome in a child with laboratory-acquired *Escherichia coli O157:H7. J Pediatr* **145:**412–414.
149. **Blaser MJ, Feldman RA.** 1980. Acquisition of typhoid fever from proficiency-testing specimens. *N Engl J Med* **303:**1481.
150. **Mermel LA, Josephson SL, Dempsey J, Parenteau S, Perry C, Magill N.** 1997. Outbreak of *Shigella sonnei* in a clinical microbiology laboratory. *J Clin Microbiol* **35:**3163–3165.
151. **Bavoil PM.** 2005. Federal indifference to laboratory-acquired infections. *ASM News* **71:**1. (Letter.)
152. **Rangel JM, Sparling PH, Crowe C, Griffin PM, Swerdlow DL.** 2005. Epidemiology of *Escherichia coli O157:H7* outbreaks, United States, 1982–2002. *Emerg Infect Dis* **11:**603–609.
153. **Kozlovac J, Gurtler J.** 2015. E. coli 0157:H7 case study. Abstr. USDA ARS 3rd International Biosafety & Biocontainment Symposium: Biorisk Management in a One-Health World, Baltimore, MD.
154. **Vraneš J, Lukšić I, Knežević J, Ljubin-Sternak S** 2015. Health care associated cutaneous abscess—a rare form of primary gonococcal infection. *Am J Med Case Rep* **3:**88–90.
155. **Centers for Disease Control and Prevention (CDC).** 2002. Update: cutaneous anthrax in a laboratory worker—Texas, 2002. *MMWR Morb Mortal Wkly Rep* **51:**482.
156. **Bhatia VN.** 1990. Possible multiplication of *M. leprae (?)* on skin and nail bed of a laboratory worker. *Indian J Lepr* **62:**226–227.
157. **Welsh HH, Lennette EH, Abinanti FR, Winn JF.** 1951. Q fever in California. IV. Occurrence of *Coxiella burnetii* in the placenta of naturally infected sheep. *Public Health Rep* **66:**1473–1477.
158. **Weigler BJ, Di Giacomo RF, Alexander S.** 2005. A national survey of laboratory animal workers concerning occupational risks for zoonotic diseases. *Comp Med* **55:**183–191.
159. **Ossewaarde JM, Hekker AC.** 1984. [Q fever infection probably caused by a human placenta]. *Ned Tijdschr Geneeskd* **128:**2258–2260.
160. **Rusnak JM, Kortepeter MG, Aldis J, Boudreau E.** 2004. Experience in the medical management of potential laboratory exposures to agents of bioterrorism on the basis of risk assessment

at the United States Army Medical Research Institute of Infectious Diseases (USAMRIID). *J Occup Environ Med* **46:**801–811.
161. **Halle S, Dasch GA.** 1980. Use of a sensitive microplate enzyme-linked immunosorbent assay in a retrospective serological analysis of a laboratory population at risk to infection with typhus group rickettsiae. *J Clin Microbiol* **12:**343–350.
162. **Perna A, Di Rosa S, Intonazzo V, Sferlazzo A, Tringali G, La Rosa G.** 1990. Epidemiology of boutonneuse fever in western Sicily: accidental laboratory infection with a rickettsial agent isolated from a tick. *Microbiologica* **13:**253–256.
163. **Norazah A, Mazlah A, Cheong YM, Kamel AG.** 1995. Laboratory acquired murine typhus—a case report. *Med J Malaysia* **50:**177–179.
164. **Oh M, Kim N, Huh M, Choi C, Lee E, Kim I, Choe K.** 2001. Scrub typhus pneumonitis acquired through the respiratory tract in a laboratory worker. *Infection* **29:**54–56.
165. **Woo JH, Cho JY, Kim YS, Choi DH, Lee NM, Choe KW, Chang WH.** 1990. A case of laboratory-acquired murine typhus. *Korean J Intern Med* **5:**118–122.
166. **Israeli E.** 2014. [A hantavirus killed an Israeli researcher: hazards while working with wild animals]. *Harefuah* **153:**443–444, 499.
167. **Sinclair JR, Carroll DS, Montgomery JM, Pavlin B, McCombs K, Mills JN, Comer JA, Ksiazek TG, Rollin PE, Nichol ST, Sanchez AJ, Hutson CL, Bell M, Rooney JA.** 2007. Two cases of hantavirus pulmonary syndrome in Randolph County, West Virginia: a coincidence of time and place? *Am J Trop Med Hyg* **76:**438–442.
168. **Gire SK, et al.** 2014. Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. *Science* **345:**1369–1372.
169. **Koebler J.** 2016. Five scientists died of Ebola while working on a single study of the virus., Update 9/3/14. Motherboard. http://motherboard.vice.com/read/five-scientists-died-of-ebola-while-working-on-a-single-study-on-the-virus.
170. **Mulders MN, Reimerink JH, Koopmans MP, van Loon AM, van der Avoort HG.** 1997. Genetic analysis of wild-type poliovirus importation into The Netherlands (1979–1995). *J Infect Dis* **176:**617–624.
171. **Foy BD, Kobylinski KC, Chilson Foy JL, Blitvich BJ, Travassos da Rosa A, Haddow AD, Lanciotti RS, Tesh RB.** 2011. Probable non-vector-borne transmission of Zika virus, Colorado, USA. *Emerg Infect Dis* **17:**880–882.
172. **Chen EC, Yagi S, Kelly KR, Mendoza SP, Maninger N, Rosenthal A, Spinner A, Bales KL, Schnurr DP, Lerche NW, Chiu CY.** 2011. Cross-species transmission of a novel adenovirus associated with a fulminant pneumonia outbreak in a new world monkey colony. *PLoS Pathog* **7:**e1002155.
173. **Heymann DL, Aylward RB, Wolff C.** 2004. Dangerous pathogens in the laboratory: from smallpox to today's SARS setbacks and tomorrow's polio-free world. *Lancet* **363:**1566–1568.
174. **Joyce MP, Kuhar D, Brooks JT.** 2015. Notes from the field: occupationally acquired HIV infection among health care workers—United States, 1985–2013. *MMWR Morb Mortal Wkly Rep* **63:**1245–1246.
175. **Ippolito G, Puro V, Heptonstall J, Jagger J, De Carli G, Petrosillo N.** 1999. Occupational human immunodeficiency virus infection in health care workers: worldwide cases through September 1997. *Clin Infect Dis* **28:**365–383.
176. **Eberle J, Habermann J, Gürtler LG.** 2000. HIV-1 infection transmitted by serum droplets into the eye: a case report. *AIDS* **14:**206–207.
177. **Centers for Disease Control (CDC).** 1992. Seroconversion to simian immunodeficiency virus in two laboratory workers. *MMWR Morb Mortal Wkly Rep* **41:**678–681.
178. **Centers for Disease Control and Prevention (CDC).** 2008. Laboratory-acquired vaccinia exposures and infections—United States, 2005–2007. *MMWR Morb Mortal Wkly Rep* **57:**401–404.
179. **Hsu CH, Farland J, Winters T, Gunn J, Caron D, Evans J, Osadebe L, Bethune L, McCollum AM, Patel N, Wilkins K, Davidson W, Petersen B, Barry MA, Centers for Disease Control and Prevention (CDC).** 2015. Laboratory-acquired vaccinia virus infection in a recently immunized person—Massachusetts, 2013. *MMWR Morb Mortal Wkly Rep* **64:**435–438.
180. **Jones L, Ristow S, Yilma T, Moss B.** 1986. Accidental human vaccination with vaccinia virus expressing nucleoprotein gene. *Nature* **319:**543.
181. **Mempel M, Isa G, Klugbauer N, Meyer H, Wildi G, Ring J, Hofmann F, Hofmann H.** 2003. Laboratory acquired infection with recombinant vaccinia virus containing an immunomodulating construct. *J Invest Dermatol* **120:**356–358.
182. **Openshaw PJ, Alwan WH, Cherrie AH, Record FM.** 1991. Accidental infection of laboratory worker with recombinant vaccinia virus. *Lancet* **338:**459.
183. **MacNeil A, Reynolds MG, Damon IK.** 2009. Risks associated with vaccinia virus in the laboratory. *Virology* **385:**1–4.
184. **Rocke TE, Dein FJ, Fuchsberger M, Fox BC, Stinchcomb DT, Osorio JE.** 2004. Limited infection upon human exposure to a recombinant raccoon pox vaccine vector. *Vaccine* **22:**2757–2760.
185. **Eisenbach C, Neumann-Haefelin C, Freyse A, Korsukéwitz T, Hoyler B, Stremmel W, Thimme R, Encke J.** 2007. Immune responses against HCV-NS3 after accidental infection with HCV-NS3 recombinant vaccinia virus. *J Viral Hepat* **14:**817–819.
186. **Centers for Disease Control and Prevention (CDC).** 2009. Laboratory-acquired vaccinia virus infection—Virginia, 2008. *MMWR Morb Mortal Wkly Rep* **58:**797–800.
187. **Health and Safety Executive.**2003. Incidents—Lessons to be learnt. Accidental infection with vaccinia virus. http://www.hse.gov.uk/biosafety/gmo/acgm/acgm32/paper8.htm.
188. **Korioth-Schmitz B, Affeln D, Simon SL, Decaneas WM, Schweon GB, Wong M, Gardner A.** 2015. Vaccinia virus—laboratory tool with a risk of laboratory-acquired infection. *Appl Biosaf* **20:**6–11.
189. **Marennnikova SS, Zhukova OA, Manenkova GM, Ianova NN.** 1988. [Laboratory-confirmed case of human infection with ratpox (cowpox)]. *Zh Mikrobiol Epidemiol Immunobiol* **6:**30–32.
190. **McCollum AM, Austin C, Nawrocki J, Howland J, Pryde J, Vaid A, Holmes D, Weil MR, Li Y, Wilkins K, Zhao H, Smith SK, Karem K, Reynolds MG, Damon IK.** 2012. Investigation of the first laboratory-acquired human cowpox virus infection in the United States. *J Infect Dis* **206:**63–68.
191. **Venter M, Steyl J, Human S, Weyer J, Zaayman D, Blumberg L, Leman PA, Paweska J, Swanepoel R.** 2010. Transmission of West Nile virus during horse autopsy. *Emerg Infect Dis* **16:**573–575.
192. **Weissenbacher MC, Cura E, Segura EL, Hortal M, Baek LJ, Chu YK, Lee HW.** 1996. Serological evidence of human hantavirus infection in Argentina, Bolivia and Uruguay. *Medicina (B Aires)* **56:**17–22.
193. **Desmyter J, Johnson KM, Deckers C, Leduc JW, Brasseur F, Van Ypersele De Strihou C. .** 1983. Laboratory rat associated outbreak of haemorrhagic fever with renal syndrome due to Hantaan-like virus in Belgium. *Lancet* 33**2:**1445–1448.
194. **Wang GD.** 1985. [Outbreak of hemorrhagic fever with renal syndrome caused by a laboratory animal (white rat) infection]. *Zhonghua Liu Xing Bing Xue Za Zhi* **6:**233–235.
195. **Zhang YZ, Dong X, Li X, Ma C, Xiong HP, Yan GJ, Gao N, Jiang DM, Li MH, Li LP, Zou Y, Plyusnin A.** 2009. Seoul virus and hantavirus disease, Shenyang, People's Republic of China. *Emerg Infect Dis* **15:**200–206.
196. **Zhang Y, Zhang H, Dong X, Yuan J, Zhang H, Yang X, Zhou P, Ge X, Li Y, Wang LF, Shi Z.** 2010. Hantavirus outbreak associated with laboratory rats in Yunnan, China. *Infect Genet Evol* **10:**638–644.

197. **Douron E, Moriniere B, Matheron S, Girard PM, Gonzalez J-P, Hirsch F, McCormick JB.** 1984. HFRS after a wild rodent bite in the Haute-Savoie—and risk of exposure to Hantaan-like virus in a Paris laboratory. *Lancet* **323:**676–677.
198. **Kawamata J, Yamanouchi T, Dohmae K, Miyamoto H, Takahaski M, Yamanishi K, Kurata T, Lee HW.** 1987. Control of laboratory acquired hemorrhagic fever with renal syndrome (HFRS) in Japan. *Lab Anim Sci* **37:**431–436.
199. **Umenai T, Woo Lee P, Toyoda T, Yoshinaga K, Horiuchi T, Wang Lee H, Saito T, Hongo M, Ishida N.** 1979. Korean haemorrhagic fever in staff in an animal laboratory. *Lancet* **313:**1314–1316.
200. **Cho SH, Yun YS, Kang D, Kim S, Kim IS, Hong ST.** 1999. Laboratory-acquired infections with hantavirus at a research unit of medical school in Seoul, 1996. *Korean J Prev Med* **32:**269–275.
201. **Lloyd G, Bowen ET, Jones N, Pendry A.** 1984. HFRS outbreak associated with laboratory rats in UK. *Lancet* **323:**1175–1176.
202. **Lloyd G, Jones N.** 1986. Infection of laboratory workers with hantavirus acquired from immunocytomas propagated in laboratory rats. *J Infect* **12:**117–125.
203. **Wong TW, Chan YC, Yap EH, Joo YG, Lee HW, Lee PW, Yanagihara R, Gibbs CJ Jr, Gajdusek DC.** 1988. Serological evidence of hantavirus infection in laboratory rats and personnel. *Int J Epidemiol* **17:**887–890.
204. **Dykewicz CA, Dato VM, Fisher-Hoch SP, Howarth MV, Perez-Oronoz GI, Ostroff SM, Gary H Jr, Schonberger LB, McCormick JB.** 1992. Lymphocytic choriomeningitis outbreak associated with nude mice in a research institute. *JAMA* **267:**1349–1353.
205. **Centers for Disease Control and Prevention (CDC).** 1998. Fatal Cercopithecine herpesvirus 1 (B virus) infection following a mucocutaneous exposure and interim recommendations for worker protection. *MMWR Morb Mortal Wkly Rep* **47:**1073–1076, 1083.
206. **Centers for Disease Control (CDC).** 1990. Update: filovirus infection in animal handlers. *MMWR Morb Mortal Wkly Rep* **39:**221.
207. **Centers for Disease Control (CDC).** 1990. Update: ebola-related filovirus infection in nonhuman primates and interim guidelines for handling nonhuman primates during transit and quarantine. *MMWR Morb Mortal Wkly Rep* **39:**22–24, 29–30.
208. **Centers for Disease Control (CDC).** 1990. Update: filovirus infection associated with contact with nonhuman primates or their tissues. *MMWR Morb Mortal Wkly Rep* **39:**404–405.
209. **Lerche NW, Switzer WM, Yee JL, Shanmugam V, Rosenthal AN, Chapman LE, Folks TM, Heneine W.** 2001. Evidence of infection with simian type D retrovirus in persons occupationally exposed to nonhuman primates. *J Virol* **75:**1783–1789.
210. **Centers for Disease Control and Prevention (CDC).** 1997. Nonhuman primate spumavirus infections among persons with occupational exposure—United States, 1996. *MMWR Morb Mortal Wkly Rep* **46:**129–131.
211. **Mouinga-Ondémé A, Betsem E, Caron M, Makuwa M, Sallé B, Renault N, Saib A, Telfer P, Marx P, Gessain A, Kazanji M.** 2010. Two distinct variants of simian foamy virus in naturally infected mandrills (Mandrillus sphinx) and cross-species transmission to humans. *Retrovirology* **7:**105.
212. **Schweizer M, Falcone V, Gänge J, Turek R, Neumann-Haefelin D.** 1997. Simian foamy virus isolated from an accidentally infected human individual. *J Virol* **71:**4821–4824.
213. **Switzer WM, Bhullar V, Shanmugam V, Cong ME, Parekh B, Lerche NW, Yee JL, Ely JJ, Boneva R, Chapman LE, Folks TM, Heneine W.** 2004. Frequent simian foamy virus infection in persons occupationally exposed to nonhuman primates. *J Virol* **78:**2780–2789.
214. **Chiu CY, Yagi S, Lu X, Yu G, Chen EC, Liu M, Dick EJ Jr, Carey KD, Erdman DD, Leland MM, Patterson JL.** 2013. A novel adenovirus species associated with an acute respiratory outbreak in a baboon colony and evidence of coincident human infection. *MBio* **4:**e00084-13.
215. **Alibek K, Handelman S.** 1999. *Biohazard*. Dell Publishing of Random House, New York.
216. **International Society for Infectious Diseases.** 2004. Ebola lab accident death—Russia (Siberia). Archive number 20040522.1377, http://www.promedmail.org.
217. **Le Guenno B, Formenty P, Wyers M, Gounon P, Walker F, Boesch C.** 1995. Isolation and partial characterisation of a new strain of Ebola virus. *Lancet* **345:**1271–1274.
218. **Fonseca K, Prince GD, Bratvold J, Fox JD, Pybus M, Preksaitis JK, Tilley P.** 2005. West Nile virus infection and conjunctival exposure. *Emerg Infect Dis* **11:**1648–1649.
219. **Smith AW, Iversen PL, Skilling DE, Stein DA, Bok K, Matson DO.** 2006. Vesivirus viremia and seroprevalence in humans. *J Med Virol* **78:**693–701.
220. **Smith AW, Berry ES, Skilling DE, Barlough JE, Poet SE, Berke T, Mead J, Matson DO.** 1998. In vitro isolation and characterization of a calicivirus causing a vesicular disease of the hands and feet. *Clin Infect Dis* **26:**434–439.
221. **Fulhorst CF, Milazzo ML, Armstrong LR, Childs JE, Rollin PE, Khabbaz R, Peters CJ, Ksiazek TG.** 2007. Hantavirus and arenavirus antibodies in persons with occupational rodent exposure. *Emerg Infect Dis* **13:**532–538.
222. **Skinhøj P, Søeby M.** 1981. Viral hepatitis in Danish health care personnel, 1974–78. *J Clin Pathol* **34:**408–411.
223. **United States Department of Labor.** 1991. Occupational exposure to bloodborne pathogens. Fed Reg **56:**64175–64182.
224. **Mahoney FJ, Stewart K, Hu H, Coleman P, Alter MJ.** 1997. Progress toward the elimination of hepatitis B virus transmission among health care workers in the United States. *Arch Intern Med* **157:**2601–2605.
225. **Wacławik J, Gasiorowski J, Inglot M, Andrzejak R, Gładysz A.** 2003. [Epidemiology of occupational infectious diseases in health care workers]. *Med Pr* **54:**535–541.
226. **Britton S, van den Hurk AF, Simmons RJ, Pyke AT, Northill JA, McCarthy J, McCormack J.** 2011. Laboratory-acquired dengue virus infection—a case report. *PLoS Negl Trop Dis* **5:**e1324.
227. **World Health Organization Western Pacific Region.** 2004. *Summary of China's Investigation into the April outbreak*. World Health Organization Western Pacific Region, Manila, Philippines.
228. **Lim PL, Kurup A, Gopalakrishna G, Chan KP, Wong CW, Ng LC, Se-Thoe SY, Oon L, Bai X, Stanton LW, Ruan Y, Miller LD, Vega VB, James L, Ooi PL, Kai CS, Olsen SJ, Ang B, Leo YS.** 2004. Laboratory-acquired severe acute respiratory syndrome. *N Engl J Med* **350:**1740–1745.
229. **World Health Organization Western Pacific Region.** 2003. Severe acute respinratory syndrome (SARS) in Taiwan, China 17 December 2003. http://www.who.int/csr/don/2003_12_17/en/.
230. **Junt T, Heraud JM, Lelarge J, Labeau B, Talarmin A.** 1999. Determination of natural versus laboratory human infection with Mayaro virus by molecular analysis. *Epidemiol Infect* **123:**511–513.
231. **Raoult D, Renesto P, Brouqui P.** 2006. Laboratory infection of a technician by mimivirus. *Ann Intern Med* **144:**702–703.
232. **van der Meyden CH, Erasmus BJ, Swanepoel R, Prozesky OW.** 1992. Encephalitis and chorioretinitis associated with neurotropic African horsesickness virus infection in laboratory workers. Part I. Clinical and neurological observations. *S Afr Med J* **81:**451–454.
233. **Scherer W.** 1980. Laboratory safety for arboviruses and certain other viruses of vertebrates. *Am J Trop Med Hyg* **29:**1359–1381.
234. **Tomori O, Monath TP, O'Connor EH, Lee VH, Cropp CB.** 1981. Arbovirus infections among laboratory personnel in Ibadan, Nigeria. *Am J Trop Med Hyg* **30:**855–861.
235. **Barry M, Russi M, Armstrong L, Geller D, Tesh R, Dembry L, Gonzalez JP, Khan AS, Peters CJ.** 1995. Brief report: treatment

of a laboratory-acquired Sabiá virus infection. *N Engl J Med* **333:** 294–296.
236. **Gaidomovich YSA, Burenko M, Leschinskaya HV.** 2000. Human laboratory acquired arbo-, arena-, and hantavirus. *Appl Biosaf* **5:**5–11.
237. **Brummer-Korvenkontio M, Vaheri A, Hovi T, von Bonsdorff CH, Vuorimies J, Manni T, Penttinen K, Oker-Blom N, Lähdevirta J.** 1980. *Nephropathia epidemica:* detection of antigen in bank voles and serologic diagnosis of human infection. *J Infect Dis* **141:**131–134.
238. **Centers for Disease Control and Prevention (CDC).** 1994. Bolivian hemorrhagic fever—El Beni Department, Bolivia, 1994. *MMWR Morb Mortal Wkly Rep* **43:**943–946.
239. **Wentworth DE, McGregor MW, Macklin MD, Neumann V, Hinshaw VS.** 1997. Transmission of swine influenza virus to humans after exposure to experimentally infected pigs. *J Infect Dis* **175:**7–15.
240. **Artenstein AW, Hicks CB, Goodwin BS Jr, Hilliard JK.** 1991. Human infection with B virus following a needlestick injury. *Rev Infect Dis* **13:**288–291.
241. **Davenport DS, Johnson DR, Holmes GP, Jewett DA, Ross SC, Hilliard JK.** 1994. Diagnosis and management of human B virus (Herpesvirus simiae) infections in Michigan. *Clin Infect Dis* **19:**33–41.
242. **Freifeld AG, Hilliard J, Southers J, Murray M, Savarese B, Schmitt JM, Straus SE.** 1995. A controlled seroprevalence survey of primate handlers for evidence of asymptomatic herpes B virus infection. *J Infect Dis* **171:**1031–1034.
243. **Holmes GP, et al.** 1990. B virus (Herpesvirus simiae) infection in humans: epidemiologic investigation of a cluster. *Ann Intern Med* **112:**833–839.
244. **Centers for Disease Control and Prevention.** 1987. B-virus infection in humans—Pensacola, Florida. MMWR Morb Mortal Wkly Rep 36**:**289–290, 295–286.
245. **Centers for Disease Control (CDC).** 1989. B virus infections in humans—Michigan. *MMWR Morb Mortal Wkly Rep* **38:** 453–454.
246. **Scinicariello F, English WJ, Hilliard J.** 1993. Identification by PCR of meningitis caused by herpes B virus. *Lancet* **341:**1660–1661.
247. **Ilkal MA, Dhanda V, Rodrigues JJ, Mohan Rao CV, Mourya DT.** 1984. Xenodiagnosis of laboratory acquired dengue infection by mosquito inoculation & immunofluorescence. *Indian J Med Res* **79:**587–590.
248. **Wu H-S, Wu W-C, Kuo H-S.** 2009. A three-year experience to implement laboratory biosafety regulations in Taiwan. *Appl Biosaf* **14:**33–36.
249. **Moore DM, MacKenzie WF, Doepel F, Hansen TN.** 1983. Contagious ecthyma in lambs and laboratory personnel. *Lab Anim Sci* **33:**473–475.
250. **Ippolito G, Puro V, Petrosillo N, De Carli G.** 1999. Surveillance of occupational exposure to bloodborne pathogens in health care workers: the Italian national programme. *Euro Surveill* **4:** 33–36.
251. **Khabbaz RF, Rowe T, Heneine WM, Kaplan JE, Folks TM, Schable CA, George JR, Pau C, Parekh BS, Curran JW, Schochetman G, Lairmore MD, Murphey-Corb M.** 1992. Simian immunodeficiency virus needlestick accident in a laboratory worker. *Lancet* **340:**271–273.
252. **Venter M, Burt FJ, Blumberg L, Fickl H, Paweska J, Swanepoel R.** 2009. Cytokine induction after laboratory-acquired West Nile virus infection. *N Engl J Med* **360:**1260–1262.
253. **Centers for Disease Control and Prevention (CDC).** 2002. Laboratory-acquired West Nile virus infections—United States, 2002. *MMWR Morb Mortal Wkly Rep* **51:**1133–1135.
254. **Moussatché N, Tuyama M, Kato SE, Castro AP, Njaine B, Peralta RH, Peralta JM, Damaso CR, Barroso PF.** 2003. Accidental infection of laboratory worker with vaccinia virus. *Emerg Infect Dis* **9:**724–726.
255. **Ertem GT, Tulek N, Oral B, Kinikli S.** 2005. Therapy of acute hepatitis C with interferon-alpha2b plus ribavirin in a health care worker. *Acta Gastroenterol Belg* **68:**104–106.
256. **Kotturi MF, Swann JA, Peters B, Arlehamn CL, Sidney J, Kolla RV, James EA, Akondy RS, Ahmed R, Kwok WW, Buchmeier MJ, Sette A.** 2011. Human $CD8^+$ and $CD4^+$ T cell memory to lymphocytic choriomeningitis virus infection. *J Virol* **85:**11770–11780.
257. **DeCarli G, Perry J, Jagger J.** 2004. Occupational co-infection with HIV and HCV. *Adv Expo Prev* **7:**13–18.
258. **Khabbaz RF, Heneine W, George JR, Parekh B, Rowe T, Woods T, Switzer WM, McClure HM, Murphey-Corb M, Folks TM.** 1994. Brief report: infection of a laboratory worker with simian immunodeficiency virus. *N Engl J Med* **330:**172–177.
259. **Langford MP, Stanton GJ, Barber JC, Baron S.** 1979. Early-appearing antiviral activity in human tears during a case of picornavirus epidemic conjunctivitis. *J Infect Dis* **139:**653–658.
260. **Ando Y, Iwasaki T, Terao K, Nishimura H, Tamura S.** 2001. Conjunctivitis following accidental exposure to influenza B virus/Shangdong/07/97. *J Infect* **42:**223–224.
261. **Webster RG, Geraci J, Petursson G, Skirnisson K.** 1981. Conjunctivitis in human beings caused by influenza A virus of seals. *N Engl J Med* **304:**911.
262. **Loeb M, Zando I, Orvidas MC, Bialachowski A, Groves D, Mahoney J.** 2003. Laboratory-acquired vaccinia infection. *Can Commun Dis Rep* **29:**134–136.
263. **Wlodaver CG, Palumbo GJ, Waner JL.** 2004. Laboratory-acquired vaccinia infection. *J Clin Virol* **29:**167–170.
264. **Lewis FM, Chernak E, Goldman E, Li Y, Karem K, Damon IK, Henkel R, Newbern EC, Ross P, Johnson CC.** 2006. Ocular vaccinia infection in laboratory worker, Philadelphia, 2004. *Emerg Infect Dis* **12:**134–137.
265. **Højlyng N, Holten-Andersen W, Jepsen S.** 1987. Cryptosporidiosis: a case of airborne transmission. *Lancet* **330:**271–272.
266. **Pohjola S, Oksanen H, Jokipii L, Jokipii AM.** 1986. Outbreak of cryptosporidiosis among veterinary students. *Scand J Infect Dis* **18:**173–178.
267. **Reif JS, Wimmer L, Smith JA, Dargatz DA, Cheney JM.** 1989. Human cryptosporidiosis associated with an epizootic in calves. *Am J Public Health* **79:**1528–1530.
268. **Philpott MS, Fautin CH, Bird KE, O'Reilly KL.** 2015. A laboratory-associated outbreak of cryptosporidiosis. *Appl Biosaf* **20:**130–136.
269. **Drinkard LN, Halbritter A, Nguyen GT, Sertich PL, King M, Bowman S, Huxta R, Guagenti M.** 2015. Notes from the field: outbreak of cryptosporidiosis among veterinary medicine students—Philadelphia, Pennsylvania, February 2015. *MMWR Morb Mortal Wkly Rep* **64:**773.
270. **Herwaldt BL, Juranek DD.** 1993. Laboratory-acquired malaria, leishmaniasis, trypanosomiasis, and toxoplasmosis. *Am J Trop Med Hyg* **48:**313–323.
271. **Centers for Disease Control and Prevention.** 1984. Malaria surveillance annual summary, 1982. *MMWR Morb Mortal Wkly Rep*
272. **Mali S, Steele S, Slutsker L, Arguin PM, Centers for Disease Control and Prevention (CDC).** 2008. Malaria surveillance—United States, 2006. *MMWR Surveill Summ* **57:**24–39.
273. **Cullen KA, Arguin PM, Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention (CDC).** 2013. Malaria surveillance—United States, 2011. *MMWR Surveill Summ* **62:**1–17.
274. **Cullen KA, Arguin PM, Centers for Disease Control and Prevention (CDC).** 2014. Malaria surveillance—United States, 2012. *MMWR Surveill Summ* **63:**1–22.
275. **Centers for Disease Control and Prevention.** 1980. Chagas disease—Michigan. *Morb Mortal Wkly Rep* **29:**147–148.
276. **Sampaio RN, de Lima LM, Vexenat A, Cuba CC, Barreto AC, Marsden PD.** 1983. A laboratory infection with *Leishmania braziliensis braziliensis. Trans R Soc Trop Med Hyg* **77:**274.

277. **Van Gompel A, Van den Enden E, Van den Ende J, Geerts S.** 1993. Laboratory infection with *Schistosoma mansoni*. *Trans R Soc Trop Med Hyg* **87:**554.
278. **Partanen P, Turunen HJ, Paasivuo RT, Leinikki PO.** 1984. Immunoblot analysis of *Toxoplasma gondii* antigens by human immunoglobulins G, M, and A antibodies at different stages of infection. *J Clin Microbiol* **20:**133–135.
279. **Hermentin K, Hassl A, Picher O, Aspöck H.** 1989. Comparison of different serotests for specific Toxoplasma IgM-antibodies (ISAGA, SPIHA, IFAT) and detection of circulating antigen in two cases of laboratory acquired Toxoplasma infection. *Zentralbl Bakteriol Mikrobiol Hyg [A]* **270:**534–541.
280. **Herwaldt BL.** 2001. Laboratory-acquired parasitic infections from accidental exposures. *Clin Microbiol Rev* **14:**659–688.
281. **Johnson M, Broady K, Angelici MC, Johnson A.** 2003. The relationship between nucleoside triphosphate hydrolase (NTPase) isoform and Toxoplasma strain virulence in rat and human toxoplasmosis. *Microbes Infect* **5:**797–806.
282. **Parker SL, Holliman RE.** 1992. Toxoplasmosis and laboratory workers: a case-control assessment of risk. *Med Lab Sci* **49:** 103–106.
283. **Villavedra M, Battistoni J, Nieto A.** 1999. IgG recognizing 21-24 kDa and 30-33 kDa tachyzoite antigens show maximum avidity maturation during natural and accidental human toxoplasmosis. *Rev Inst Med Trop Sao Paulo* **41:**297–303.
284. **Delgado O, Guevara P, Silva S, Belfort E, Ramirez JL.** 1996. Follow-up of a human accidental infection by *Leishmania (Viannia) braziliensis* using conventional immunologic techniques and polymerase chain reaction. *Am J Trop Med Hyg* **55:**267–272.
285. **Sadick MD, Locksley RM, Raff HV.** 1984. Development of cellular immunity in cutaneous leishmaniasis due to *Leishmania tropica*. *J Infect Dis* **150:**135–138.
286. **Evans TG, Pearson RD.** 1988. Clinical and immunological responses following accidental inoculation of *Leishmania donovani*. *Trans R Soc Trop Med Hyg* **82:**854–856.
287. **Blagburn BL, Current WL.** 1983. Accidental infection of a researcher with human Cryptosporidium. *J Infect Dis* **148:**772–773.
288. **Williams JL, Innis BT, Burkot TR, Hayes DE, Schneider I.** 1983. Falciparum malaria: accidental transmission to man by mosquitoes after infection with culture-derived gametocytes. *Am J Trop Med Hyg* **32:**657–659.
289. **Freedman DO, MacLean JD, Viloria JB.** 1987. A case of laboratory acquired Leishmania donovani infection; evidence for primary lymphatic dissemination. *Trans R Soc Trop Med Hyg* **81:**118–119.
290. **Hofflin JM, Sadler RH, Araujo FG, Page WE, Remington JS.** 1987. Laboratory-acquired Chagas disease. *Trans R Soc Trop Med Hyg* **81:**437–440.
291. **Baker CC, Farthing CP, Ratnesar P.** 1984. Toxoplasmosis, an innocuous disease? *J Infect* **8:**67–69.
292. **Knobloch J, Demar M.** 1997. Accidental *Leishmania mexicana* infection in an immunosuppressed laboratory technician. *Trop Med Int Health* **2:**1152–1155.
293. **Jensen JB, Capps TC, Carlin JM.** 1981. Clinical drug-resistant falciparum malaria acquired from cultured parasites. *Am J Trop Med Hyg* **30:**523–525.
294. **Felinto de Brito ME, Andrade MS, de Almeida ÉL, Medeiros ÂCR, Werkhäuser RP, Araújo AIF, Brandão-Filho SP, Paiva de Almeida AM, Gomes Rodrigues EH.** 2012. Occupationally acquired american cutaneous leishmaniasis. *Case Rep Dermatol Med* **2012:**279517.
295. **Larson DM, Eckman MR, Alber RL, Goldschmidt VG.** 1983. Primary cutaneous (inoculation) blastomycosis: an occupational hazard to pathologists. *Am J Clin Pathol* **79:**253–255.
296. **Tenenbaum MJ, Greenspan J, Kerkering TM, Utz JP.** 1982. Blastomycosis. *Crit Rev Microbiol* **9:**139–163.
297. **Cooper CR, Dixon DM, Salkin IF.** 1992. Laboratory-acquired sporotrichosis. *J Med Vet Mycol* **30:**169–171.
298. **Ishizaki H, Ikeda M, Kurata Y.** 1979. Lymphocutaneous sporotrichosis caused by accidental inoculation. *J Dermatol* **6:** 321–323.
299. **Mochizuki T, Watanabe S, Kawasaki M, Tanabe H, Ishizaki H.** 2002. A Japanese case of tinea corporis caused by *Arthroderma benhamiae*. *J Dermatol* **29:**221–225.
300. **van Gool T, Biderre C, Delbac F, Wentink-Bonnema E, Peek R, Vivarès CP.** 2004. Serodiagnostic studies in an immunocompetent individual infected with *Encephalitozoon cuniculi*. *J Infect Dis* **189:**2243–2249.
301. **Hilmarsdottir I, Coutellier A, Elbaz J, Klein JM, Datry A, Guého E, Herson S.** 1994. A French case of laboratory-acquired disseminated *Penicillium marneffei* infection in a patient with AIDS. *Clin Infect Dis* **19:**357–358.
302. **Kamalam A, Thambiah AS.** 1979. *Trichophyton simii* infection due to laboratory accident. *Dermatologica* **159:**180–181.
303. **Contreras-Barrera ME, Moreno-Coutiño G, Torres-Guerrero DE, Aguilar-Donis A, Arenas R.** 2009. Eritema multiforme secundario a infección por Trichophyton mentagrophytes. [Erythema multiforme secondary to cutaneous Trichophyton mentagrophytes infection]. *Rev Iberoam Micol* **26:**149–151.
304. **Hironaga M, Fujigaki T, Watanabe S.** 1981. *Trichophyton mentagrophytes* skin infections in laboratory animals as a cause of zoonosis. *Mycopathologia* **73:**101–104.
305. **Shi ZC, Lei PC.** 1986. Occupational mycoses. *Br J Ind Med* **43:**500–501.
306. **United States Food and Drug Agency.**2009. *Bad Bug Book*. http://www.fda.gov/Food/FoodSafety/FoodborneIllness/FoodborneIllnessFoodbornePathogens Natural Toxins/ BadBugBook /ucm071372.
307. **Cohn AC, MacNeil JR, Clark TA, Ortega-Sanchez IR, Briere EZ, Meissner HC, Baker CJ, Messonnier NE, Centers for Disease Control and Prevention (CDC).** 2013. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* **62**(RR-2)**:**1–28.
308. **Kortepeter MG, Martin JW, Rusnak JM, Cieslak TJ, Warfield KL, Anderson EL, Ranadive MV.** 2008. Managing potential laboratory exposure to ebola virus by using a patient biocontainment care unit. *Emerg Infect Dis* **14:**881–887.
309. **Kuhar DT, Henderson DK, Struble KA, Heneine W, Thomas V, Cheever LW, Gomaa A, Panlilio AL, US Public Health Service Working Group.** 2013. Updated US Public Health Service guidelines for the management of occupational exposures to human immunodeficiency virus and recommendations for postexposure prophylaxis. *Infect Control Hosp Epidemiol* **34:**875–892. [corrected in Infect Control Hosp Epidemiol 2013;Nov;34:1238 (Note: Dosage error in article text.)]
310. **U.S. Public Health Service.** 2001. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. *MMWR Recomm Rep* **50**(RR-11)**:**1–52.
311. **Gannon CK.** 2003. Anatomy of an exposure: a hospital lab's recovery of *Brucella melitensis*. *MLO Med Lab Obs* **35:**22–25.
312. **Centers for Disease Control and Prevention (CDC).** 2004. Laboratory exposure to *Burkholderia pseudomallei*—Los Angeles, California, 2003. *MMWR Morb Mortal Wkly Rep* **53:**988–990.
313. **Cahn A, Koslowsky B, Nir-Paz R, Temper V, Hiller N, Karlinsky A, Gur I, Hidalgo-Grass C, Heyman SN, Moses AE, Block C.** 2009. Imported melioidosis, Israel, 2008. *Emerg Infect Dis* **15:** 1809–1811.
314. **Maley MW, Kociuba K, Chan RC.** 2006. Prevention of laboratory-acquired brucellosis: significant side effects of prophylaxis. *Clin Infect Dis* **42:**433–434.
315. **Rusnak JM, Kortepeter MG, Hawley RJ, Boudreau E, Aldis J, Pittman PR.** 2004. Management guidelines for laboratory exposures to agents of bioterrorism. *J Occup Environ Med* **46:** 791–800.

316. **Benoit TJ, Blaney DD, Gee JE, Elrod MG, Hoffmaster AR, Doker TJ, Bower WA, Walke HT, Centers for Disease Control and Prevention (CDC).** 2015. Melioidosis cases and selected reports of occupational exposures to *Burkholderia pseudomallei*—United States, 2008–2013. *MMWR Surveill Summ* **64:**1–9.
317. **Goldman R (ed).** 1995. *Medical Surveillance Program*. Marcel Dekker, Inc, New York..
318. **Centers for Disease Control and Prevention (CDC).** 2000. Laboratory-acquired human glanders—Maryland, May 2000. *MMWR Morb Mortal Wkly Rep* **49:**532–535.
319. **Weinberg ED.** 1999. Iron loading and disease surveillance. *Emerg Infect Dis* **5:**346–352.
320. **Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchmann SD, Hospital Infection Control Practices Advisory Committee.** 1998. Guideline for infection control in healthcare personnel, 1998. *Infect Control Hosp Epidemiol* **19:**407–463.
321. **Agrup G, Belin L, Sjöstedt L, Skerfving S.** 1986. Allergy to laboratory animals in laboratory technicians and animal keepers. *Br J Ind Med* **43:**192–198.
322. **Committee AIHAB.**1995. Biogenic allergens, p 44–48, *Biosafety Reference Manual,* 2nd ed. American Industrial Hygiene Association, Fairfax, VA.
323. **Phillips GB.** 1965. *Causal Factors in Microbiology Laboratory Accidents and Infections.* National Technical Information Service, Fort Detrick, MD.
324. **Martin JC.** 1980. Behavior factors in laboratory safety: personnel characteristics and modification of unsafe acts, p 321–342. *In* Fuscaldo AA, Erlick BJ, Hindman B (ed), *Laboratory Safety: Theory and Practice.* Academic Press, New York.
325. **Kaiser J.** 2011. Updated: University of Chicago Microbiologist Infected from Possible Lab Accident. *Science*, AAAS online. http://www.sciencemag.org/news/2011/09/updated-university-chicago-microbiologist-infected-possible-lab-accident.
326. **Mansheim BJ, Kasper DL.** 1979. Detection of anticapsular antibodies to *Bacteroides asaccharolyticus* in serum from rabbits and humans by use of an enzyme-linked immunosorbent assay. *J Infect Dis* **140:**945–951.
327. **Burstyn DG, Baraff LJ, Peppler MS, Leake RD, St Geme J Jr, Manclark CR.** 1983. Serological response to filamentous hemagglutinin and lymphocytosis-promoting toxin of *Bordetella pertussis. Infect Immun* **41:**1150–1156.
328. **Al Dahouk S, Nöckler K, Hensel A, Tomaso H, Scholz HC, Hagen RM, Neubauer H.** 2005. Human brucellosis in a nonendemic country: a report from Germany, 2002 and 2003. *Eur J Clin Microbiol Infect Dis* **24:**450–456.
329. **Breton I, Burucoa C, Grignon B, Fauchere JL, Becq Giraudon B.** 1995. Brucellose acquise au laboratoire. [Laboratory-acquired brucellosis.] *Med Mal Infect* **25:**549–551.
330. **Elidan J, Michel J, Gay I, Springer H.** 1985. Ear involvement in human brucellosis. *J Laryngol Otol* **99:**289–291.
331. **Fabiansen C, Knudsen JD, Lebech AM.** 2008. [Laboratory-acquired brucellosis]. *Ugeskr Laeger* **170:**2161.
332. **Grist NR, Emslie JA.** 1991. Infections in British clinical laboratories, 1988-1989. *J Clin Pathol* **44:**667–669.
333. **Marianelli C, Petrucca A, Pasquali P, Ciuchini F, Papadopoulou S, Cipriani P.** 2008. Use of MLVA-16 typing to trace the source of a laboratory-acquired Brucella infection. *J Hosp Infect* **68:**274–276.
334. **Martin-Mazuelos E, Nogales MC, Florez C, Gómez-Mateos JM, Lozano F, Sanchez A.** 1994. Outbreak of *Brucella melitensis* among microbiology laboratory workers. *J Clin Microbiol* **32:**2035–2036.
335. **Podolak E.** 2010. Researcher suspended for authorized experiments. *Biotechniques*. http://www.biotechniques.com/news/Researcher-suspended-for-unauthorized-experiments/biotechniques-296880.html
336. **Rees RK, Graves M, Caton N, Ely JM, Probert WS.** 2009. Single tube identification and strain typing of *Brucella melitensis* by multiplex PCR. *J Microbiol Methods* **78:**66–70.
337. **Rodrigues AL, Silva SK, Pinto BL, Silva JB, Tupinambás U.** 2013. Outbreak of laboratory-acquired *Brucella abortus* in Brazil: a case report. *Rev Soc Bras Med Trop* **46:**791–794.
338. **Sayin-Kutlu S, Kutlu M, Ergonul O, Akalin S, Guven T, Demiroglu YZ, Acicbe O, Akova M, Occupational Infectious Diseases Study Group.** 2012. Laboratory-acquired brucellosis in Turkey. *J Hosp Infect* **80:**326–330.
339. **Smith JA, Skidmore AG, Andersen RG.** 1980. Brucellosis in a laboratory technologist. *Can Med Assoc J* **122:**1231–1232.
340. **Wansbrough L.** 2010. Brucella in Hospital Laboratory Workers: Epi Update, a publication of the Bureau of Immununology, June 2010. Florida Department of Health. http://floridahealth.gov/diseases-and-conditions/disease-reporting-and management/florida-epidemic-intelligence-service/_documents/2009-2011/documents/june2010epiupdate.pdf.
341. **Wünschel M, Olszowski AM, Weissgerber P, Wülker N, Kluba T.** 2011. [Chronic brucellosis: a rare cause of septic loosening of arthroplasties with high risk of laboratory-acquired infections]. *Z Orthop Unfall* **149:**33–36.
342. **Ashdown LR.** 1992. Melioidosis and safety in the clinical laboratory. *J Hosp Infect* **21:**301–306.
343. **Oates JD, Hodgin UG Jr.** 1981. Laboratory-acquired *Campylobacter enteritis. South Med J* **74:**83.
344. **Penner JL, Hennessy JN, Mills SD, Bradbury WC.** 1983. Application of serotyping and chromosomal restriction endonuclease digest analysis in investigating a laboratory-acquired case of *Campylobacter jejun*i enteritis. *J Clin Microbiol* **18:**1427–1428.
345. **Hyman CL, Augenbraun MH, Roblin PM, Schachter J, Hammerschlag MR.** 1991. Asymptomatic respiratory tract infection with *Chlamydia pneumoniae TWAR. J Clin Microbiol* **29:**2082–2083.
346. **Surcel HM, Syrjälä H, Leinonen M, Saikku P, Herva E.** 1993. Cell-mediated immunity to *Chlamydia pneumoniae* measured as lymphocyte blast transformation in vitro. *Infect Immun* **61:**2196–2199.
347. **Tuuminen T, Salo K, Surcel HM.** 2002. A casuistic immunologic response in primary and repeated *Chlamydophila pneumoniae* infections in an immunocompetent individual. *J Infect* **45:**202–206.
348. **Egawa T, Hara H, Kawase I, Masuno T, Asari S, Sakurai M, Kishimoto S.** 1990. Human pulmonary infection with *Corynebacterium equi. Eur Respir J* **3:**240–242.
349. **Johanson RE.** 2004. *Enterobacter aerogenes* needlestick leads to improved biological management system. *Appl Biosaf* **9:**65–67.
350. **Booth L, Rowe B.** 1993. Possible occupational acquisition of *Escherichia coli O157* infection. *Lancet* **342:**1298–1299.
351. **Campbell MJ.** 2015. Characterizing accidents, exposures, and laboratory-acquired infections reprted to the National Institutes of Health Office of Biotechnology Activities (NIH/OBA) Division Under the NIH Guidelines for Work with Recombinant DNA materials from 1976–2010. *Appl Biosaf* **20:**12–26.
352. **Ostroff SM, Kobayashi JM, Lewis JH.** 1989. Infections with *Escherichia coli O157:H7* in Washington State. The first year of statewide disease surveillance. *JAMA* **262:**355–359.
353. **Parry SH, Abraham SN, Feavers IM, Lee M, Jones MR, Bint AJ, Sussman M.** 1981. Urinary tract infection due to laboratory-acquired *Escherichia coli:* relation to virulence. *Br Med J (Clin Res Ed)* **282:**949–950.
354. **Public Health Service Laboratory.** 1996. Escherichia coli O 157 infection acquired in the laboratory. *Commun Dis Rep CDR Wkly* **6:**239.
355. **Gilbert GL.** 2015. Laboratory testing in management of patients with suspected Ebolavirus disease: infection control and safety. *Pathology* **47:**400–402.

356. **Rao GG, Saunders BP, Masterton RG.** 1996. Laboratory acquired verotoxin producing *Escherichia coli (VTEC)* infection. *J Hosp Infect* **33:**228–230.
357. **Donnelly TM, Behr M.** 2000. Laboratory-acquired lymphadenopathy in a veterinary pathologist. *Lab Anim (NY)* **29:**23–25.
358. **Hornick R.** 2001. Tularemia revisited. *N Engl J Med* **345:**1637–1639.
359. **Janovská S, Pávková I, Reichelová M, Hubálek M, Stulík J, Macela A.** 2007. Proteomic analysis of antibody response in a case of laboratory-acquired infection with *Francisella tularensis subsp. tularensis*. *Folia Microbiol (Praha)* **52:**194–198.
360. **Lam ST, Sammons-Jackson W, Sherwood J, Ressner R.** 2012. Laboratory-acquired tularemia successfully treated with ciprofloxacin. *Infect Dis Clin Pract* **20:**204–207.
361. **Mailles A, V. Vaillant, V. Bilan.** 2013. Bilan de 10 annees de surbeillance de la tularemie chez l'homme en France. Institue de Veile Sanitaire, Legal depot September 2013.
362. **Trees DL, Arko RJ, Hill GD, Morse SA.** 1992. Laboratory-acquired infection with *Haemophilus ducreyi* type strain CIP 542. *Med Microl Lett* **1:**330–337.
363. **Matysiak-Budnik T, Briet F, Heyman M, Mégraud F.** 1995. Laboratory-acquired *Helicobacter pylori* infection. *Lancet* **346:** 1489–1490.
364. **Raymond J, Bingen E, Brahimi N, Bergeret M, Kalach N.** 1996. Randomly amplified polymorphic DNA analysis in suspected laboratory *Helicobacter pylori* infection. *Lancet* **347:**975.
365. **Takata T, Shirotani T, Okada M, Kanda M, Fujimoto S, Ono J.** 1998. Acute hemorrhagic gastropathy with multiple shallow ulcers and duodenitis caused by a laboratory infection of *Helicobacter pylori*. *Gastrointest Endosc* **47:**291–294.
366. **Broughton ES, Flack LE.** 1986. The susceptibility of a strain of *Leptospira interrogans* serogroup icterohaemorrhagiae to amoxycillin, erythromycin, lincomycin, tetracycline, oxytetracycline and minocycline. *Zentralbl Bakteriol Mikrobiol Hyg [A]* **261:**425–431.
367. **Gilks CF, Lambert HP, Broughton ES, Baker CC.** 1988. Failure of penicillin prophylaxis in laboratory acquired leptospirosis. *Postgrad Med J* **64:**236–238.
368. **Sugunan AP, Natarajaseenivasan K, Vijayachari P, Sehgal SC.** 2004. Percutaneous exposure resulting in laboratory-acquired leptospirosis—a case report. *J Med Microbiol* **53:**1259–1262.
369. **Cooke MM, Gear AJ, Naidoo A, Collins DM.** 2002. Accidental *Mycobacterium bovis* infection in a veterinarian. *N Z Vet J* **50:** 36–38.
370. **Brutus JP, Lamraski G, Zirak C, Hauzeur JP, Thys JP, Schuind F.** 2005. Septic monoarthritis of the first carpo-metacarpal joint caused by *Mycobacterium kansasii*. *Chir Main* **24:**52–54.
371. **Weber T, Tumani H, Holdorff B, Collinge J, Palmer M, Kretzschmar HA, Felgenhauer K.** 1993. Transmission of Creutzfeldt-Jakob disease by handling of dura mater. *Lancet* **341:** 123–124.
372. **Washington State Department of Labor and Industries.**2004. Region 2- Seattle Office. Inspection report on laboratory associated infections due to *Mycobacterium tuberculosis*. Inspection 307855056. http://www.sunshine-project.org/idriuwmadchamber.pdf.
373. **Duray PH, Flannery B, Brown S.** 1981. Tuberculosis infection from preparation of frozen sections. *N Engl J Med* **305:**167.
374. **Leyten EM, Mulder B, Prins C, Weldingh K, Andersen P, Ottenhoff TH, van Dissel JT, Arend SM.** 2006. Use of enzyme-linked immunospot assay with *Mycobacterium tuberculosis*-specific peptides for diagnosis of recent infection with *M. tuberculosis* after accidental laboratory exposure. *J Clin Microbiol* **44:**1197–1201.
375. **Mazurek GH, Cave MD, Eisenach KD, Wallace RJ Jr, Bates JH, Crawford JT.** 1991. Chromosomal DNA fingerprint patterns produced with IS6110 as strain-specific markers for epidemiologic study of tuberculosis. *J Clin Microbiol* **29:**2030–2033.
376. **Sharma VK, Kumar B, Radotra BD, Kaur S.** 1990. Cutaneous inoculation tuberculosis in laboratory personnel. *Int J Dermatol* **29:**293–294.
377. **Sugita M, Tsutsumi Y, Suchi M, Kasuga H.** 1989. High incidence of pulmonary tuberculosis in pathologists at Tokai University Hospital: an epidemiological study. *Tokai J Exp Clin Med* **14:**55–59.
378. **Alonso-Echanove J, Granich RM, Laszlo A, Chu G, Borja N, Blas R, Olortegui A, Binkin NJ, Jarvis WR.** 2001. Occupational transmission of *Mycobacterium tuberculosis* to health care workers in a university hospital in Lima, Peru. *Clin Infect Dis* **33:**589–596.
379. **Bruins SC, Tight RR.** 1979. Laboratory-acquired gonococcal conjunctivitis. *JAMA* **241:**274.
380. **Centers for Disease Control (CDC).** 1981. Gonococcal eye infections in adults—California, Texas, Germany. *MMWR Morb Mortal Wkly Rep* **30:**341–343.
381. **Malhotra R, Karim QN, Acheson JF.** 1998. Hospital-acquired adult gonococcal conjunctivitis. *J Infect* **37:**305.
382. **Podgore JK, Holmes KK.** 1981. Ocular gonococcal infection with minimal or no inflammatory response. *JAMA* **246:**242–243.
383. **Zajdowicz TR, Kerbs SB, Berg SW, Harrison WO.** 1984. Laboratory-acquired gonococcal conjunctivitis: successful treatment with single-dose ceftriaxone. *Sex Transm Dis* **11:**28–29.
384. **Christen G, Tagan D.** 2004. Infection à Neisseria meningitidis acquise en laboratoire. [Laboratory-acquired Neisseria meningitidis infection]. *Med Mal Infect* **34:**137–138.
385. **Guibourdenche M, Darchis JP, Boisivon A, Collatz E, Riou JY.** 1994. Enzyme electrophoresis, sero- and subtyping, and outer membrane protein characterization of two *Neisseria meningitidis* strains involved in laboratory-acquired infections. *J Clin Microbiol* **32:**701–704.
386. **Petty BG, Sowa DT, Charache P.** 1983. Polymicrobial polyarticular septic arthritis. *JAMA* **249:**2069–2072.
387. **Public Health Service Laboratory.** 1992. Laboratory-acquired meningococcal infection. *Commun Dis Rep CDR Wkly* **2:**39.
388. **Woods JP, Cannon JG.** 1990. Variation in expression of class 1 and class 5 outer membrane proteins during nasopharyngeal carriage of *Neisseria meningitidis*. *Infect Immun* **58:**569–572.
389. **Ashdown L, Cassidy J.** 1991. Successive *Salmonella Give* and *Salmonella Typhi* infections, laboratory-acquired. *Pathology* **23:** 233–234.
390. **Barker A, Duster M, Van Hoof S, Safdar N.** 2015. Nontyphoidal *Salmonella*: an occupational hazard for clinical laboratory workers. *Appl Biosaf* **20:**72–74.
391. **Holmes MB, Johnson DL, Fiumara NJ, McCormack WM.** 1980. Acquisition of typhoid fever from proficiency-testing specimens. *N Engl J Med* **303:**519–521.
392. **Koay AS, Jegathesan M, Rohani MY, Cheong YM.** 1997. Pulsed-field gel electrophoresis as an epidemiologic tool in the investigation of laboratory acquired *Salmonella typhi* infection. *Southeast Asian J Trop Med Public Health* **28:**82–84.
393. **Lester A, Mygind O, Jensen KT, Jarløv JO, Schønheyder HC.** 1994. [Typhoid and paratyphoid fever in Denmark 1986–1990. Epidemiologic aspects and the extent of bacteriological follow-up of patients]. *Ugeskr Laeger* **156:**3770–3775.
394. **Mermin JH, Townes JM, Gerber M, Dolan N, Mintz ED, Tauxe RV.** 1998. Typhoid fever in the United States, 1985–1994: changing risks of international travel and increasing antimicrobial resistance. *Arch Intern Med* **158:**633–638.
395. **Thong K-L, Cheong Y-M, Pang T.** 1996. A probable case of laboratory-acquired infection with salmonella typhi: evidence from phage typing, antibiograms, and analysis by pulsed-field gel electrophoresis. *Int J Infect Dis* **1:**95–97.
396. **Dadswell JV.** 1983. Laboratory acquired shigellosis. *Br Med J (Clin Res Ed)* **286:**58.
397. **Aleksić S, Bockemühl J, Degner I.** 1981. Imported shigellosis: aerogenic *Shigella boydii 74* (Sachs A 12) in a traveller followed

by two cases of laboratory-associated infections. *Tropenmed Parasitol* **32:**61–64.
398. **Kolavic SA, Kimura A, Simons SL, Slutsker L, Barth S, Haley CE.** 1997. An outbreak of *Shigella dysenteriae* type 2 among laboratory workers due to intentional food contamination. *JAMA* **278:**396–398.
399. **Van Bohemen CG, Nabbe AJ, Zanen HC.** 1985. IgA response during accidental infection with *Shigella flexneri*. *Lancet* **326:** 673.
400. **Gosbell IB, Mercer JL, Neville SA.** 2003. Laboratory-acquired *EMRSA-15* infection. *J Hosp Infect* **54:**324–325.
401. **Wagenvoort JH, De Brauwer EI, Gronenschild JM, Toenbreker HM, Bonnemayers GP, Bilkert-Mooiman MA.** 2006. Laboratory-acquired meticillin-resistant *Staphylococcus aureus* (MRSA) in two microbiology laboratory technicians. *Eur J Clin Microbiol Infect Dis* **25:**470–472.
402. **Anderson LC, Leary SL, Manning PJ.** 1983. Rat-bite fever in animal research laboratory personnel. *Lab Anim Sci* **33:**292–294.
403. **Hawkey PM, Pedler SJ, Southall PJ.** 1980. *Streptococcus pyogenes:* a forgotten occupational hazard in the mortuary. *BMJ* **281:**1058.
404. **Kurl DN.** 1981. Laboratory-acquired human infection with group A type 50 streptococci. *Lancet* **318:**752.
405. **Little JS, O'Reilly MJ, Higbee JW, Camp RA.** 1984. Suppurative flexor tenosynovitis after accidental self-inoculation with *Streptococcus pneumoniae type I*. *JAMA* **252:**3003–3004.
406. **Raviglione MC, Tierno PM, Ottuso P, Klemes AB, Davidson M.** 1990. Group G streptococcal meningitis and sepsis in a patient with AIDS. A method to biotype group G streptococcus. *Diagn Microbiol Infect Dis* **13:**261–264.
407. **Anonymous.** 1991. Sveskt kolerafall trolig smitta i laboratorium. [A Swedish case of cholera of probable laboratory origin.] *Lakartidningen* **89:**3668.
408. **Lee KK, Liu PC, Huang CY.** 2003. *Vibrio parahaemolyticus* infectious for both humans and edible mollusk abalone. *Microbes Infect* **5:**481–485.
409. **Graham T.** 2013. I am the laboratory-acquired infection. Abstr., Biological Safety Conference, American Biological Safety Association, Mundelein, IL.
410. **Graham CJ, Yamauchi T, Rountree P.** 1989. Q fever in animal laboratory workers: an outbreak and its investigation. *Am J Infect Control* **17:**345–348.
411. **Hall CJ, Richmond SJ, Caul EO, Pearce NH, Silver IA.** 1982. Laboratory outbreak of Q fever acquired from sheep. *Lancet* **319:**1004–1006.
412. **Hamadeh GN, Turner BW, Trible W Jr, Hoffmann BJ, Anderson RM.** 1992. Laboratory outbreak of Q fever. *J Fam Pract* **35:**683–685.
413. **Henning K, Hotzel H, Peters M, Welge P, Popps W, Theegarten D.** 2009. [Unanticipated outbreak of Q fever during a study using sheep, and its significance for further projects]. *Berl Munch Tierarztl Wochenschr* **122:**13–19.
414. **Meiklejohn G, Reimer LG, Graves PS, Helmick C.** 1981. Cryptic epidemic of Q fever in a medical school. *J Infect Dis* **144:**107–113.
415. **Simor AE, Brunton JL, Salit IE, Vellend H, Ford-Jones L, Spence LP.** 1984. Q fever: hazard from sheep used in research. *Can Med Assoc J* **130:**1013–1016.
416. **Whitney EA, Massung RF, Kersh GJ, Fitzpatrick KA, Mook DM, Taylor DK, Huerkamp MJ, Vakili JC, Sullivan PJ, Berkelman RL.** 2013. Survey of laboratory animal technicians in the United States for *Coxiella burnetii* antibodies and exploration of risk factors for exposure. *J Am Assoc Lab Anim Sci* **52:** 725–731.
417. **Herrero JI, Ruiz R, Walker DH.** 1993. La técnica de western immunoblotting en situaciones atípicas de infección por *Rickettsia conorii*. Presentación de 2 casos. [The western immunoblotting technique in atypical situations of *Rickettsia conorii* infection. Presentation of 2 cases.] *Enferm Infecc Microbiol Clin* **11:** 139–142.
418. **The Subcommittee on Arbovirus Laboratory Safety of the American Committee on Arthropod-Borne Viruses.** 1980. Laboratory safety for arboviruses and certain other viruses of vertebrates. *Am J Trop Med Hyg* **29:**1359–1381.
419. **Schnurrenberger PR, Swango LJ, Bowman GM, Luttgen PJ.** 1980. Bovine papular stomatitis incidence in veterinary students. *Can J Comp Med* **44:**239–243.
420. **Langford MP, Anders EA, Burch MA.** 2015. Acute hemorrhagic conjunctivitis: anti-coxsackievirus A24 variant secretory immunoglobulin A in acute and convalescent tear. *Clin Ophthalmol* **9:**1665–1673.
421. **Sitwell L, Lach B, Atack E, Atack D, Izukawa D.** 1988. Creutzfeldt-Jakob disease in histopathology technicians. *N Engl J Med* **318:**853–854.
422. **Miller DC.** 1988. Creutzfeldt-Jakob disease in histopathology technicians. *N Engl J Med* **318:**853–854.
423. **Chen LH, Wilson ME.** 2004. Transmission of dengue virus without a mosquito vector: nosocomial mucocutaneous transmission and other routes of transmission. *Clin Infect Dis* **39:**e56–e60.
424. **Okuno Y, Fukunaga T, Tadano M, Fukai K.** 1982. Serological studies on a case of laboratory dengue infection. *Biken J* **25:** 163–170.
425. **Le Guenno B.** 1995. Emerging viruses. *Sci Am* **273:**56–64.
426. **Mertens T, Hager H, Eggers HJ.** 1982. Epidemiology of an outbreak in a maternity unit of infections with an antigenic variant of Echovirus 11. *J Med Virol* **9:**81–91.
427. **Hager H, Mertens T, Eggers HJ.** 1980. [An epidemic in a maternity unit caused by an echo virus 11 variant (author's transl)]. *MMW Munch Med Wochenschr* **122:**619–622.
428. **Spalton DJ, Palmer S, Logan LC.** 1980. Echo 11 conjunctivitis. *Br J Ophthalmol* **64:**487–488.
429. **Sudeep AB, Jadi RS, Mishra AC.** 2009. Ganjam virus. *Indian J Med Res* **130:**514–519.
430. **Rao CV, Dandawate CN, Rodrigues JJ, Rao GL, Mandke VB, Ghalsasi GR, Pinto BD.** 1981. Laboratory infections with Ganjam virus. *Indian J Med Res* **74:**319–324.
431. **Centers for Disease Control and Prevention.** 1994. Laboratory management of agents associated with hantavirus pulmonary syndrome: interim biosafety guidelines. *MMWR Recomm Rep* **43**(RR-7)**:**1–7.
432. **Lee HW, Johnson KM.** 1982. Laboratory-acquired infections with Hantaan virus, the etiologic agent of Korean hemorrhagic fever. *J Infect Dis* **146:**645–651.
433. **Weissenbacher MC, Merani MS, Hodara VL, de Villafañe G, Gajdusek DC, Chu YK, Lee HW.** 1990. Hantavirus infection in laboratory and wild rodents in Argentina. *Medicina (B Aires)* **50:**43–46.
434. **Anderson RA, Woodfield DG.** 1982. Hepatitis B virus infections in laboratory staff. *N Z Med J* **95:**69–71.
435. **Sampliner R, Bozzo PD, Murphy BL.** 1984. Frequency of antibody to hepatitis B in a community hospital laboratory. *Lab Med* **15:**256–257.
436. **Takahashi K, Miyakawa Y, Gotanda T, Mishiro S, Imai M, Mayumi M.** 1979. Shift from free "small" hepatitis B e antigen to IgG-bound "large" form in the circulation of human beings and a chimpanzee acutely infected with hepatitis B virus. *Gastroenterology* **77:**1193–1199.
437. **Weissenbacher MC, Edelmuth E, Frigerio MJ, Coto CE, de Guerrero LB.** 1980. Serological survey to detect subclinical Junín virus infection in laboratory personnel. *J Med Virol* **6:**223–226.
438. **Johnson K, Winters T.** 2012. Herpes B virus: Implications in lab workers, travelers, and pet owners. Harvard School of Public Health Grand Rounds. http://www.hsph.harvard.edu/oemr/files/2012/08/Grand-Rounds-Herpes-B-Final-Johnson-Winters.pdf.
439. **Beer B, Kurth R, Bukreyev A.** 1999. Characteristics of Filoviridae: marburg and Ebola viruses. *Naturwissenschaften* **86:**8–17.

440. **Nikiforov VV, Turovskiĭ Iul, Kalinin PP, Akinfeeva LA, Katkova LR, Barmin VS, Riabchikova EI, Popkova NI, Shestopalov AM, Nazarov VP, et al.** 1994. [A case of a laboratory infection with Marburg fever]. *Zh Mikrobiol Epidemiol Immunobiol* **May–June:**104–106.
441. **Pedrosa PB, Cardoso TA.** 2011. Viral infections in workers in hospital and research laboratory settings: a comparative review of infection modes and respective biosafety aspects. *Int J Infect Dis* **15:**e366–e376.
442. **Morgan C.** 1987. Import of animal viruses opposed after accident at laboratory. *Nature* **328:**8.
443. **Erdman DD, Gary GW, Anderson LJ.** 1989. Serum immunoglobulin A response to Norwalk virus infection. *J Clin Microbiol* **27:**1417–1418.
444. **Cohen BJ, Brown KE.** 1992. Laboratory infection with human parvovirus B19. *J Infect* **24:**113–114.
445. **Shiraishi H, Sasaki T, Nakamura M, Yaegashi N, Sugamura K.** 1991. Laboratory infection with human parvovirus B19. *J Infect* **22:**308–310.
446. **Coimbra TL, Nassar ES, de Souza LT, Ferreira IB, Rocco IM, Burattini MN, da Rosa AT, Vasconcelos PF, Pinheiro FP, LeDuc JW, Rico-Hesse R.** 1994. New arenavirus isolated in Brazil. *Lancet* **343:**391–392.
447. **Willems WR, Kaluza G, Boschek CB, Bauer H, Hager H, Schütz HJ, Feistner H.** 1979. Semliki forest virus: cause of a fatal case of human encephalitis. *Science* **203:**1127–1129.
448. **Heneine W, Switzer WM, Sandstrom P, Brown J, Vedapuri S, Schable CA, Khan AS, Lerche NW, Schweizer M, Neumann-Haefelin D, Chapman LE, Folks TM.** 1998. Identification of a human population infected with simian foamy viruses. *Nat Med* **4:**403–407.
449. **Schweizer M, Turek R, Hahn H, Schliephake A, Netzer KO, Eder G, Reinhardt M, Rethwilm A, Neumann-Haefelin D.** 1995. Markers of foamy virus infections in monkeys, apes, and accidentally infected humans: appropriate testing fails to confirm suspected foamy virus prevalence in humans. *AIDS Res Hum Retroviruses* **11:**161–170.
450. **von Laer D, Neumann-Haefelin D, Heeney JL, Schweizer M.** 1996. Lymphocytes are the major reservoir for foamy viruses in peripheral blood. *Virology* **221:**240–244.
451. **Centers for Disease Control (CDC).** 1992. Anonymous survey for simian immunodeficiency virus (SIV) seropositivity in SIV-laboratory researchers—United States, 1992. *MMWR Morb Mortal Wkly Rep* **41:**814–815.
452. **Vasconcelos PF, Travassos da Rosa AP, Rodrigues SG, Tesh R, Travassos da Rosa JF, Travassos da Rosa ES.** 1993. Infecção humana adquirida em laboratório causada pelo virus SP H 114202 (Arenavirus: família Arenaviridae): aspectos clínicos e laboratoriais. [Laboratory-acquired human infection with SP H 114202 virus (Arenavirus: Arenaviridae family): clinical and laboratory aspects]. *Rev Inst Med Trop Sao Paulo* **35:**521–525.
453. **Flanagan ML, Oldenburg J, Reignier T, Holt N, Hamilton GA, Martin VK, Cannon PM.** 2008. New world clade B arenaviruses can use transferrin receptor 1 (TfR1)-dependent and -independent entry pathways, and glycoproteins from human pathogenic strains are associated with the use of TfR1. *J Virol* **82:**938–948.
454. **Avšič-Županc T, Poljak M, Matičič M, Radšel-Medveščck A, LeDuc JW, Stiasny K, Kunz C, Heinz FX.** 1995. Laboratory acquired tick-borne meningoencephalitis: characterisation of virus strains. *Clin Diagn Virol* **4:**51–59.
455. **Costa GB, Moreno EC, de Souza Trindade G, Studies Group in Bovine Vaccinia.** 2013. Neutralizing antibodies associated with exposure factors to Orthopoxvirus in laboratory workers. *Vaccine* **31:**4706–4709.
456. **Fillis CA, Calisher CH.** 1979. Neutralizing antibody responses of humans and mice to vaccination with Venezuelan encephalitis (TC-83) virus. *J Clin Microbiol* **10:**544–549.
457. **Reif JS, Webb PA, Monath TP, Emerson JK, Poland JD, Kemp GE, Cholas G.** 1987. Epizootic vesicular stomatitis in Colorado, 1982: infection in occupational risk groups. *Am J Trop Med Hyg* **36:**177–182.
458. **New York State Department of Health.** 2001. West Nile Virus Update- January 1, 2001–December 31, 2001.
459. **Anderson BC, Donndelinger T, Wilkins RM, Smith J.** 1982. Cryptosporidiosis in a veterinary student. *J Am Vet Med Assoc* **180:**408–409.
460. **Centers for Disease Control (CDC).** 1982. Human cryptosporidiosis—Alabama. *MMWR Morb Mortal Wkly Rep* **31:**252–254.
461. **Current WL, Reese NC, Ernst JV, Bailey WS, Heyman MB, Weinstein WM.** 1983. Human cryptosporidiosis in immunocompetent and immunodeficient persons. Studies of an outbreak and experimental transmission. *N Engl J Med* **308:**1252–1257.
462. **Gait R, Soutar RH, Hanson M, Fraser C, Chalmers R.** 2008. Outbreak of cryptosporidiosis among veterinary students. *Vet Rec* **162:**843–845.
463. **Levine JF, Levy MG, Walker RL, Crittenden S.** 1988. Cryptosporidiosis in veterinary students. *J Am Vet Med Assoc* **193:**1413–1414.
464. **Preiser G, Preiser L, Madeo L.** 2003. An outbreak of cryptosporidiosis among veterinary science students who work with calves. *J Am Coll Health* **51:**213–215.
465. **Reese NC, Current WL, Ernst JV, Bailey WS.** 1982. Cryptosporidiosis of man and calf: a case report and results of experimental infections in mice and rats. *Am J Trop Med Hyg* **31:**226–229.
466. **Dillon NL, Stolf HO, Yoshida EL, Marques MEA.** 1993. Leishmaniose cutânea acidental. [Accidental cutaneous leishmaniasis]. *Rev Inst Med Trop Sao Paulo* **35:**385–387.
467. **Herwaldt BL.** 2006. Protozoa and helminths. *In* Fleming DO, Hunt DL (ed), *Biological Safety: Principles and Practices*, 4th ed. ASM Press, Washington, DC.
468. **Druilhe P, Trape JF, Leroy JP, Godard C, Gentilini M.** 1980. [Two accidental human infections by Plasmodium cynomolgi bastianellii. A clinical and serological study]. *Ann Soc Belg Med Trop* **60:**349–354.
469. **Bending MR, Maurice PD.** 1980. Malaria: a laboratory risk. *Postgrad Med J* **56:**344–345.
470. **Grist NR.** 1981. Hepatitis and other infections in clinical laboratory staff, 1979. *J Clin Pathol* **34:**655–658.
471. **Hajeer AH, Balfour AH, Mostratos A, Crosse B.** 1994. *Toxoplasma gondii:* detection of antibodies in human saliva and serum. *Parasite Immunol* **16:**43–50.
472. **Hermentin K, Picher O, Aspöck H, Auer H, Hassl A.** 1983. A solid-phase indirect haemadsorption assay (SPIHA) for detection of immunoglobulin M antibodies to *Toxoplasma gondii:* application to diagnosis of acute acquired toxoplasmosis. *Zentralbl Bakteriol Mikrobiol Hyg [A]* **255:**380–391.
473. **Payne RA, Joynson DH, Balfour AH, Harford JP, Fleck DG, Mythen M, Saunders RJ.** 1987. Public Health Laboratory Service enzyme linked immunosorbent assay for detecting Toxoplasma specific IgM antibody. *J Clin Pathol* **40:**276–281.
474. **Peters SE, Gourlay Y, Seaton A.** 2002. *Listeria meningitis* as a complication of chemoprophylaxis against laboratory acquired toxoplasma infection: a case report. *J Infect* **44:**126.
475. **Woodison G, Balfour AH, Smith JE.** 1993. Sequential reactivity of serum against cyst antigens in *Toxoplasma* infection. *J Clin Pathol* **46:**548–550.
476. **Añez N, Carrasco H, Parada H, Crisante G, Rojas A, Gonzalez N, Ramirez JL, Guevara P, Rivero C, Borges R, Scorza JV.** 1999. Acute Chagas' disease in western Venezuela: a clinical, seroparasitologic, and epidemiologic study. *Am J Trop Med Hyg* **60:**215–222.
477. **Emeribe AO.** 1988. *Gambiense trypanosomiasis* acquired from needle scratch. *Lancet* **331:**470–471.

478. **Herbert WJ, Parratt D, Van Meirvenne N, Lennox B.** 1980. An accidental laboratory infection with trypanosomes of a defined stock. II. Studies on the serological response of the patient and the identity of the infecting organism. *J Infect* **2:**113–124.
479. **Receveur MC, LeBras M, Vincendeau P.** 1993. Laboratory-acquired Gambian trypanosomiasis. *N Engl J Med* **329:**209–210.
480. **Buitrago MJ, Gonzalo-Jimenez N, Navarro M, Rodriguez-Tudela JL, Cuenca-Estrella M.** 2011. A case of primary cutaneous histoplasmosis acquired in the laboratory. *Mycoses* **54:** e859–e861.
481. **Loth EA, Dos Santos JH, De Oliveira CS, Uyeda H, Simão RD, Gandra RF.** 2015. Infection caused by the yeast form of *Paracoccidioides brasiliensis*. *JMM Case Rep* **2.** doi:10.1099/jmmcr.0.000016
482. **Kenny MT, Sabel FL.** 1968. Particle size distribution of Serratia marcescens aerosols created during common laboratory procedures and simulated laboratory accidents. *Appl Microbiol* **16:** 1146–1150.
483. **Blacklow NR, Dolin R, Fedson DS, Dupont H, Northrup RS, Hornock RB, Chanock RM.** 1972. Acute infectious nonbacterial gastroenteritis: etiology and pathogenesis. *Ann Intern Med* **76:**993–1008.
484. **Riley RL.** 1957. Aerial dissemination of pulmonary tuberculosis. *Am Rev Tuberc* **76:**931–941.
485. **Riley RL.** 1961. Airborne pulmonary tuberculosis. *Bacteriol Rev* **25:**243–248.
486. **Kulagin SM, Fedorova NI, Ketiladze ES.** 1962. Laboratory outbreak of hemorrhagic fever with renal syndrome: clinoco-epidemiological characteristics. *Zh Mikrobiol Epidemiol Immunobiol* **33:**121–126.
487. **Gottlieb SJ, Garibaldi E, Hutcheson PS, Slavin RG.** 1993. Occupational asthma to the slime mold Dictyostelium discoideum. J Occup Med 35**:**1231–1235.
488. **Shireman PK.** 1992. Endometrial tuberculosis acquired by a health care worker in a clinical laboratory. Arch Pathol Lab Med 116**:**521–523.