Ulster Med J 2021;**90(1):**28-31

Medical History

A SHORT HISTORY OF OCCUPATIONAL DISEASE: 1. LABORATORY-ACQUIRED INFECTIONS

Petts D, Wren MWD, Nation BR, Guthrie G, Kyle B, Peters L, Mortlock S, Clarke S, Burt C.

ABSTRACT

Laboratory-acquired infections are as old as laboratories themselves. As soon as the culture of microorganisms was introduced, so too was their transfer to laboratory workers. It is only in relatively recent history that such infections have been fully understood, and methods of spread and their prevention or avoidance developed. This paper endeavours to provide an overview of the history of laboratory-acquired infection and the steps taken, particularly in the UK, for its prevention.

INTRODUCTION

Infections acquired in the laboratory are as old as microbiology laboratories themselves. As soon as the culture of microorganisms was established, so too was their transfer to laboratory workers. The manipulation of samples and cultures has always posed a risk to the health of workers. The first recorded laboratory-acquired infection (LAI) was a case of typhoid fever in 1885 (reported in Kisskalt[1]) and was soon followed by cases of brucellosis, tetanus, cholera, diphtheria and sporotrichosis, all recorded in the years from 1887 to 1904.

Kisskalt in 1915[1] published the first survey of LAIs. Between 1885 and 1915, he found 50 cases of typhoid fever, six of which were fatal. The routes of transmission included aerosol generation, sharps injuries, ingestion, mouth pipetting and splashes onto mucous membranes.

American surveys in 1915, 1929 and 1939 recorded infections with psittacosis and Q fever (primarily in microbiologists) that followed the grinding and centrifugation of yolk sac cultures, thus indicating the importance of the aerosol route.

Widespread interest in LAIs began in the 1950s. Studies by Pike *et al*. (1965),[2] Sulkin (1961)[3] and Grist (in a series of studies from 1979 to 1989)[4-6] all revealed the most common infections to be tuberculosis (25.3%), shigellosis (27.4%), hepatitis (type unspecified, 20.0%), salmonellosis (11.6%), typhoid (3.2%) and brucellosis (2.1%). The numbers of infections and the associated deaths from these studies are listed in Table 1.

Table 1. Laboratory-acquired infection and associated death rate in the USA and Europe 1951-1978.

Study / report	Infections (*n*)	Associated deaths (*n*)
Sulkin and Pike, 1951 [8]	1275	39
Sulkin and Pike, 1961 [3]	1073	68
Pike, et al. 1965 [2]	641	13
Pike, 1976 [9]	3921	164
Pike, 1978 [10]	158	4

The relative risks of infection for laboratory workers and those in the general population (Table 2), as recorded by Baron and Miller,[7] shows the higher risks to laboratory staff of brucellosis, infection with *Escherichia coli* O157 and meningococcal sepsis and meningitis. Additionally, the studies by Grist in the UK showed the preponderance of tuberculosis, hepatitis, shigellosis and *Salmonella* infection in microbiologists.[4-6]

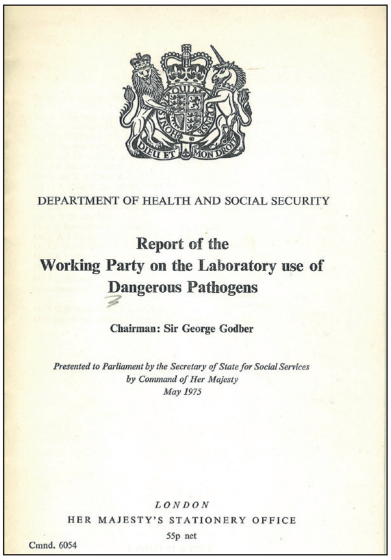
Table 2. Relative risk of infection between laboratory workers and the general population (after Baron and Miller [7]).

Organism / disease	Risk /100,000 microbiologists	Risk /100,000 general population
Brucellosis	64.1	0.08
E. coli O157	8.3	0.96
Meningococcal sepsis/meningitis	25.3	0.62
Salmonellosis	1.5	17.9
Shigellosis	6.6	6.6

In 1919 the first laboratory safety manual was published by Fricke[11] in Germany. It recommended the use of wraparound laboratory gowns with long sleeves, no eating in the laboratory, the avoidance of mouth pipetting and the decontamination of pipettes.

The published literature records five major routes for the acquisition of a laboratory-acquired infection. Generation of aerosols was the most common route described. Surveys show that they may have caused between 35% and 65% of cases. Reitman and Wendum (1956)[12] recovered 118 viable particles of *Serratia indica* per cubic foot of room air sampled over 10 minutes when a tube containing 50 mL of a broth

The History Committee, Institute of Biomedical Science,
12 Coldbath Square, London EC1R 5HL, United Kingdom.
Received: 11th March 2020
Provenance: Internally peer-reviewed.
Correspondence to: Brian Nation CSci FIBMS
E-mail: briannation@ibms.org



DEPARTMENT OF HEALTH AND SOCIAL SECURITY

Report of the Working Party on the Laboratory use of Dangerous Pathogens

Chairman: Sir George Godber

Presented to Parliament by the Secretary of State for Social Services by Command of Her Majesty May 1975

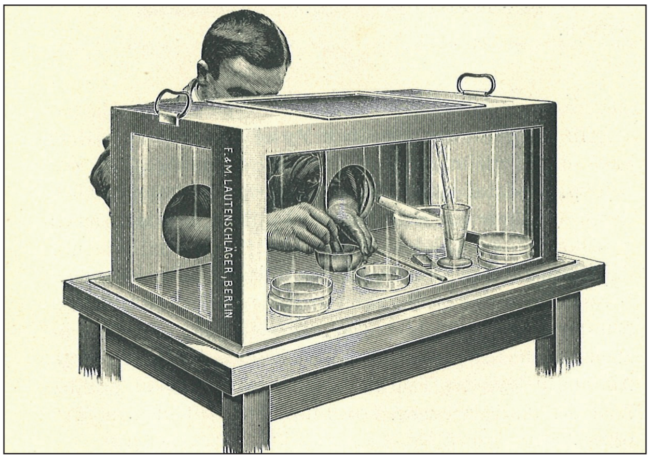
LONDON
HER MAJESTY'S STATIONERY OFFICE
55p net

Cmnd. 6054

The 1975 Report of the Working Party on the Laboratory Use of Dangerous Pathogens (chaired by Sir George Godber) provided safety advice for handling Category A (now Category 4) pathogens and their classification.

culture was broken during the operation of a centrifuge, demonstrating that aerosol dispersion from a centrifuge was a major hazard.

The Biological Safety Cabinet (BSC) was developed to protect the worker from aerosols. The first cabinet was described by Robert Koch in 1905 followed by Fricke in 1915. They first became available commercially in Germany in 1919.



The first Biological Safety Cabinet was described by Robert Koch in 1905, followed by Fricke in 1915, becoming available commercially in Germany in 1919.

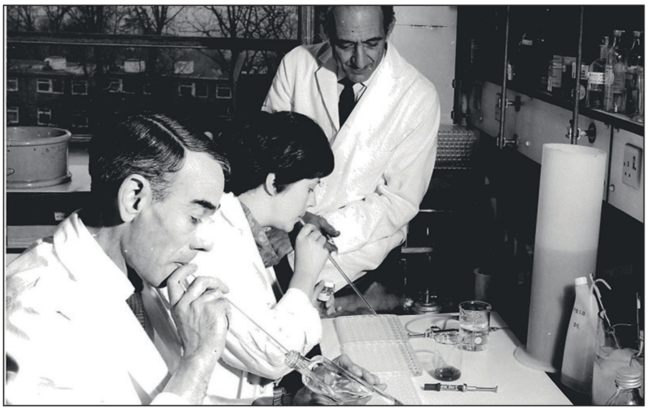
Van der Ende (1940)[13] published the first formal description of a BSC, but it was not until 1948 that stainless steel cabinets with a glass viewing front and an exhaust fan were introduced and not widely used until the late 1960s.

In 1957, Reid[14] reported the incidence of tuberculosis in laboratory workers, the lowest incidence occurring in chief technicians, the highest in junior and student technicians, but both of these were greatly exceeded by the incidence in mortuary workers.

Accidental inoculation caused by needlestick injuries were the most commonly described LAI in some surveys and accounted for up to 25% of infections.

Mouth pipetting, especially of liquid cultures, blood and serum was the cause of approximately 13% of all LAIs in the study by Pike.

Mouth pipetting was recognised by Paneth[15] as a serious hazard and recommended a rubber balloon (teat) to avoid mouth contact, but this was not universally accepted until the 1950s.



Mouth pipetting was recognised as a serious hazard as far back as 1915, but was still widely practised in the 1960s – some 62% of laboratories still mouth pipetted and this figure was not improved by 1977.

Studies by Phillips (1961)[16] and Harrington and Shannon (1978)[17] revealed that mouth pipetting was still widely practised in the 1960s, indeed 62% of laboratories still mouth pipetted and this figure was not improved by 1977.

Phillips and Bailey (1966)[18] demonstrated the considerable aerosol generation with the use of needles and syringes, especially from pressure in the syringe, and recommended the removal of the needle using forceps. Aerosols were also generated from pipettes (especially when the last few drops were expelled).

Splashes and spillages, particularly to the eyes and face, were particularly common when separating a needle from its syringe while still under pressure. Pike's study of 1976 included 177 cases (a quarter of the total cases) due to needle and syringe accidents. Spillages of cultures, noticed and unnoticed, onto bench surfaces and subsequently onto fingers and hands were reported. In the same study, hand to mouth and hand to eye transfer occurred in a further 25% of cases.

Eating, drinking and smoking, once accepted as normal practice in a laboratory but now forbidden, have been implicated in a number of acquired infections. Similar cases have occurred with milk samples. One case of laboratory-acquired anthrax occurred in a laboratory worker who smoked while working with cultures of the organism. Historical examples include cases where food submitted for laboratory testing was wrongly labelled as safe and subsequently eaten by staff members.

A number of high-profile incidents of laboratory-associated outbreaks of serious infections in the UK involving

Table 3. The path of legislation.

Report	Year	Content
Rosenheim Report	1972	Review of precautions to be taken in renal dialysis units. Review of precautions to be taken in laboratories.
Maycock Report	1973	Updated advice given in 1972. Further updated in 2002 to cover hepatitis C and HIV.
Safety in Pathology Laboratories	1972-1974	Booklet produced by a working party chaired by JF Heggie giving safety advice. Further developed by CH Collins into the PHLS Monograph No 6 entitled *The Prevention of Laboratory Acquired Infection* in 1974
Godber Report	1974	Safety advice for handling Category A (now category 4) pathogens and their classification. Reclassified other pathogens into B and C (now 1, 2, and 3). Prompted by outbreaks of Marburg disease and Lassa fever, it recommended the establishment of the Dangerous Pathogens Advisory Group (DPAG). DPAG publishes a Code of Practice for handling samples containing Category A pathogens.
Health and Safety at Work Act	1974	Forms the Health and Safety Executive (HSE). Protection under the Act is extended to laboratory workers in 1976. Introduction of safety representatives who had to be members of a trades union.
Howie Report and Code of Practice	1978	Categorises pathogens into categories 1, 2, 3 and 4. Deals with samples containing hepatitis B virus. Defines duties of the safety officer. Advice on laboratory design, microbiological hazards, notification of laboratory-acquired infections, safety committees and the planning, building and equipping of laboratories.
Shooter Report	1980	Followed the Birmingham smallpox incident in 1978. Recommended the formation of the Advisory Committee on Dangerous Pathogens (ACDP). ACDP has to issue regular updates and advice on newly discovered pathogens and new information on existing pathogens.

healthcare-associated workers and members of the public occurred in the 1960s and 1970s led to a heightened public and legislative interest in LAIs. The most widely known were outbreaks of smallpox and the large number of cases of hepatitis associated with renal dialysis units.

In 1973 a science technician working with equipment used for smallpox research became ill with symptoms that were subsequently diagnosed as this disease. Prior to the diagnosis, her mother and two visitors also contracted the disease. Unfortunately, the technician and her visitors died, but the mother survived. Five years later, in 1978, a medical photographer in Birmingham contracted smallpox. Research into the virus was being carried out nearby, but it was not possible to determine the route of transmission.

In Edinburgh, 40 cases of hepatitis occurred in a renal dialysis unit (26 patients, 12 staff and two home contacts). Eleven of these cases died. The index case was thought to be a patient incubating the infection while undergoing dialysis. Inadequate disinfection of the machine led to the spread of the virus to subsequent patients. The likely routes of transmission to the staff members include the handling of the contaminated machine itself, needlestick injuries and contamination of mucous membranes via aerosol generation.

These incidents highlighted the potential danger of laboratory work with microorganisms to the wider population, but also the risks to laboratory workers themselves. The Thomlinson Report of 1958 focused on the excessive incidence of tuberculosis in laboratory and post-mortem room staff, and listed precautions to be taken in laboratories, PM rooms and animal houses.

These incidents also gave rise to a series of inquiries and reports that led to the development of improved codes of practice and legislation in the UK. These are summarised in Table 3.

The laboratory coat had gone through many incarnations finally resulting in the coat now commonly used, described and published by Dowsett and Heggie[19] in 1972.

CONCLUSIONS

Laboratory-acquired infections have long been known to be a major hazard to those working in healthcare and similar laboratories. However, it has required outbreaks or an accumulation of many cases before the dangers were officially recognised, the routes of acquisition were identified and the necessary control measures put in place. Spread of infection into the wider population led to the development and introduction of legislation, both to protect laboratory workers and the public. Thankfully, we are now more aware of the dangers and how to regulate and minimise the risks.

This article is based on, and expands, the subject of the IBMS History Committee posters exhibited at the Biomedical Science Congress, held at the International Convention Centre, Birmingham, in September 2019. The five posters may be viewed and downloaded as PDF files from the IBMS website (www.ibms.org/historyposters/occupational_health/).

REFERENCES

1. Kisskalt K. Laboratory infections with typhoid bacilli. *Z Hyg Und Infektionskrahkh*. 1915; **80**: 145-62
2. Pike RM, Sulkin SE, Schulze ML. Continuing importance of laboratory-acquired infections. *Am J Public Health Nations Health*. 1965; **55**(2): 190-9.
3. Sulkin SE. Laboratory-acquired infections. *Bacteriol Rev*. 1961; **25**(3): 203-9.
4. Grist NR. Infections in British clinical laboratories, 1980-81. *J Clin Pathol*. 1983; **36**(2): 121-6.
5. Grist NR, Emslie J. Infections in British clinical laboratories, 1982-3. *J Clin Pathol*. 1985; **38**(7): 721-5.
6. Grist NR, Emslie J. Infections in British clinical laboratories, 1984-5. *J Clin Pathol*. 1987; **40**(8): 826-9.
7. Baron EJ, Miller JM. Bacterial and fungal infections among diagnostic laboratory workers: evaluating the risks. *Diag Microbiol Infect Dis*. 2008; **60**(3): 241-6.
8. Sulkin SE, Pike RM. Survey of laboratory-acquired infections. *Am J Public Health*. 1951; **41**(7): 769-81.
9. Pike RM. Laboratory-associated infections: summary and analysis of 3921 cases. *Health Lab Sci*. 1976; **13**(2): 105-14.
10. Pike RM. Past and present hazards of working with infectious agents. *Arch Pathol Lab Med*. 1978; **102**(7): 333-6.
11. Fricke W. Schutamassmahmen bei Bakteriologischem und Serolo'ischem Arbeiten Custum. Für Ärzte, Studierende und Laboratoriumsgehilfen zum Gebrauch im Laboratorium und bei bakteriologischen Kursen. [Protective measures for bacteriological and serological work. For doctors, students and laboratory assistants for use in the laboratory and in bacteriological courses.] Jena, Germany: Verlag von Gustav Fischer; 1919. German.
12. Reitman M, Wedum, AG. Microbiological safety. *Public Health Rep* 1956; **71**(7) :659-65.
13. Van der Ende M. An apparatus for the safe inoculation of animals with dangerous pathogens. *J Hyg (Lond)*. 1943; **43**(3): 189-95.
14. Reid DD. Incidence of tuberculosis among workers in medical laboratories. *Br Med J*. 1957; **2** (5035): 10-4.
15. Paneth L. The prevention of laboratory infection. *Med Klin* 1915; **11**: 1398-9.
16. Phillips GB, Microbiological safety in US and foreign laboratories. Technical Study 35. (AD No 268-635) Fort Deidrick, MD: Safety Division. Office of the Safety Director; 1961.
17. Harrington JM, Shannon HS. Incidence of TB, hepatitis, brucellosis and shigellosis in British medical laboratory workers. *Br Med J*. 1976; **1** (6012): 759-62.
18. Phillips GB, Bailey SP. Hazards of mouth pipetting. *Am J Med Technol*. 1966; **32**(2): 127-9.
19. Dowsett EG, Heggie JF. Protective pathology-laboratory coat. *Lancet*. 1972; **1** (7763): 1271.