In pursuit of safety*

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Presidential addresses come in a great variety of forms: it is considered respectable for them to be erudite, autobiographical, topical, or even trivial. Despite the number of committees, meetings, and reports on the subject of laboratory safety, I felt that there could be some interest in a backward glance to see how we have got to where we are, and a forward look to consider where we ought to go. Profusion of advice in the field is no new thing: even 3000 years ago Solomon¹ advised that 'In the multitude of counsellors there is safety'. Something of the more recent historical perspective is afforded by a graphical presentation of Collins² bibliography on microbiological aspects of laboratory safety (Figure).

Number of papers published on aspects of microbiological safety in laboratories, adapted from Collins.²

Between one and six publications a year was the unchanging norm between 1951 and 1971, a period when the total number of microbiological papers published each year was increasing very considerably. Since 1971 there has been the spate, of which we are all too well aware.

The existence of a hazard in laboratory work was not a new discovery in the late 1960s. Indeed, as early as 1951 Sulkin and Pike³ were able to collect from the published literature and from a questionnaire sent to some 5000 laboratories, mostly in the United States, a record of 1342 cases of infection

(with 39 deaths) in laboratory workers, at least half of which had been regarded as definitely contracted in the laboratory.

In 1957, Reid⁴ published evidence from British laboratories which indicated that workers in medical laboratories experienced between three and four times as much notified tuberculosis as comparable individuals in the general population. At about the same time Merger⁵ had shown that medical laboratory technicians in Canada had between four and 23 times as much tuberculosis as the general population. In 1961, Phillips⁶ reported on his inquiries, made during a tour of laboratories in 18 different countries on behalf of the US army; he obtained anecdotal records of a total of 426 infections. By 1965 Pike⁷ was able to report, in a paper entitled 'Continuing importance of laboratory-acquired infections', that his tally, still based on publications supplemented by questionnaire, had increased from the 1342 of his 1951 survey to 1983; and, in 1968, Hammon⁸ quoted an American committee as having records of over 2700 cases of laboratory-acquired infection, 107 of them being fatal.

The 1970s flood of papers has not included very much new evidence. Pike⁹ published a further update in 1976, and in the same year Harrington and Shannon¹⁰ published the results of a retrospective postal questionnaire on the incidence of infection in some 21 000 workers in United Kingdom laboratories in 1971 (1973 in Scotland). They had reports of 21 cases of tuberculosis, estimated still to be about four to five times the number 'expected' from national notification figures (themselves of doubtful accuracy) although the actual incidence, like that in the population generally, was lower than Reid's figures published in 1957. Harrington and Shannon also reported figures for the incidence of hepatitis (35 cases) and shigellosis (37 cases). Grist¹¹⁻¹⁴ has reported a series of postal surveys conducted through the Association of Clinical Pathologists on the frequency of hepatitis in laboratory workers, summarised in Table 1, which suggest a declining attack rate during the last six years, a suggestion confirmed by an analysis of

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Table 1 Hepatitis in laboratory workers

Year	CDR* No. of reports of acute hepatitis B	Grist's† questionnaires	
		Cases of hepatitis per year	No/10 ⁶ /yr(B)
1970	—	14	111 —
1971	—		
1972	8		
1973	9	16	143 —
1974	7		
1975	3	4	35 (13)
1976	3		
1977	4	4	29 (22)
1978	3		

*Reports to PHLS Communicable Disease Report.

†Grist¹¹⁻¹⁴.

cases of hepatitis B reported to the Public Health Laboratory Service.

Nor was there any dearth, long before 1971, of papers describing the ways in which various laboratory manipulations could liberate microbes; indeed, the wheel was invented again and again in the 30 years from 1940 to 1970. This was an era when aerobiology was fashionable, and from the American Association for Advancement of Science monograph¹⁵ on 'Aerobiology' in 1942 onwards there was a steady stream of papers showing the production of bacterial aerosols by various seemingly harmless bench manipulations. For example, Johansson and Ferris¹⁶ photographed the spray liberated from the tip of a pipette. Anderson and colleagues¹⁷ collected large numbers of bacteria from the air close to a bench on which a variety of laboratory manoeuvres were carried out, using a thick suspension of *Serratia marcescens*. The hazards of lyophilised cultures were well illustrated by Reitman and others.¹⁸ Reitman and Wedum¹⁹ concluded that 'practically every manipulation in the microbiological laboratory creates aerosols, and these aerosols are probably the source of many laboratory infections'. Whitwell *et al.*²⁰ described the risks of dispersal of aerosols from centrifuges, while Tomlinson²¹ demonstrated the liberation of droplets from the opening of screw-capped containers. These reports were supplemented by a number of 'symposium' volumes, contributed very largely by workers in major research institutes, on the elaborate safety precautions recommended in them and, by extrapolation, for use in other microbiological laboratories.

It is a general impression now that not much notice was taken of the admonitions, that the experimental demonstration of potential hazards was ignored by both laboratory staff and laboratory

directors, and that the occurrence of infection was either attributed to personal carelessness or regarded as an inevitable concomitant of working with pathogens.

Phillips⁶ visited laboratories in 18 countries in 1959-60, and his report, after noting that in Europe laboratory directors were held in high esteem and commonly had, attached to their laboratories, log fires, steam bathrooms, and chauffeurs, quotes some opinions on laboratory safety. These include such gems as:

'Retirement of present Director will enable our staff to establish a realistic safety program.'

'Everyone is doing too much to provide protective equipment and not enough toward eliminating causes.'

'The chief technician is the safety officer but he has no power and none of his suggestions is used.'

'Two infractions of the no mouth-pipetting rule are a cause for discharge.'

These quotations and others like them indicate that indeed, even in 1960, some held that safety was being overplayed, and others were striving for improved facilities.

Pike⁹ analysed the reported 'sources' or 'causes' of the laboratory infections he listed (Table 2), which, it must be remembered, were largely gathered from published reports and must be highly selective. 'Accidents' naturally figure largely, doubtless because they are readily recognised when they occur. Although explicit evidence for 'aerosol infection' was obtained in very few cases, it has been very generally assumed that a great proportion of the cases for which no specific incident was recognised were due to airborne infection. This faith in the aerial route has informed a great part of the preventive rituals that have been developed and preached during the last two decades.

Table 2 'Sources' and 'causes' of laboratory-acquired infections (after Pike⁹)

Total number surveyed	3921
Percentage attributable to:	
Accident	17.9
Infection from animal or ectoparasite	16.8
Contact with clinical or necropsy specimen	9.2
Aerosol	13.3
Other recognised event	2.1
No event recognised but worked with agent	21.1
Unknown	19.6

There is no way of knowing how general was the underplaying of the risks or how many laboratories were actually making steady improvements. But, if the response was less than it might have been, perhaps there were good reasons.

I believe that one reason for the relative lack of

attention to the possibilities of laboratory-acquired infection during the 1950s and early 1960s was that the principal infections reported in the literature as 'laboratory-acquired' were either characterised by a long incubation period, like tuberculosis, or were exotic infections not commonly encountered in diagnostic laboratories (Table 3). Another reason may have been the fact that so many of the publications dealing with the subject seemed to refer to work in laboratories concerned with microbiological research—often on a large scale—rather than to the clinical laboratory. Thus, 72% of the infections recorded by Pike⁹ occurred in research laboratories, and Darlow²² prefaced an informative paper on 'Safety in the microbiological laboratory' by reference to the 'involvement of large research teams'.

Table 3 *Top five laboratory infections*

Phillips ^a		Pike et al. ^a	
USPHS 1910-50 (231)	18 Countries (426)	Cases (1669)	Deaths (164)
Q Fever	Tuberculosis	Brucellosis	Typhoid
Typhus	Q Fever	Q Fever	B virus
Tularaemia	Brucellosis	Typhoid	Spotted fever
Spotted fever	Psittacosis	Hepatitis	Psittacosis
Psittacosis	Tularaemia	Tularaemia	Leptospirosis

The 1960s and early 1970s saw events that changed the whole approach to laboratory safety. This was a time when science was suffering from the blows administered by Rachel Carson in *Silent spring* and other books, and when the phenomenon of consumerism was flourishing. Ralph Nader was the scourge of American industry and Government, propagating a vehement crusade claiming to protect consumers of goods and services against the supposed rapacity of manufacturers, often thought to be aided and abetted by supine governments. To Nader, it was said, 'the possibility of the invidious immediately becomes the fact of it'. We have seen similar attitudes elsewhere. One began to have the feeling that many members of the public had come to consider that they had a statutory right to immortality, and that any infraction of that right must be someone's fault.

In 1970, Barbara Castle invited Lord Robens to chair a Committee on Safety and Health at Work; the committee's report,²³ published in 1972, recommended the establishment of a new statutory authority to unify the administration of all safety regulations and to extend them to the whole working population. It emphasised the importance of self-regulation, education, and the application of non-statutory codes of practice. The resultant Health

and Safety at Work, etc, Act became law in 1974. This Act explicitly involved the trade unions in the machinery of control, and the unions have themselves become acutely concerned with all manner of safety problems. The Health and Safety Executive was set up under the Act although it did not extend its activity into the laboratory field until 1978.

More important, in the early 1970s, were some obvious, acute examples of laboratory infections leading to death. The recognition that hepatitis B could be transferred from patients to staff, particularly in dialysis units, was emphasised by a few incidents in which laboratory workers became infected and in some cases died. One outbreak, which had a profound effect on attitudes to hepatitis in laboratory workers despite the fact that it seems never to have been published in adequate detail, occurred in Edinburgh in 1969-70.²⁴

Equally dramatic, though further from home, were the outbreaks of viral haemorrhagic fevers at Marburg in 1966 and at Lassa and Jos in Nigeria in 1969. The quite extraordinary facility with which these infections were, according to early reports, transmitted to medical attendants and laboratory workers, and the apparent high mortality, as well as the publicity given to Casal's decision to destroy his stocks of Lassa virus, brought the concept of laboratory-acquired infection into a prominence from which it has not looked back.

The hepatitis risk was unequivocally a real one and, moreover, one of the first posing a recognisable infective hazard to workers in laboratories other than those for microbiology. Interest in this hazard was kept alive by a number of reports such as that of the Advisory Group chaired by Lord Rosenheim²⁵ on the hepatitis problems in the treatment of chronic renal failure, and that of Polakoff and others²⁶ on hepatitis in dialysis units.

Then in 1973 two events occurred that signalled the take-off of the current safety bonanza: the infection of a laboratory worker with smallpox at the London School of Hygiene, and the publication of a letter by Singer and Soll alerting the scientific world to the hazards arising from new techniques for manipulating the genes of bacteria.

The molecular biologists' irruption into the safety scene was signalled by a letter²⁷ that appeared in *Science* in September 1973, drawing attention to the possible hazards to man of experimentation in the field of genetic engineering of microorganisms. Methods had been found by which the genetic material of an animal tumour virus, SV40, could be inserted into, and replicate in, *Escherichia coli*. By 1972 it was clear that the genomes of bacteria could be chopped up at will by the use of restriction enzymes and made to accept inserted DNA se-

quences not only from other bacteria but from viruses and higher animals, including man, and it was predicted that the bacteria would manufacture the products—viral or animal—coded for by the inserted DNA. And the recipient microbe of choice was, because of the enormous fund of knowledge of its genetics, *E. coli*, a normal constituent of the gut flora of man.

The potential benefits—admittedly then thought to be distant—were immense: the manufacture of insulin by *E. coli* rather than by extraction from pancreas; the manufacture of viral vaccines from pure antigen unmixed by toxic debris from the virus or egg; an unravelling of the nature of the genetic disorder in cancer cells. But the scenarios also envisaged the engineered *E. coli* acquiring the characters of doom-bugs: they might spread in epidemic fashion through the human population, causing an outbreak of cancer or some other fell disease; they might be resistant to all known and unknown antibiotics; they might liberate insulin, or growth hormone, or botulinum toxin in a way as uncontrolled as the flood liberated by the sorcerer's apprentice.

There seems to have been a fair volume of argument among the small group of pioneers, mostly working in the United States, on the appropriate response to this variety of scenarios, from those who claimed that they had a mission to control cancer, and that for this they should accept some risk—five or 10 deaths from experimentation might be a small price for the number saved—to those who asserted that in no way did big benefits justify big risks. In the end caution, or real fear of microbial monsters, won the day, and the 26 July 1974 issue of *Science* carried the letter from Berg and 10 colleagues,²⁸ all molecular biologists rather than epidemiologists, calling on scientists throughout the world to defer experiments of various categories postulated as being specially hazardous.

The hazard was then—and still is—entirely conjectural, but so dramatic were the scenarios that the proposed moratorium seems to have been very widely accepted. In Britain the Medical Research Council forbade those workers supported by its funds to continue or initiate work in the defined fields. The Advisory Board for the Research Councils set up a working party under Lord Ashby, which reviewed oral presentations of the various scenarios by 25 of the active workers in Britain, and produced a report²⁹ in less than six months. The working party considered that the potential benefits of genetic engineering of microbes outweighed the possible hazards and came down strongly in favour of continuing work, but with appropriate safety precautions. Unfortunately, Lord Ashby's Working

Party had not been asked to define those safety precautions or to provide a code of practice, and indeed we tended to shelter behind admonitions to 'good microbiological practice'. In consequence, the publication of the report was not considered to provide the all-clear for work to proceed; the journal *Nature* discussed it under the title 'Amber light for genetic manipulation'. So the Department of Education and Science set up another working party to draw up codes of practice for genetic manipulators. Although we still had no evidence that the engineered bacteria would actually have enhanced, or indeed any, ability to cause disease, we set up³⁰ a hierarchy of conjectural hazards and a corresponding hierarchy of supposedly relevant methods for containment with detailed codes of practice—the 'Williams Guidelines'.

The Williams Guidelines, which categorised hazard principally on the basis of the source of the DNA inserted into the new carrier, were destined to have a short life, but the working party also proposed that the Government should set up a Genetic Manipulation Advisory Group (GMAG), comprising both scientists knowledgeable in the field and individuals able to take account of the interests of employees and the general public, to advise on all work in the field of genetic manipulation in the United Kingdom. I say 'advise' because we believed that the provisions of the Health and Safety at Work etc. Act already provided sufficient in the way of legal sanctions to back up a voluntary notification system. In fact, the Health and Safety Executive (HSE) later issued regulations requiring formal notification to them and to GMAG of an intention to work in the field of genetic manipulation but, for the assessment of the proposed experiments and inspection of laboratory facilities, HSE has continued to rely on GMAG.

But the story does not stop there. While our working party was deliberating, the American Association for the Advancement of Science convened a meeting at Asilomar in California in February 1975 at which a set of guidelines very similar to ours were discussed and, after much further debate, these were in June 1976 adopted by the National Institutes of Health (NIH) which set up the Office of Recombinant DNA Activities (ORDA). NIH could legislate only for work that it was funding, a fact that led politicians into devising a variety of Bills for submission to Congress to provide for control of commercial as well as NIH-funded work, none of which got as far as the Statute Book.

Meanwhile, the science was progressing apace, both in achieving the objective of inserting the desired fragments of DNA into bacteria and in obtaining the desired product, and, by conducting

some risk assessment experiments, convincing the regulating authorities that the hazards were in any case less than had been postulated. It was considered that the precautions could be enormously reduced by using bacteria and gene vectors that could be shown by experiment not to survive in the normal human body or environment and could not transfer their genes to normal commensal microbes. Moreover, discovery of the rather fundamental differences in the ways in which prokaryotic and eukaryotic genes are organised made it apparent that bacteria would be unable to interpret an eukaryotic gene that had not been specially modified. In the USA, NIH issued revised and less stringent guidelines in December 1978, and in Britain Sydney Brenner proposed, and GMAG eventually accepted,³¹ a new philosophy for conjecturing hazard. Brenner's scheme involved assessing separately the possible risks in the form of three questions: What is the probability of the genetically manipulated plasmid having access to a potential target? What is the probability that, gaining access, a genetically manipulated genome will be expressed in the form of some active product? What damage could be caused by the product? A range of probabilities has been constructed for a range of different biological systems, and these are used as guidelines to the level of physical containment required for the experiment. The outcome, in Britain as in the United States, has been to release many categories of experiment for work without the necessity for elaborate high containment.

The evolution of the genetic manipulation scene has been a fascinating one, quite apart from the astounding scientific achievement: the doom-ridden scenarios of 1972-3, which actually paid scant respect to epidemiological reality; the self-righteous air with which the scientists conformed to the moratorium; the development—in this country—of a broadly acceptable, because scientifically guided, advisory system for control; and the attempts at real experiment and analysis to try to measure risks. The edifice is all the more remarkable because there is still no evidence for actual hazard.

There was, of course, no doubt whatever about the danger of smallpox; it was well recognised as an infection still carrying a substantial mortality; it was, in 1973, still endemic in the Indian subcontinent; and memories of epidemic spread within Britain were not too distant. The occurrence of three cases of the disease arising by spread from a research laboratory naturally led to calls for full investigation, and within six weeks the Secretary of State for Social Services had set up a formal inquiry presided over by Mr PJ Cox, QC, supported by Professor McCarthy and Dr Millar. The inquiry sat in public

for 29 days and heard 40 witnesses who were represented and cross-examined by Counsel.

The Cox Committee³² was able to point to a number of defects in the safety routines in the relevant laboratories but, in addition, made a number of far-reaching recommendations on the management of microbiological work and on the control of epidemic infection. Arising from one of these recommendations, the Department of Health and Social Security set up a working party, chaired by Sir George Godber (then Chief Medical Officer), to make recommendations on 'The laboratory use [sic] of dangerous pathogens'.³³

The Godber Working Party had first to decide what the term 'dangerous pathogens' should comprise, a difficult task when the medicals and veterinarians were involved and when there was debate whether the relevant danger should be that to the human community (as implied by the committee's parentage in the Cox Committee), that to the human and animal community, or that to the laboratory worker, or all three. In the end the committee embraced all three types of danger with the definition that included 'organisms so dangerous as to present great risks to the health either of laboratory workers or of the human or animal community' (category A). Despite a grammatical variant when this phrase was translated in the later Howie Code, it has been interpreted to mean that the very dangerous category A organisms are those that are hazardous either in the laboratory or in the community, or both. This had the inevitable—and recognised—consequence that any single set of protective precautions would contain elements legitimately regarded as redundant for some purposes.

Included in the report of the Godber Working Party³³ was a set of rules for the construction and operation of a 'category A' dangerous pathogens laboratory; these were based on the procedures developed for research work at the Ministry of Defence Microbiological Research Establishment. That they were neither designed nor suitable for laboratories solely concerned with diagnostic work was recognised by the working party, which admonished authorities to exercise discretion in judging the adequacy of the precautions adopted in individual laboratories according to the work to be done. Unfortunately, the working party offered no guidance on the ways in which such discretion might be exercised.

Sir George Godber's Working Party had two progeny: the Dangerous Pathogens Advisory Group (DPAG), which was set up by DHSS to advise the Health Departments, and to some extent the Ministry of Agriculture, on the arrangements for handling 'very dangerous pathogens', and a

working party under Sir James Howie to prepare a Code of Practice for the Prevention of Infection in Clinical Laboratories.

The DPAG, chaired by Professor Shooter, although intended by its parent to be small and expert, grew by the accretion not only of experts but of representatives of several departmental and health authority interests (but not of trade unions, lay, or other general interests) to a total of over 30 members, officers, and observers. It took its task to be to apply the 'Word of Godber', and it arranged for the inspection of laboratories that wished to work with very dangerous pathogens, including those that wished to do no more than seek more conventional pathogens in material that might possibly contain one of the very dangerous viruses. It exercised its discretion—as the Godber Working Party had indicated—but, like that working party, failed to formalise in time the distinctive routines appropriate on the one hand to research with dangerous pathogens and on the other to work directed at the diagnosis or exclusion of other agents. I say 'in time' because of the tragic escape, in August 1978, of smallpox virus from a research laboratory in Birmingham for which DPAG had exercised a discretion that it can now be seen would have been better reserved for laboratories in which dangerous pathogens were never to be handled in bulk.

The work of Sir James Howie's Working Party, whose Code³⁴ was published in 1979, is now abundantly familiar to all who work in clinical laboratories and to many who work in laboratories for quite remote disciplines. Suffice it to say that the working party codified what it saw to be the best practicable methods for work in clinical diagnostic laboratories and that its form and tone inevitably reflected the climate of public (rather than professional) opinion of the mid 1970s, which, as I have already tried to indicate, had been conditioned by a mixture of science fiction, real tragedy, and not entirely altruistic propaganda. The Howie Working Party had as its parent Godber on dangerous pathogens and grandparent Cox on smallpox; facts, rumours, and committees on hepatitis had been legion; and the report of Harrington and Shannon¹⁰ seemed to indicate that laboratory spread of tuberculosis was still not controlled. There was enough general background of real concern without invoking Rumour in Shakespeare's *Henry IV* who spoke 'of peace, while covert enmity, under the smile of safety, wounds the world'.

The Howie Code of Practice was languishing unpublished but prematurely leaked when in August 1978 the smallpox virus struck again, escaping from a research laboratory in Birmingham,

seeming to justify the complaints that our safety precautions are often inadequate. (The report of Professor Shooter's committee which investigated that incident was likewise destined to languish unpublished, but leaked, for over a year.)

The contrast between the 'official' response to the hazards of genetic manipulation and those of clinical laboratory practice is interesting and striking. The initial response to the conjecture of possible hazards from the new methods of gene transfer in bacteria was massive overkill: to stop all experimentation for months, and to follow this by gradual relaxation as analysis and experiment seemed to define the dangers more clearly—and this despite the fact that some of the scenarios are far more threatening than anything that real dangerous pathogens can offer. In contrast, clinical pathology, which has known real pathogens for decades, started in a too relaxed way but seems now to be risking serious overkill.

The genetic manipulators have attempted semi-quantitative risk assessment as a guide to the levels of protection to be applied. They have measured survival of manipulated bacteria in the gut, tried to determine the risk of gene transfer from their transformed bacteria, and provided at least estimates of the probability of escape from safety cabinets, and from the laboratory, and of the risk of entry into a new host, of doing harm after entry, or of that harm being contagious. Most of the figures are filled in—in the first place—by pure thought rather than by measurement, but when added together (or strictly when multiplied together, since they are probabilities) the real risk has appeared to be almost vanishingly small.

Genetic manipulation has a great incentive, both scientific and commercial. The benefit that is set against any risk has a positive character: we shall get *E. coli* manufacturing insulin or growth hormone at a reduced cost or in greater volume.

The clinical laboratory worker's end product is not a marketable insulin but the correct and useful diagnosis arrived at quickly to facilitate the care or cure of some sick person. To listen to some polemicists one might think that the cost of that product was measurable not so much in the time, effort, skill, and materials used to achieve the diagnosis but in hazard to the staff performing the tests. The prevention of this hazard can seem to become a more important objective than providing a good diagnostic service. Perhaps this is another example of the truism that eliminating risks for the unfortunate few may markedly increase the risk for the rest of a much larger group, an idea that is difficult to defend politically when the unfortunate few are

easily recognised while the unfortunate many are nameless.

It seems worth considering what more quantitative analysis and experiment could enable us to put more figures to the real costs and to the twofold benefit of doing more good for patients and less harm to the laboratory workers.

The most effective way of preventing infection in laboratory staff is to make sure that the laboratory does not receive material containing pathogens. This ultimate method has been adopted for the prevention of laboratory acquired Lassa fever and the like, and there have been limited moves to follow the same principle with hepatitis B and tuberculosis. Although this may perhaps be justified with a few exotic virus infections, in general it seems a bad principle since it almost certainly implies protecting laboratory staff at the expense of optimum treatment of patients, and there can be very few circumstances in which that is ethically justifiable.

What then are the sort of 'costs' imposed by protection of staff that have to be met in one way or another from funds that could be used for other aspects of patient care or preventive medicine? Broadly, the costs comprise equipment, space, staff, and time. Equipment needs have loomed very large in the agonising that has followed publication of the Howie Code of Practice. A particular dilemma is posed by the recognition or assertion that model B of some item is safer than model A, perhaps because it liberates fewer microbes into the air while operating, or is marginally more difficult to operate wrongly. It is difficult enough to measure the 'improvements' precisely, impossible to judge whether the improvements, if real, make a significant contribution to greater safety. When we cannot even assert in any quantitative way how much the introduction of safety cabinets has contributed to the control of tuberculosis, it is manifestly impossible even to guess how much benefit might result from a relatively small improvement in the aerosol retention efficiency of a new design of cabinet.

The limited evidence that we have indicates that the incidence of laboratory-acquired infections is declining, though how much this is due to improvements in technique and equipment, and how much to a decline in the number of infected specimens received, cannot be judged. We need to know more precisely what is the extent of the harm suffered by laboratory workers, and we must surely take this beyond the anecdotal or the limitation to one or two 'traditional' hazards like tuberculosis or brucellosis—for neither of these is likely to exist as a significant hazard much longer simply because of their disappearance from the population of patients under examination. Harrington and Shannon's¹⁰

analysis revealed that shigellosis was marginally more common in laboratory workers than hepatitis, and had twice the incidence of tuberculosis. Probably many of these cases were the relatively trivial Sonne dysentery, and doubtless more of them, than of the more serious infections, were actually contracted outside the laboratory. We ought to be able to discover whether there is any detectable excess in laboratory workers of infections due to any of the other microbes we encounter reasonably regularly in clinical laboratories. What information can we get by looking for non-symptomatic carriage of indicator organisms commonly handled at the bench? Petrocheilou and Richmond³⁵ reported a limited study in which they looked for (and failed to find) in their own faeces a nalidixic-resistant *E. coli* K12, with which they worked for two years, but further studies seeking faecal or upper respiratory carriage might be rewarding.

One step further back in analysing risks would be to measure more precisely the actual exposure of bench workers, working normally, to the microbes with which they are working. Too much of the literature of laboratory hazard depends on fearfully unrealistic experiments with heavy suspensions of marker organisms, and almost all relates to aerosol infection. The risks of contact infections are presumably much more intermittent and therefore more difficult to assess but the task is not necessarily impossible. It is, of course, true that, even given that we can measure the numbers of microbes dispersed in various manoeuvres, we do not know sufficient of minimal infecting doses to extrapolate the risks; probably few microbes can infect from a dose as small as that apparently effective in tuberculosis. But these limitations do not absolve us from the duty to measure the real risks realistically.

It must ordinarily be some accident or error in technique that lets the microbes escape. Can we measure how often relevant accidents or mistakes happen? And can we relate this error frequency to different methods of working? How often do containment methods, designed to protect against aerosols, carry a penalty of an increased frequency of accident? Is it true that a tendency to rely on a range of protective equipment is liable to atrophy technical skills or to generate the belief that, if work is carried out within a safety cabinet, there is no need to practise the skills that, used on the open bench, have by and large protected us for years?

How real is the assertion that our safety is bought by penalty for patients? Much has also been made of the slower working imposed by safety rules, but I doubt if we have real quantitative evidence. Is working to rule really slower, and does it delay reporting results? How often do some safety-

generated prohibition prevent or delay the performance of a test vitally needed for patient care, with consequent ineffective or at best prolonged treatment? How great are the additional costs imposed on the laboratory services and necessarily diverted from other functions?

Although many people had been working for years in the pursuit of laboratory safety we were not well armed with hard evidence on real risks or the real incidence of trouble when, for a mixture of reasons, safety became transformed from something we all work together to achieve to something management had failed to do enough about. We now need concerted attempts to get more facts to help us not only to improve laboratory safety but also to educate the public and the powers that be, so that the pursuit of safety does not simply become a wild goose chase.

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