Health and safety in medical laboratories*

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There has been a large increase in the number of persons employed in medical laboratories in the last 25 years. These workers are exposed to a variety of infective agents in the course of their work, the most important being Mycobacterium tuberculosis, Salmonella typhi, Brucella spp., and serum hepatitis virus. Chemical and physical hazards include toxic chemicals, lacerations, skin disease, and possibly cancer. Current knowledge of safe working practice in laboratories leaves much to be desired and there is an urgent need for both internationally agreed codes of safe practice and the development of guidelines for the medical surveillance of laboratory workers. The World Health Organization is developing such guidelines in an attempt to protect the health of workers employed in the investigation of ill health in others.

The technological advances of the past 150 years have transformed medicine from an art to a modern science. A growing number of clinical investigations are available to the physician and there is an increasing need for technicians to perform these laboratory tests. The advent of nationalized health services in many countries has resulted in the employment of large numbers of people in medical and paramedical occupations. For example, in the United Kingdom, approximately 1 out of every 20 workers is employed in the National Health Service and experience in the United States of America suggests that the demand for more health care will continue. Western European countries have a doctor to patient ratio as high as 1 per 1000 population, and ancillary workers in the health field generally outnumber the physicians.

Medical laboratory workers form one of the larger subgroups and, in England and Wales, there are currently more than 25,000. Such work is not without its occupational hazards and these risks have recently received considerable publicity as a result of some unfortunate laboratory-acquired infections. Ironically, the global extinction of smallpox as an endemic disease coincided with two deaths from smallpox in the United Kingdom, both of which were traced back to laboratory sources of the virus. These isolated events have focused attention on the microbiological hazards of laboratory work but, at the same time, have obscured the degree of risk and overshadowed the chemical and physical hazards inherent in laboratory activities.

The purpose of this article is to review the risks associated with work in medical laboratories and to outline practical ways in which health and safety measures can be instituted to minimize them.

OCCUPATIONAL HAZARDS

General considerations

Laboratory workers are exposed to a wide range of hazards associated with the materials they employ and the methods they use in the course of their work. The subject has been of

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increasing interest in recent years and the hazards to health professionals have been reviewed by Tolonen and Harrington. Research establishments may be especially hazardous places as the danger associated with a substance or process may not be realized until some unforeseen accident, illness, or death occurs. Routine and diagnostic laboratories handle a wide range of materials and a large number of potentially dangerous, pathogenic agents. The control of many infectious diseases following the introduction of effective antimicrobial drugs has, moreover, added a new and insidious danger to the laboratory workers’ job. There is now less likelihood that a particular specimen contains pathogenic material, and this can lull the laboratory technician into a false sense of security. For example, in the United Kingdom pulmonary tuberculosis is now a relatively rare disease, yet it is sometimes discovered inadvertently during post-mortem examination or during the analysis of a sputum specimen submitted for cytological rather than bacteriological analysis. Moreover, in these circumstances, the organism is frequently resistant to first line antituberculosis therapy and is therefore especially dangerous.

In addition to the handling of infective or potentially infective material, normal laboratory practice also includes the use of chemical reagents, gases, and solvents that may constitute a non-microbiological hazard. These agents may be explosive, flammable, or toxic, and fires, gassings, and explosions occasionally occur in laboratories. To these immediate dangers must be added the longer term risk involved in handling carcinogenic chemical reagents.

The literature on medical laboratory hazards has largely centred on infections and, therefore, on microbiological establishments. This is partly because laboratory-acquired infections tend to be more easily remembered than other hazardous events. The cause and effect pathway may also be clearer although the mode of transmission for most laboratory infections remains speculative; a large number of reports of infections are anecdotal and few are more than case reports. Such circumstances preclude an accurate assessment of risk for even the more unusual infective agents and it is likely that infections due to the commoner organisms such as streptococci or staphylococci are underreported. It is often difficult to acquire definitive evidence that an infection common to the community at large has, in a particular instance, been acquired in the laboratory. Nevertheless, the first human cases of several diseases were seen in laboratory workers, e.g., herpes B virus, American Q fever, Marburg disease, louping-ill, and Newcastle disease.

Infectious diseases

Early attempts to survey large populations of laboratory workers were little more than collections of cases. The surveys of Sulkin and Pike are among the most extensive and in one of the later reports Pike describes 3921 cases. Attempts to link the infections with specific laboratory accidents or incidents were only partially successful. In a review of 426 cases of laboratory infections covering 32 diseases in 12 countries, Phillips noted that tuberculosis, Q fever, brucellosis, psittacosis, and tularaemia were most common. However, in over 80% of the cases, it was difficult to establish the incident that had precipitated the infection. The most frequently cited causes were self-inoculation, aerosol spread, and glassware injuries. Occasionally, a single laboratory can be the source of widespread illness; an example of this was reported from the USSR, where there were 46 cases of laboratory-acquired encephalitis.

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between 1950 and 1963, 24 of which resulted from a single accident in a laboratory handling Venezuelan equine encephalitis.

**Tuberculosis**

This disease has been traditionally considered an occupational disease of health workers. The risk is now more insidious because, in several western European countries, the diagnosis is made post mortem in up to half of all reported cases in the general population. These occupational risks were not quantified until 1957 when Reid\(^e\) reported that for British pathologists the risk of acquiring tuberculosis was many times higher than for a comparable population of post office workers. Studies undertaken between 1971 and 1974 by the present author confirmed a continuing threat to the health of British laboratory personnel, when it was noted that laboratory technicians were at greatest risk (7 times higher than for a comparison population), medically qualified staff slightly lower (4 times that for a comparison population), with clerical staff having a 2-fold excess. Morbid anatomy department staff and, in particular, post-mortem room technicians were particularly at risk, but it is disturbing to note that non-technical personnel such as clerks and secretaries also ran a higher risk than their counterparts outside the laboratory.

There is little information on the relative risks to laboratory staff in countries where pulmonary tuberculosis is more prevalent in the general population, though it could be presumed than a higher population prevalence would be translated into a higher laboratory risk. Alternatively, a high community prevalence might ensure that laboratory personnel take greater care with, say, sputum specimens than do their opposite numbers in countries where the disease is generally rare.

**Serum hepatitis**

Serum hepatitis is usually transmitted parenterally, the first outbreaks having been described in association with vaccination procedures for smallpox and arsphenamine therapy for venereal disease. Infection with the type B hepatitis virus has become of much greater significance during the last decade or so, and severe, even fatal, outbreaks of the disease have occurred in association with haemodialysis units and clinical chemistry laboratories. Self-inoculation is the most likely route of infection for the laboratory worker. In Britain the introduction of stringent control over the handling of high-risk specimens of blood and urine has reduced laboratory-acquired infection rates from 0.12% (all staff) and 0.49% (clinical chemistry technicians) in 1972, to much lower levels now. Indeed, in 1980 there were no reported cases of hepatitis B infection among laboratory workers in Britain (N. R. Grist, personal communication). This dramatic reduction has been attributed to increased safety awareness rather than the introduction of expensive safety measures. What little hepatitis still occurs in laboratories is largely restricted to biochemistry and haematology staff rather than microbiologists.

**Salmonellosis**

The typhoid bacillus was one of the first organisms to be closely studied as a laboratory-acquired infection. Between 1915 and 1939, Kisskalt reported on 165 cases from Germany. Sporadic reports from elsewhere have suggested that typhoid fever remains a potentially serious threat, though in Britain only 12 cases of laboratory-acquired infection were noted between 1964 and 1979, accounting for 0.9% of all cases not acquired abroad. In the United States of America, laboratory-acquired *Salmonella typhi* infections account for 2% of indigenous infection, and, disturbingly, most of these cases were acquired during labora-

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tory proficiency-testing procedures to identify "unknown" organisms. The next most common source was *S. typhi* cultures used for teaching purposes. These figures raise some important issues. As most of the laboratory-acquired typhoid fevers are not caused through routine diagnostic or even research procedures, the suitability of employing such a pathogenic organism for routine proficiency testing or teaching must be called into question.

**Brucellosis**

An early report of laboratory-acquired brucellosis cited laboratory teaching rooms as the source of the infection. These is clearly a need to revise the list of microorganisms that can be considered appropriate for student work. Indeed, infection with *Brucella* organisms can be difficult to diagnose, though the risk is low in laboratories serving urban populations and is very small compared with the occupational risk of brucellosis to veterinarians and agricultural workers.

**Other infections**

The list of microorganisms that have been implicated in laboratory-acquired illness is long but particular note should be taken of the herpes B group. Outbreaks of infection with Marburg and Lassa fever viruses can be especially serious and have caused fatalities among laboratory workers handling specimens from patients with the disease. In view of the high infectivity of these organisms and the relatively weak therapeutic measures available to combat the disease, it is essential that such organisms are handled only in maximum containment facilities.

Despite the extensive literature on laboratory-acquired infections, much of the information is anecdotal and highly selective. Little attempt has been made to quantify the risks to laboratory staff though many people have advocated extensive and expensive protection procedures.

**Non-infectious illnesses**

**Accidents**

Although infection is the most obvious hazard in a medical laboratory, it is likely that non-infectious conditions cause a greater toll of absence from work. Sickness absence rates in British laboratories are relatively low, but absences due to diarrhoea of unspecified origin occur with three times the frequency of control populations. Accident rates, however, seem to be inordinately high. In a survey of a 12% random sample of English laboratories, comprising 2520 workers in 39 laboratories, followed for one year, the accident-with-injury rate was 25 per 100 person-years. Technicians, who made up 64% of the population, experienced 76% of the injuries. Three-quarters of these injuries were lacerations, with knife injuries most prevalent in morbid anatomists, and glassware injuries more common in haematologists. Few comparable studies are available, but a Danish study noted that lacerations were more frequent in the laboratory environment than in other work places, while a French study showed that 13.5% of laboratory personnel had an accident during a 5-year period. The sites of the injuries reported in these studies strongly suggest that the use of simple protective clothing could greatly reduce the trauma. For example, in our studies, 7% of the injuries occurred when glass or liquid entered the eyes while 87.5% of the injuries affected the eyes and/or the hands.
Skin disease

The failure to protect vulnerable areas of skin can have other damaging effects. A recent study of skin disorders in laboratory workers noted that one-fifth of the work force had skin problems and about one-third of these were directly related to occupational hazards. The causes included irritants such as antiseptics, acids, and alkalis, and allergens such as rodent urinary protein, xylol, and formaldehyde. Formaldehyde is a potent, if rare, cause of asthma in some susceptible individuals, and a particular hazard for morbid anatomists and embalmers. These exposures are of special interest in view of the recent evidence of carcinogenesis in rats following exposure to formaldehyde vapour.

Cancer

There is little definitive evidence that laboratory workers are at greater risk of developing cancer than the general population. However, there is little doubt that carcinogenic substances have been and are handled in laboratories. Chemicals such as 2-naphthylamine, 1-naphthylamine, benzidine, o-tolidine, and benzene are known or suspected carcinogens. In the mid 1970s these substances were being used in a few British clinical laboratories, but a mortality study of pathologists and laboratory technicians covering the period 1955 – 73 failed to reveal an excess of bladder cancer. It did, however, show a small excess of lymphoma among pathologists. The number of subjects involved was small, but in the light of reports of a similar tumour excess among American and Swedish chemists, the subject merits further study. No clear-cut link was noted with virological work.

Other illnesses

Toxic and anaesthetic gases are a potential source of inhalation hazards and the explosive or inflammable nature of some of these materials carries a risk of fire and explosion, though in the author’s experience, such events are rare. Most laboratories, however, seem to have suffered at one time or another from a centrifuge accident, which frequently carries the dual risk of injury from airborne fragments of glass or metal and the possibility that the contents of the centrifuge bucket may be infective and become aerosolized. Finally, for reasons that are largely unknown, laboratory workers commit suicide more frequently than their non-laboratory counterparts. Moreover, they are more likely to use poison for such purposes; cyanide is a particularly popular agent.

In summary, though infectious hazards are usually associated with laboratory work, it is important to remember that laboratories are also places where non-infective occupational hazards may be present. Indeed, these non-microbial agents may be a more common cause of staff morbidity.

HEALTH AND SAFETY PRACTICE

General considerations

It is generally accepted that reduction of the occupational hazards associated with laboratory work will require well organized and effective preventive health and safety surveillance combined with the establishment of codes of laboratory practice. Such codes for safe working with microbiological agents have been promulgated in a number of countries, and the World Health Organization is currently developing practical guidelines for dealing with these hazards. A number of working parties have been convened to draft
proposals for dealing with various facets of the problem, including ways of handling a major laboratory accident and appropriate procedures for the health and medical surveillance of laboratory personnel.

Safe working requires attention to be given to the plant and the personnel. The fabric of the laboratory and its equipment must be safely assembled, and maintained in safe working order. Hazardous materials such as solvents, corrosive liquids, and explosive gases must be stored and used correctly and all laboratory methods must be approved and executed according to a written code of practice. Personnel must be trained in safe working, provided with appropriate protective clothing, and subjected to agreed monitoring procedures to ensure that they are healthy when they start work and remain so during the course of their employment.

Current practice

Most laboratories in developed countries have codes of practice, some of which are recommendations, while others are mandatory and enforceable by law. In the United Kingdom, the *Code of practice for the prevention of infections in clinical laboratories*¹ was published in 1978 and superseded earlier, less stringent codes. Although these latest controls are not, strictly speaking, legally enforceable, they carry considerable weight with the government factory inspectors who visit clinical premises. However, evidence from Britain and elsewhere suggests that, in practice, there is great variation in the quality and extent of safe laboratory working practices. For example, health surveillance of laboratory personnel is variable. Some receive a full pre-employment medical examination and periodic reappraisals combined with an active immunization programme. Others are not even required to complete a pre-employment health questionnaire, do not have to have a chest X-ray before starting work, and are not subjected to periodic health monitoring.

Safety cabinets have, until recently, been inadequately maintained in many laboratories and they do not necessarily meet the safety needs of the procedure for which they are used. Ideally, laboratory equipment of sophisticated design should be subject to routine maintenance by the manufacturer or his agent, but it is not uncommon for laboratory staff themselves to tinker with faulty equipment. Regulations governing the storage and use of toxic and flammable chemicals have not been enforced with the same thoroughness as might occur on factory premises. Furthermore, the regulations and codes vary from country to country.

The World Health Organization has attempted to establish internationally acceptable criteria as a basis for health care, and one of the first steps was to classify the risks associated with the organisms handled in medical laboratories. Clearly, it was not possible to specify the risk group for all organisms in every country, but four broad categories have been defined:

*Risk group I* (low individual and community risk): includes biological agents that are unlikely to cause human disease or animal disease of veterinary importance.

*Risk group II* (moderate individual risk with limited community risk): biological agents that can cause human or animal disease but are unlikely to be a serious hazard to laboratory workers, the community, livestock, or other elements of the environment. Laboratory exposure rarely produces serious infections, effective treatment and preventive measures are available, and the risk of spread is limited.

Risk group III (high individual risk with low community risk): biological agents that usually produce serious human disease but do not ordinarily spread from one infected individual to another.

Risk group IV (high individual and community risk): biological agents that usually produce serious human or animal disease and are readily transmitted from one individual to another, directly or indirectly.

Examples of risk group IV microorganisms are variola virus or Lassa fever virus. Mycobacterium tuberculosis, hepatitis B virus, S. typhi, and Vibrio cholerae might be categorized as group II or III depending on the country. These designations enable safety and health measures to be tailored to the specific laboratory, though, clearly, a number of routine diagnostic laboratories, while normally handling mainly group I or II organisms, would require a suite to be available for work with group III organisms.

Future considerations

A general tightening up of laboratory safety procedures is called for throughout the world. The risk group categorizations enable specific guidelines to be laid down, which, if adopted, would go a long way towards reducing the risks inherent in medical laboratory work.

Several precepts underscore these plans, including the need (a) to exclude highly susceptible individuals from working with dangerous pathogens, (b) to provide a means for the early detection of laboratory-acquired infections, (c) to assess by epidemiological means the risks inherent in the work, and (d) to determine, by biological monitoring, the adequacy of currently used protective devices.

Examples of measures suitable for adoption in risk group III and IV laboratories include:

1. The appointment of a biosafety officer and the establishment of a hierarchy of responsibility.
2. The maintenance of a complete record of accidents and illnesses suffered by the laboratory staff.
3. The adoption of a detailed pre-employment medical examination, which, if passed, would be followed up by annual checks relevant to the particular laboratory.
4. The drafting of a contingency plan to deal with individuals accidentally exposed to microorganisms of risk groups III and IV.

Similar but less stringent plans could be drafted for risk group I and II laboratories. Work with nucleic acid fractions of microorganisms, such as genetic manipulation techniques, should, in the absence of evidence for or against, be assumed to be equivalent to working with group III or IV organisms. This suggestion might need to be revised later when more is known of the risks involved in such work.

A further consideration is the need for valid epidemiological studies of populations of laboratory workers in order to quantify the occupational risks and to establish priorities for preventive measures. Such studies are at present planned in certain countries including the Soviet Union, the United Kingdom, and the USA, but international comparisons would be valuable. WHO is currently considering the possibility of a multicentre international study and a working party may be convened to draw up a suitable protocol.

One of the major difficulties in discussing laboratory-acquired infections is the dearth of sound data in the face of a wealth of anecdotal information and speculative pronouncements. A large-scale study might provide a firm basis from which future health and safety measures could be developed.
INTERNATIONAL IMPLICATIONS

The growth of health care facilities in developing countries emphasizes the need for internationally agreed safe working practices in laboratories. Laboratory safety is still somewhat haphazard in some developed countries and developing countries are probably even less well equipped to provide effective occupational health services to laboratory employees.

Moreover, the risks are not confined to the laboratory as the recent smallpox incidents in the United Kingdom have demonstrated. Group III and group IV organisms, by definition, carry significant community health risks. These risks are magnified by the ease and speed with which people can travel across continents, thereby distributing the hazard to places remote from the source. It is essential, therefore, that safe laboratory practices and efficient health surveillance of those occupationally exposed to dangerous pathogens are established and agreed internationally. WHO is attempting to achieve these ends through the Special Programme on Safety Measures in Microbiology which was instituted in 1976. It is hoped that this programme will in large measure help to protect the health of those who investigate and treat the illnesses of others.

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