

RETURN to an Order of
the Honourable The
House of Commons
dated 22nd July, 1980

**REPORT OF THE
INVESTIGATION INTO
THE CAUSE OF
THE 1978 BIRMINGHAM
SMALLPOX OCCURRENCE**

*Ordered by The House of Commons to be printed
22nd July, 1980*

LONDON
HER MAJESTY'S STATIONERY OFFICE

REPORT OF THE INVESTIGATION INTO THE CAUSE OF THE 1978 BIRMINGHAM SMALLPOX OCCURRENCE

Foreword by The Secretary of State for Social Services

I have arranged for this Report, which was submitted to my predecessor in December 1978, to be published on the first practicable day after receiving assurance that there was no longer any legal obstacle. Readers will recognise that the investigation by Professor Shooter and his colleagues was carried out in circumstances of great public concern in which speed seemed to them, to my predecessor and, I believe, to Parliament to be of the essence. Their task was not only to enquire into the circumstances of the occurrence of smallpox at Birmingham but also to ensure that immediate precautions were taken to prevent any further escape of infection. The University of Birmingham collaborated fully with them.

The Report now published was based on such information as was available to Professor Shooter and his colleagues at the time, or was derived from investigations they commissioned, and appeared relevant to their remit and to their aim of helping to prevent a similar occurrence in the future. They reached no definite conclusion on the way in which the outbreak of smallpox occurred but presented certain explanations which they believed to be possibilities.

Subsequently a great deal of evidence and argument on the facts and causes of the outbreak was made public in the course of the hearing by the Birmingham Justices of a prosecution of the University by the Health and Safety Executive. The case against the University was dismissed. The way in which the outbreak of infection occurred remained unexplained.

The University have stated that they regard the outcome of the Court hearing as establishing that they were in no way at fault and that much of the assessment in this Report is substantially incorrect. The Justices did not make public their reasons for dismissing the case and it is not for me to enter into controversy about matters on which the evidence may be in conflict. The Report is clearly to be read in the knowledge of the circumstances in which it was prepared, of the conclusion of the Justices and of the persisting uncertainty about the way in which the outbreak occurred.

The assessment of the facts in the Report and the criticisms made or implied in it were vigorously contested in evidence given before the Justices. However, that does not detract from the public importance and value of the general recommendations it contains about the inspection of laboratories where work with very dangerous pathogens is carried out and about procedures for notification and control of such work. I believe it important that these recommendations should be widely known. On some of them action has already been taken, and on others consultations initiated by the Health and Agriculture Departments and the Health and Safety Executive are in progress.

My colleagues and I are grateful to Professor Shooter and the members of his group for the effort they put into their investigation and for the important suggestions they made to contribute to the greater safety of laboratory staff and of the general public.

PATRICK JENKIN

INVESTIGATION INTO THE CAUSE
OF THE 1978 BIRMINGHAM
SMALLPOX OCCURRENCE

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21st December 1978

THE RT. HON. DAVID ENNALS, M.P.
Secretary of State for Social Services,
Alexander Fleming House,
Elephant and Castle,
London SE1 6BY.

Dear Secretary of State,

On 30th August 1978 you asked me to conduct an investigation into the occurrence of smallpox in Birmingham in 1978 with a team of experts and observers from the World Health Organisation, the Health and Safety Executive and the Trades Union Congress.

In the report that accompanies this letter we have set out our findings, and we hope that our observations and recommendations will help to prevent a similar tragedy happening in the future.

Yours sincerely,

PROFESSOR R. A. SHOOTER

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MRS. M. C. MOORAT.

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MR. S. W. F. RESTALL—Microbiological Research Establishment, Porton.

WEST MIDLANDS REGIONAL HEALTH AUTHORITY

PROFESSOR P. WILDY.

THE WORLD HEALTH ORGANISATION

We wish to thank the Chief Constables of Merseyside and West Midlands, and the Ambulance Service for their assistance in transporting smallpox virus to St. Mary's Hospital Medical School, London.

We also wish to thank Lord Hunter, Vice-Chancellor of Birmingham University, Professor Owen Wade, Dean of the Medical School, the staff of the Medical School and representatives of the staff associations and trades unions for all the help and co-operation they have given us, without which this investigation would not have been possible.

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REPORT OF THE INVESTIGATION INTO THE CAUSE OF THE 1978 BIRMINGHAM SMALLPOX OCCURRENCE

TO: THE RT. HON. DAVID ENNALS, M.P.
Secretary of State for Social Services

PART I

THE SCIENTIFIC INVESTIGATION

CHAPTER 1

INTRODUCTION

1. On 24th August 1978, smallpox was diagnosed in a medical photographer, Mrs. Janet Parker, aged 40 years, of King's Norton in Birmingham, who worked in the Anatomy Department of the Birmingham University Medical School and had not been abroad during the past year.

2. Mrs. Parker first became unwell with headache and muscular pains, on Friday, 11th August 1978. She went to work that day, and travelled to and from work with her husband in their own car. On Saturday, 12th August, she felt better and went out for a brief walk in King's Norton, and on Sunday, 13th August, she called on a neighbour. She again became unwell on Sunday, 13th August. She developed a rash on Tuesday, 15th August, or Wednesday, 16th August. On Wednesday, 16th August, she was visited by her doctor who prescribed an antibiotic, and two days later she was visited by his partner who noticed the rash and, considering it likely to be a drug rash, stopped the medication. She remained unwell with spots developing on her face, limbs and trunk, and on 21st August she was transferred to her parents' home in her father's car. On Thursday, 24th August, she was visited by her parent's doctor who referred her to hospital.

3. She was admitted to an isolation cubicle in Ward 32 at East Birmingham Hospital at 3.00 p.m. on Thursday, 24th August. Smallpox was suspected, and that evening specimens of vesicle fluid were taken to the Department of Medical Microbiology of the Birmingham University Medical School, where the smallpox laboratory functioned as the Regional Diagnostic Smallpox Laboratory. Professor Bedson, who was head of the Department of Medical Microbiology and in charge of the smallpox laboratory, undertook virological examination of the specimens. Electron microscopy revealed brick-shaped particles characteristic of pox viruses. At 10 p.m. that night Mrs. Parker was admitted to Catherine-de-Barnes Isolation Hospital, Birmingham. Sadly, Mrs. Parker never recovered from her illness and she died on 11th September. Examination of her medical records showed that she had not over the past year received any treatment that would alter her immunity to infection; she was vaccinated against smallpox in 1966.

4. Mrs. Parker's mother, Mrs. Hilda Whitcomb, aged 70 who had been vaccinated on 24th August, 1978, developed smallpox on 7th September and was also admitted to Catherine-de-Barnes Hospital. She recovered from her illness and was discharged on 22nd September. No further cases of smallpox have been reported. Records of all deaths registered in the Birmingham Area Health Authority areas during June and July 1978 have been scrutinized in case any deaths registered as due to other causes may have been due to smallpox, but no suspect case was found. Eight other people, mainly close contacts of Mrs. Parker, who developed mild illnesses such as fever and/or a rash, were admitted to hospital as a precaution but in none was the diagnosis of smallpox confirmed, and almost all were finally considered to be cases of reaction to vaccination.

Containment of the Infection

5. We would like to record our appreciation of the speed and thoroughness with which Dr. Nicol, the Area Medical Officer, and his staff, and also the staff of the Birmingham University Medical School, reacted to contain the spread of illness when smallpox had been diagnosed. Their action in dealing with the task of tracing, isolating and vaccinating all close contacts of Mrs. Parker, and in disinfecting all areas of possible contamination, was impressive and contributed considerably to preventing a far wider spread of infection.

The Source of Infection Committee

6. A Source of Infection Committee was set up by the University of Birmingham and the Area Health Authority and met on 28th August to, "enquire into and try to establish the source of infection of the patient Mrs. Janet Parker." The Committee's enquiries were overtaken by the setting up of this investigation a few days later. The Committee's preliminary report, which they made available to us, is given in Appendix 1.

Public Concern over the Birmingham Occurrence

7. Following the success of the World Health Organisation's (WHO) smallpox eradication campaign which began in 1967, the scourge of smallpox has probably now been eradicated from the world. The last known "natural" case of smallpox occurred in Somalia in October 1977, and when the Birmingham case occurred WHO was about to certify formally that the world was completely free of the disease.

Naturally the case aroused considerable national and international disquiet, particularly as the source of the infection appeared to be the smallpox laboratory of the Birmingham University Medical School situated on the floor below the photographic studio where the patient worked. Disquiet was also expressed in that this case followed, 5 years later, a similar one in London in April 1973, when two people died of smallpox as a result of infection originating from a laboratory in the London School of Hygiene and Tropical Medicine. At that time a public enquiry was held*, and recommendations, designed to improve the safety in laboratories handling smallpox virus, were made in order to prevent further laboratory escapes. We consider below how far the lessons of the London incident were learned. Furthermore, attention was drawn to an outbreak of

*Cmnd 5626, HMSO London, June 1974.

smallpox in the West Midlands in 1966 which affected 73 people, when the primary case was thought to be a photographer employed in the Anatomy Department in the Birmingham University Medical School.

The Investigation

8. Following this latest incident in Birmingham, public concern was expressed about the adequacy of the safety measures employed by laboratories working with smallpox viruses and the question was raised whether it was desirable or even necessary to continue to work with such dangerous organisms when the disease was probably eradicated from the world. The present investigation was constituted by your invitation to Professor R. A. Shooter of 30th August 1978, with the following terms of reference: "To conduct an investigation into the occurrence of smallpox in Birmingham in 1978, all the relevant circumstances leading up to it, and the lessons to be learned; and to report to the Secretary of State for Social Services." Members of the investigation included four who were members of the Dangerous Pathogens Advisory Group, and two who have no association with the Group. They were invited in consultation with the Chief Medical Officer of the Department of Health and Social Security.

9. We were assisted in our task by experts from the World Health Organisation, the Health and Safety Executive and the Trades Union Congress, who, though assigned to our investigation as observers, nevertheless took a full and active part in it.

10. We saw the aims of our investigation as follows:—

- i. To find out how Mrs. Parker was infected.
- ii. If the smallpox laboratory in the Department of Medical Microbiology of the University of Birmingham Medical School was the source of the infection, to find out whether infection occurred because of
 - a. failure to carry out safety regulations;
 - b. failure of those responsible to make sufficiently severe regulations;
 - c. something unforeseen that was not planned for in the regulations.
- iii. To identify lessons to be learned for the future.
- iv. To make general recommendations about holding smallpox virus.

11. There were several aspects relating to this incident that we did not consider because we felt them to lie outside our terms of reference. For example, we did not make a detailed examination of the clinical course of Mrs. Parker's illness, we did not investigate the containment measures employed by the Area Health Authority or the efficiency of the system of liaison between the various parties concerned in the occurrence, nor did we explore the state of industrial relations insofar as they had an impact on safety, in the University of Birmingham. Our report, however, covers a very wide range of issues both leading up to and following on from Mrs. Parker's infection.

12. After preliminary investigations, made when the strain of smallpox that infected Mrs. Parker has not yet been identified with certainty, we considered that there were five possible sources of Mrs. Parker's infection.

- i. The smallpox laboratory, the virus reaching Mrs. Parker through the air, or by human contact, or by contact with contaminated material or equipment.
- ii. A person suffering from smallpox or a form of smallpox modified by previous vaccination.
- iii. An animal infected with an animal pox virus in the Department of Anatomy's primate colony.
- iv. Virus that had survived in Mrs. Parker's studio and dark room since 1966 when a photographer who was working there developed smallpox.
- v. Virus deliberately or accidentally removed from the smallpox laboratory.

Each of these possibilities was investigated. Our task was made more difficult as we were not able to talk to Mrs. Parker or Professor Bedson.

13. We held 8 formal meetings, and in between these the Chairman, individual members and observers and the two secretaries made numerous visits to the Birmingham Medical School to interview staff, arrange for scientific tests to be carried out and to inspect the Department of Medical Microbiology and the surrounding areas in the East Wing of the Birmingham Medical School.

CHAPTER 2

SMALLPOX

14. Smallpox virus belongs to a large family of pox viruses, and in nature its ravages are confined to man. It occurs in two forms, *Variola major* and *Variola minor*. The most serious, *Variola major*, is a single species, but strains of this virus isolated from different parts of the world may show some differences. These strains are usually identified by the name of the patient from whom they were isolated or the country in which the outbreak occurred.

15. Man is infected by inhaling smallpox virus. The illness is characterised by a sudden onset of fever, headache, vomiting, marked prostration and sometimes delirium. The incubation period may extend from 7 to 17 days, but usually 10 to 12 days elapse from the date of infection before the onset of illness. The rash begins as tiny discrete pink spots which enlarge and become slightly raised papules. Each of these becomes, by the third day, a vesicle about 6 mm in diameter, deep in the skin. After two more days the fluid inside becomes turbid and the lesions are now in the form described as pustules. They gradually shrink and dry up to become hard crusts in the skin, eventually separating from it and leaving a sunken scar or pock. The hard material which comes away contains smallpox virus in its substance.

16. The distribution of the rash is characteristic, affecting the head and extremities much more than the trunk. There are, however, variations in this characteristic pattern which can cause considerable clinical diagnostic difficulties. In its most atypical form, known as *Variola sine eruptione*, which is sometimes the result of residual immunity from a previous vaccination, no rash follows the onset of illness. Even these patients may very occasionally be infectious.

17. Complete protection from smallpox is nearly always achieved by successful vaccination carried out in the period up to two years before exposure. Vaccination within three days after exposure is also generally protective. Immunity, however, is never absolute and a heavy infection with smallpox virus may give rise to illness even in the presence of considerable immunity. Mrs. Whitcomb, Mrs. Parker's mother, was vaccinated successfully and given anti-vaccinial immunoglobulin on 24th August, when her daughter's illness was diagnosed. She was also given methisazone on 25th August. However, she developed smallpox on 7th September. The disease ran a mild course and she was discharged free from infection on 22nd September.

18. Vaccinia virus is used for vaccination of humans against smallpox. Its exact origin is uncertain. Its antigens are similar to those of smallpox but the two viruses are readily distinguished in the laboratory.

19. Other members of the pox virus family are frequently named after the animals they attack, or from which they were first isolated. Among them there

are such viruses as cowpox, camelpox, buffalopox and monkeypox. Monkeypox is known to have infected some thirty people overseas, producing a smallpox-like disease, but it spreads with difficulty even among susceptible close contacts, and is thought not to be sufficiently transmissible to allow continuing infection to become established in man. Viruses known as whitepox have been isolated from the tissues of monkeys and rodents; they are generally indistinguishable by available methods from variola virus, but are not known to have caused human infection.

20. Hybrid (or cross bred) virus can be obtained experimentally by infecting one culture with two viruses. These hybrid viruses have properties of which some are drawn from one parent virus, and some from the other. These may be called recombinants, but the method used is not included as work in "genetic manipulation" as defined and controlled by the Genetic Manipulation Advisory Group (GMAG) and the Health and Safety Executive.

CHAPTER 3

THE UNIVERSITY OF BIRMINGHAM MEDICAL SCHOOL

21. The University of Birmingham Medical School dates back to 1779. At the time of the events under consideration, Professor E. Brodie Hughes was Dean, he retired at the end of August 1978 and was succeeded by Professor O. L. Wade. The present Medical School was erected in the 1930's and is a solidly constructed brick building on four floors. The East Wing houses, on the ground floor and lower ground floor, the Department of Medical Microbiology, within which is the smallpox laboratory. On the first floor, above the Microbiology Department, is the Department of Anatomy in which Mrs. Parker worked. The second floor houses tutorial rooms. (See Figures 1 and 2).

The Department of Medical Microbiology

22. The Department of Medical Microbiology, in which research on animal pox and smallpox viruses was being conducted, is the successor to previous Departments of Bacteriology and Virology established over many years. It had as its head Professor Henry Bedson. The pox virus laboratory was identified by the World Health Organisation as one of the three laboratories in the United Kingdom still holding variola viruses at 25th July 1978. The others were at the Medical School, Liverpool University and St. Mary's Hospital Medical School, London. The number has since been reduced to one laboratory, at St. Mary's Hospital Medical School.

23. Professor Bedson, who was responsible for the running of the pox virus laboratory, died tragically on 6th September from self-inflicted throat wounds, shortly after our enquiry began. He had been acutely concerned about Mrs. Parker's illness and the press and public reaction to it.

24. Professor Bedson, who was aged 49 years, qualified in medicine in 1952 from the London Hospital, where he became first assistant in the Medical Professorial Unit. Later he was lecturer in bacteriology at Liverpool University where he developed his interest in pox virus work. He was appointed to Birmingham University in 1964 as senior lecturer in virology and bacteriology, became reader in virology in 1969, and held the Chair in Medical Microbiology from 1976. His work was considered by WHO to be vital in their campaign to eradicate smallpox. Present knowledge of the relationship of white pox viruses to variola virus owes much to his studies and he had played a major role in the smallpox eradication campaign. Professor Bedson was a member of the Dangerous Pathogens Advisory Group, a member of the International Commission for the assessment of Smallpox Eradication in Pakistan and Afghanistan 1976, and a member of the WHO Informal Group on Monkeypox and related Viruses.

Approval of the Smallpox Laboratory

25. In 1976, approval for work with smallpox virus was given to the laboratory by the Department of Health and Social Security who were acting on the

advice of the Dangerous Pathogens Advisory Group (DPAG). The DPAG is an expert group representative of medical, scientific and veterinary specialities set up to advise Government Departments on the suitability of particular laboratories to work with dangerous pathogenic organisms. The smallpox laboratory had been inspected in 1976 on behalf of DPAG which, on the basis of the report received, had considered it suitable for smallpox work.

26. The smallpox laboratory was supported financially by WHO and the MRC to carry out research. It was, however, due to cease all smallpox work by the end of 1978 following a decision by WHO to limit the number of centres holding smallpox virus to five—London; Atlanta, USA; Moscow; Tokyo; and Bilthoven, Holland. Inspectors from the World Health Organisation visited the laboratory in early May 1978. They expressed to Professor Bedson their concern at the lack of certain safety measures and recommended improvements in others, but saw no reason to alter the timetable by which the laboratory should continue smallpox work until the end of 1978.

27. The approval of the smallpox laboratory by the DPAG and the action of WHO in agreeing that the smallpox work should continue have, in the wake of Mrs. Parker's infection from smallpox, raised serious questions about the standards and the system by which they judge the facilities of a laboratory suitable for the containment of a classified dangerous pathogen. A detailed examination of the role played by DPAG and WHO appears later in this report.

The Pox Virus Laboratory

General Description

28. The pox virus laboratory of the Department of Medical Microbiology consisted of a large room—the animal pox room—at one end of which there was an office, and at the other, two rooms, one the smallpox room and the other the tissue culture room in which there were incubation facilities for eggs. The layout of the laboratory is shown on the attached plan in Fig. 1, and its relation to the Anatomy Department in Fig. 2.

29. The smallpox room was about 8' square, had a sealed window, and contained an MSE 25 ultra-centrifuge (6)*, a portable autoclave (5) for materials and articles which were likely to be contaminated, and a Class I PHLS-type (visual indicator) biological safety cabinet (3) exhausting through filters and thence by a short length of ducting through the window to the exterior. The safety cabinet fan when working was thought to cause a negative pressure in the smallpox room. Its fan was not in operation all day or for prolonged periods, but only when work was in progress and for a time afterwards. The cabinet contained a gas burner, but we noticed that the inlet holes in the side of the cabinet, designed to admit the rubber tubing for other pieces of apparatus such as an aspirator, had been sealed with adhesive tape. The cabinet sat on a wooden bench (2). Also on the bench was an aspirator operated by a water pump (1). This was used outside the cabinet to suck off media from Petri dishes during harvesting of viruses. Cold water was supplied to the sink by two taps. The one used for hand washing was foot-operated, the other, connected to the

*Figures in brackets refer to the "Key" numbers in the plan in Fig. 1.

Figure 1. Layout of Pox Virus Laboratory Suite

KEY

Smallpox Room

- 1 Foot-operated sink with aspirator
- 2 Bench
- 3 Safety Cabinet with ultrasonicator
- 4 Service duct B – Shaded areas represent hatches
- 5 Portable autoclave
- 6 MSE 25 High speed centrifuge
- 7 ‘Tacmat’

Tissue Culture Room

- 8 Sink
- 9 Ultra-violet lamp
- 10 Incubators
- 11 Bench

Animal Pox Room

- 12 Freezer holding stocks of smallpox and other viruses
- 13 Refrigerator
- 14 Large plastic bins containing used glassware immersed in chlorox
- 15 Trolley with metal buckets on top containing used infected material, in plastic bags, for auto claving
- 16 Table
- 17 Trolley carrying anaerobic jar and pump, used in the preparation of absorbed serum
- 18 Incubator containing smallpox virus
- 19 Incubator containing smallpox inoculated eggs
- 20 Incubator containing animal pox virus
- 21 Bench with microscopes
- 22 Low speed centrifuge
- 23 Duct C – Shaded area is the hatch
- 24 Sink with aspirator
- 25 Safety cabinet with ultrasonicator
- 26 Bench
- 27 Sink
- 28 Sliding door
- 29 Swing barrier
- 30 Ventilation duct

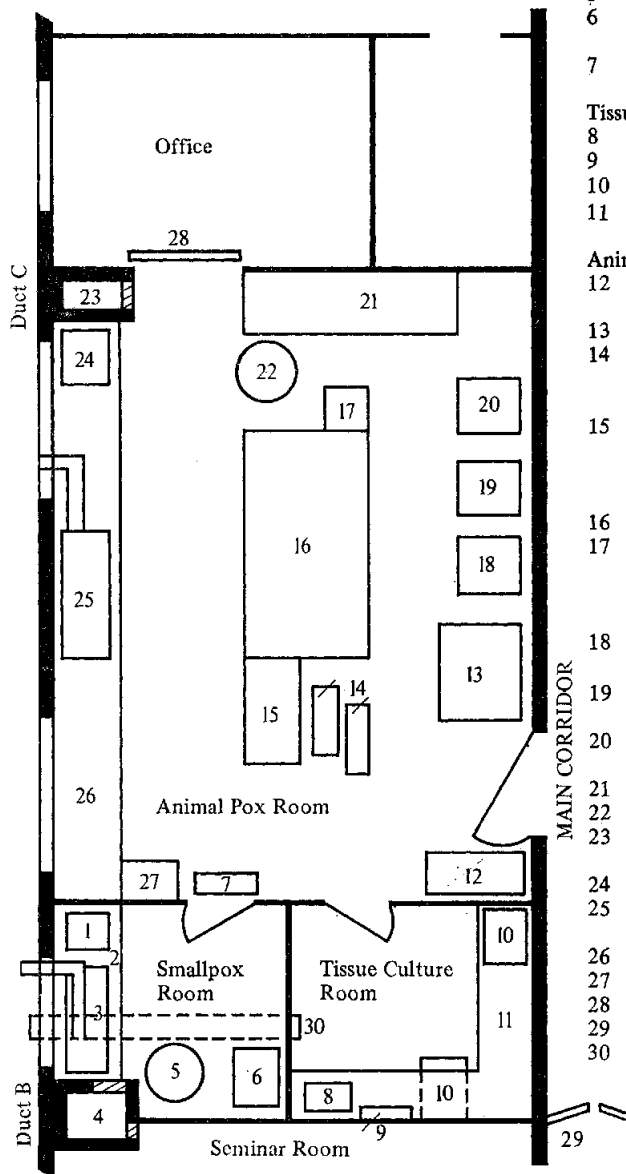
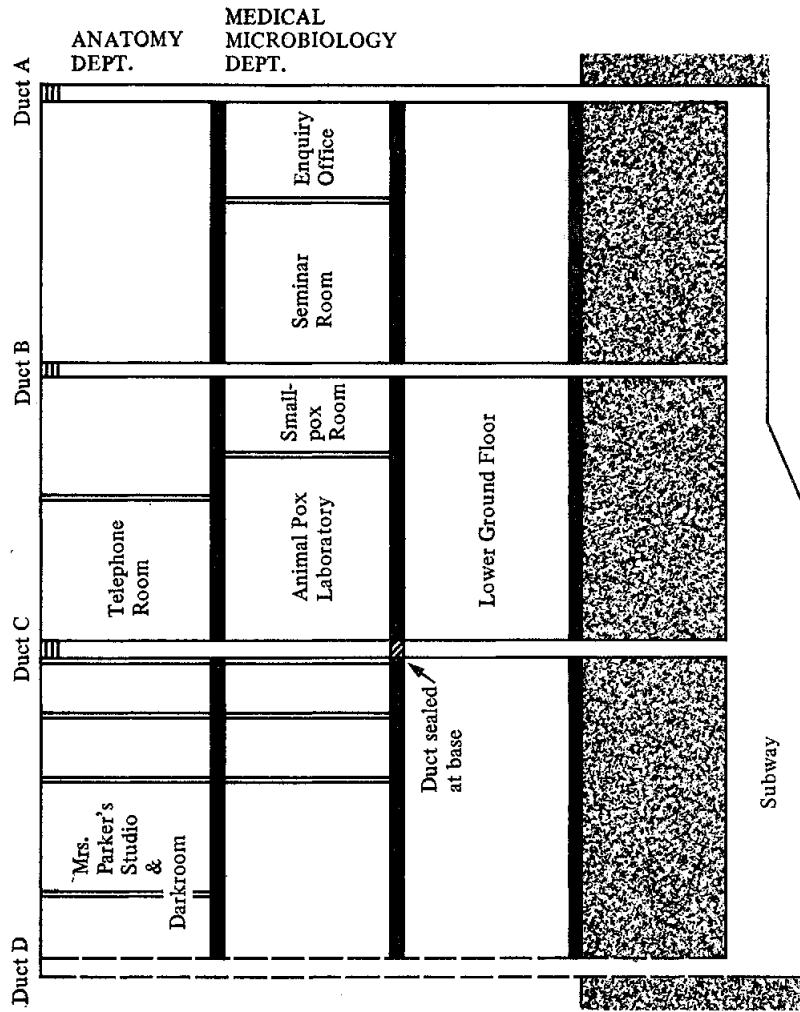
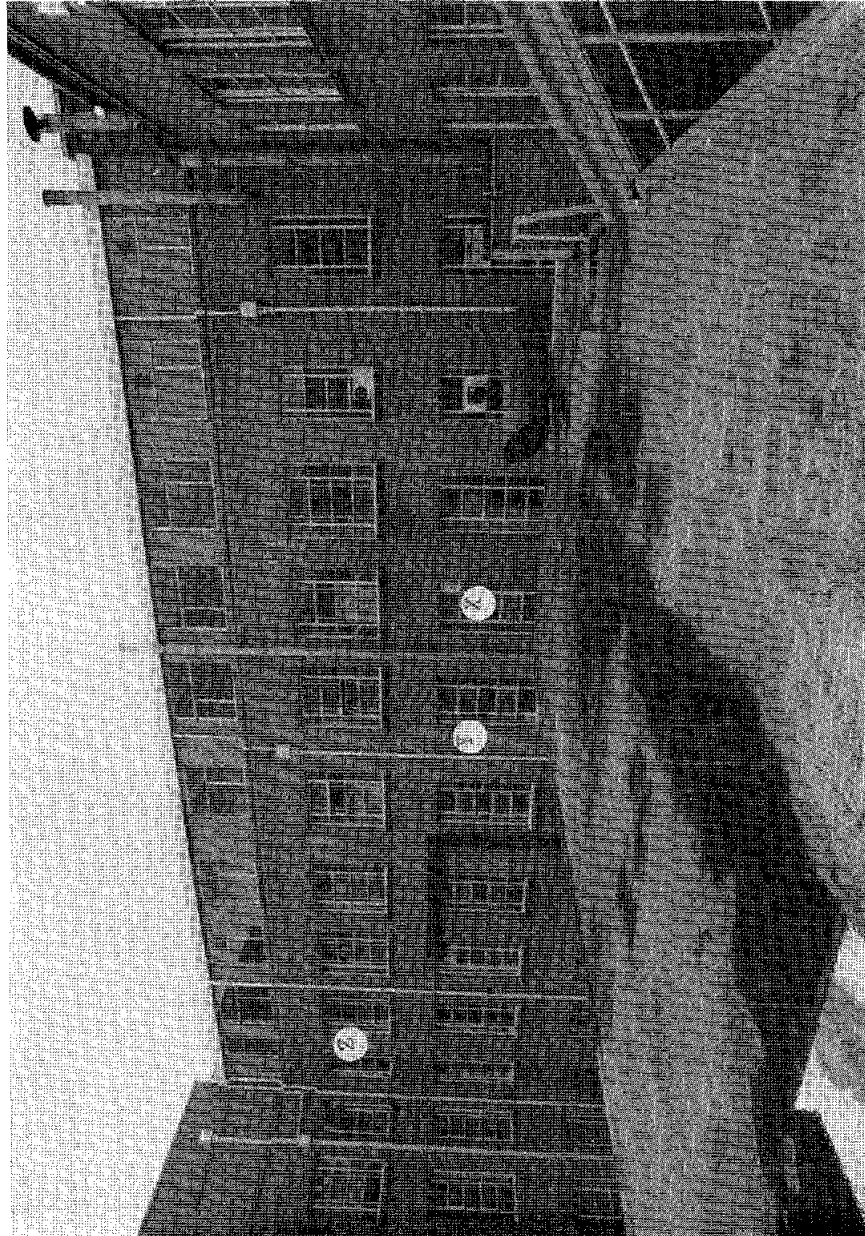


Figure 2. Diagram showing the Medical Microbiology and Anatomy Department floors (viewed from the East Courtyard) and the service ducts running through them.

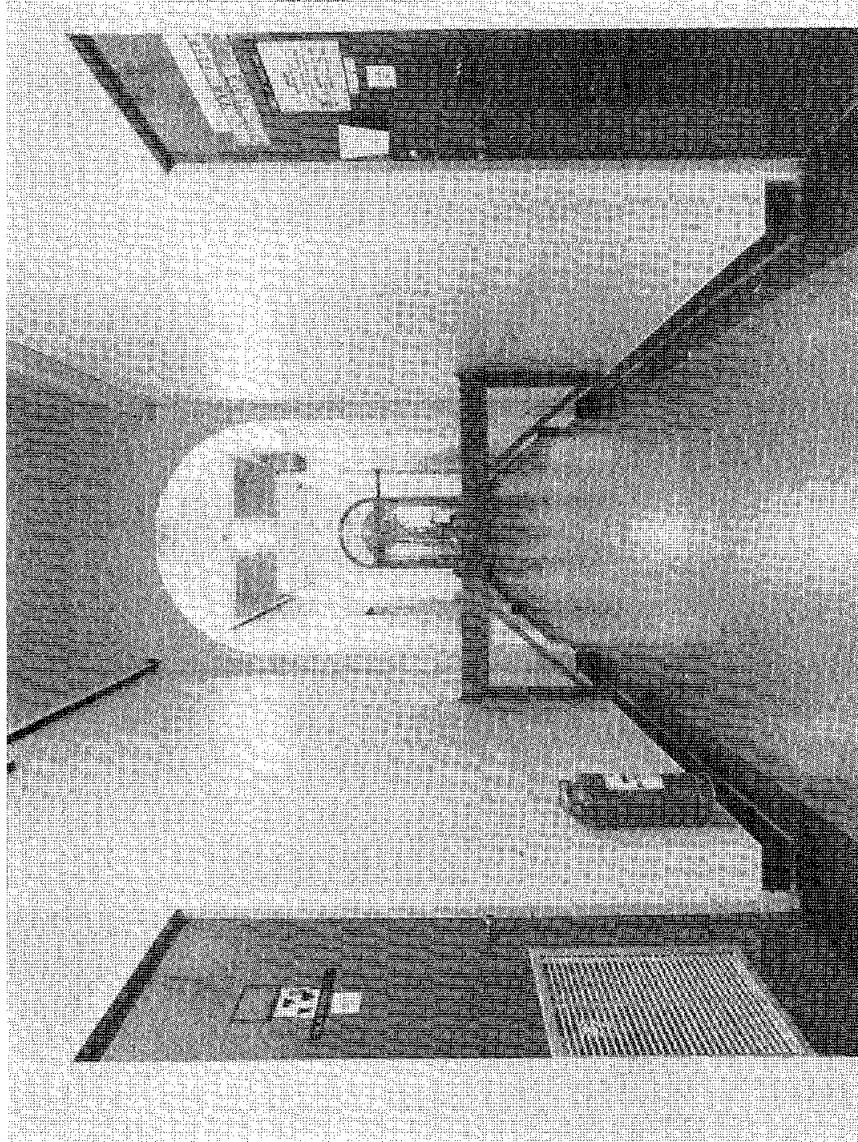


ANATOMY AND MEDICAL MICROBIOLOGY

Floors from the East Courtyard—X marks the smallpox room, Y the animal
pox room, and Z Mrs. Parker's photographic studio.

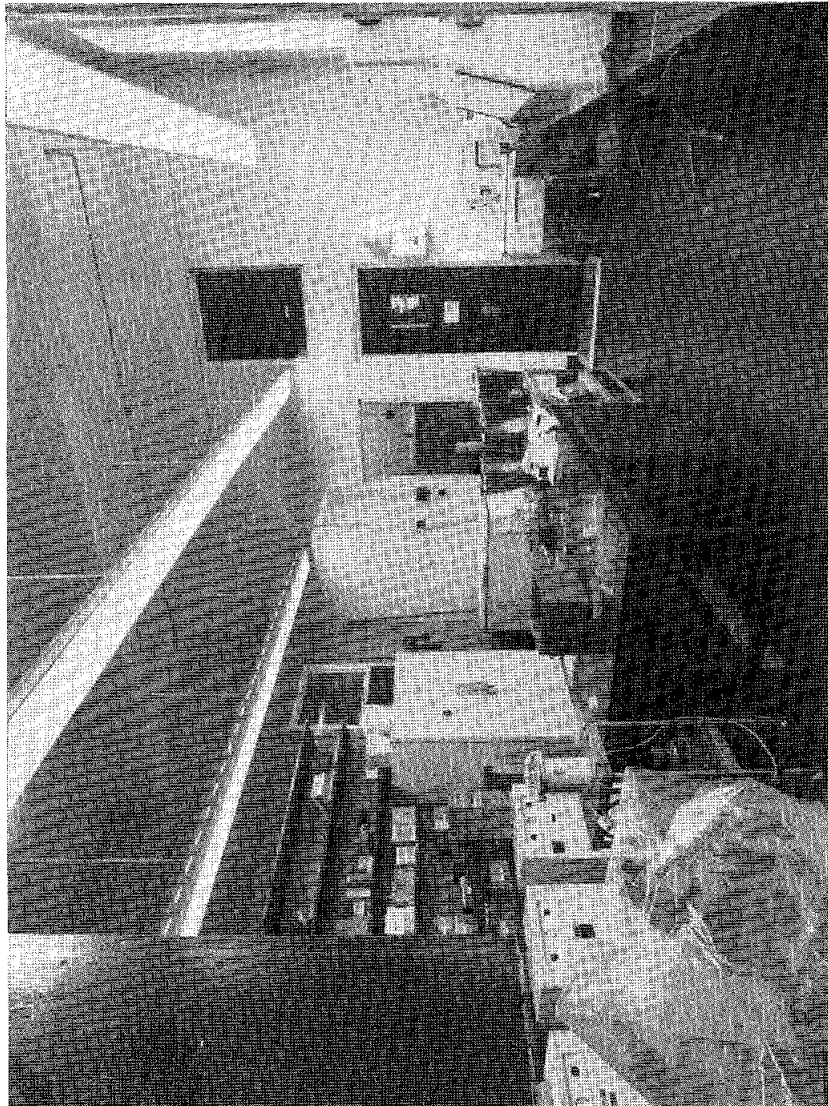


THE MEDICAL MICROBIOLOGY DEPARTMENT CORRIDOR
Showing the door to the pox virus laboratory suite and one of the “swing-barriers”.

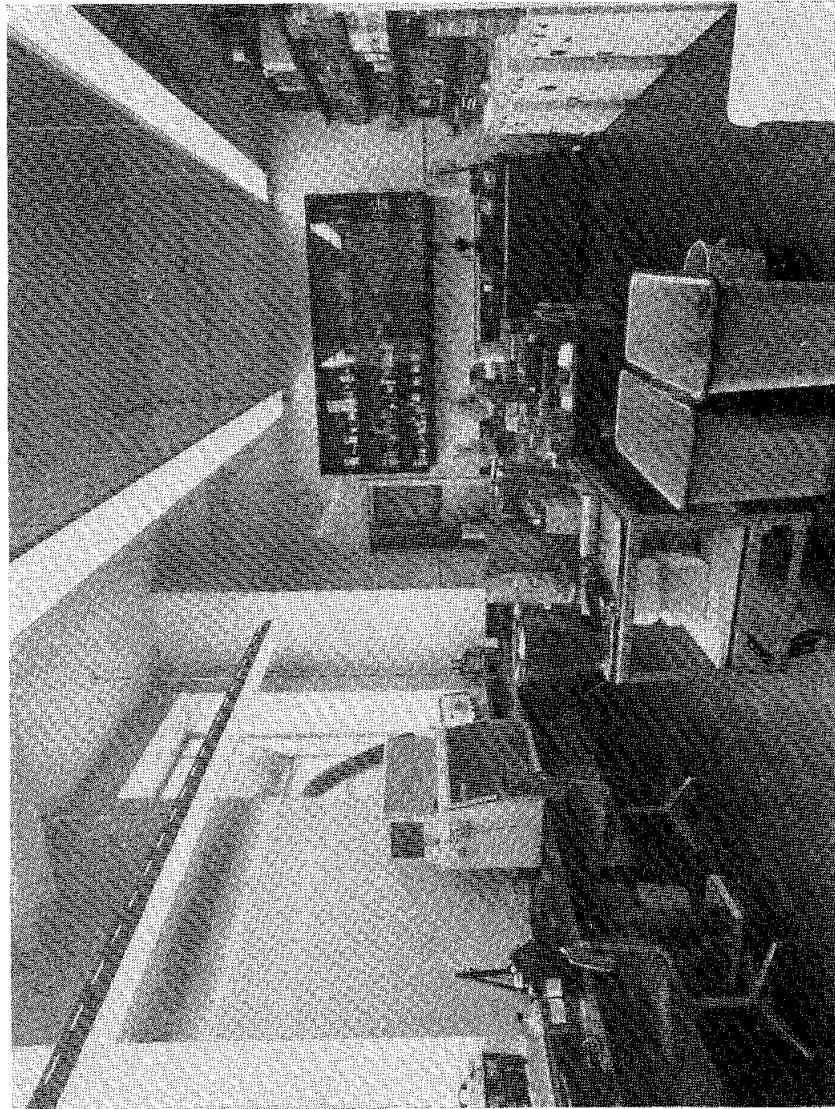


ANIMAL POX ROOM

Looking towards the smallpox room. Showing (l. to r.): three incubators, refrigerator, door from corridor (behind refrigerator), freezer for storage of smallpox viruses, door to tissue culture room, door to smallpox room, sink, safety cabinet.

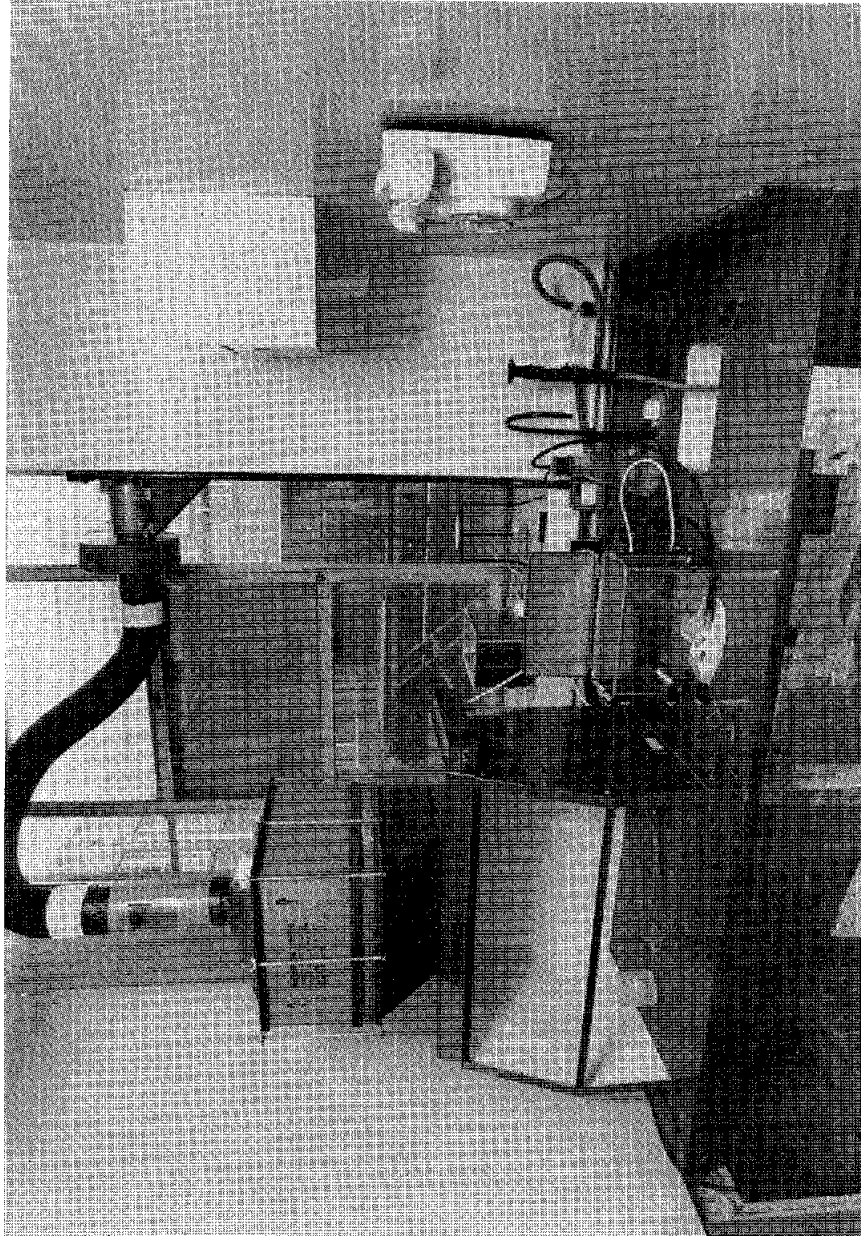


ANIMAL POX ROOM
Looking towards the office.

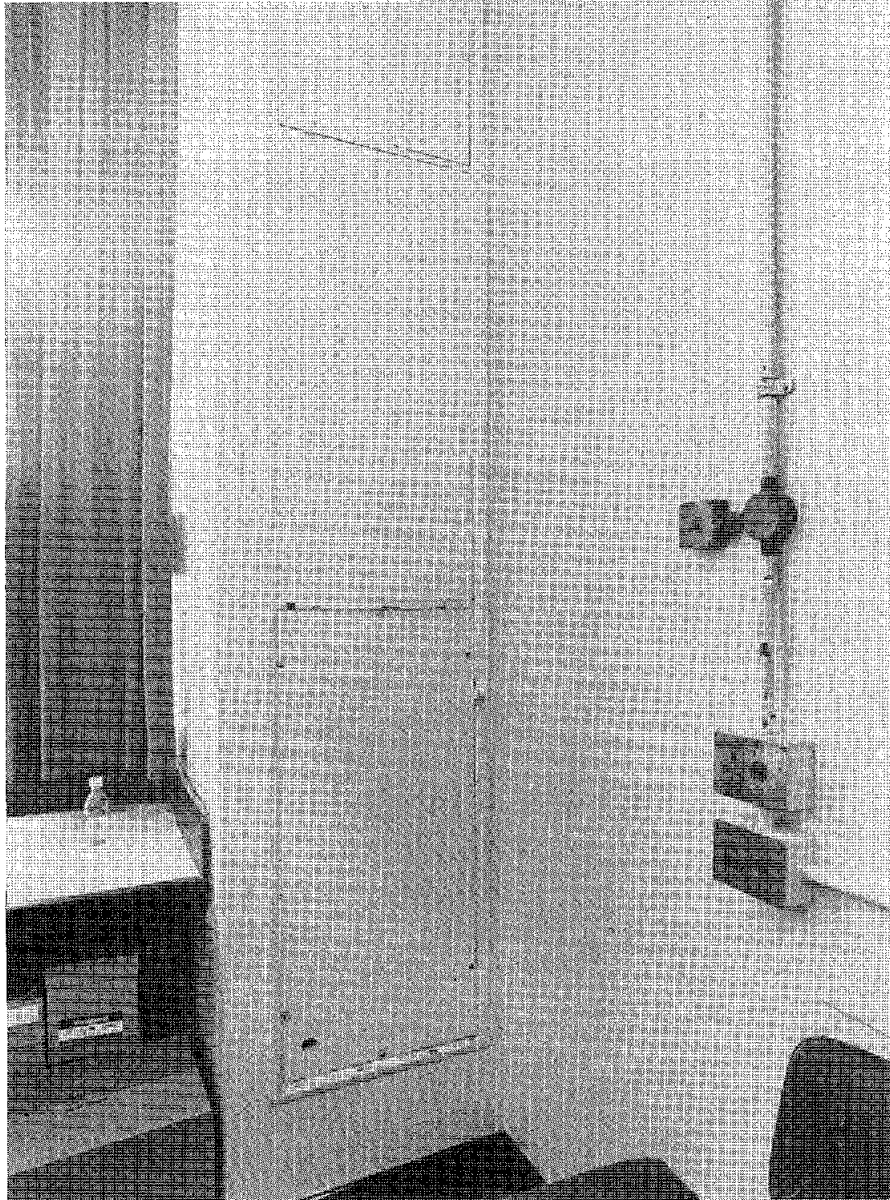


SMALLPOX ROOM

Laboratory bench. Showing (l. to r.): safety cabinet, bath-type ultrasonicator, sink with aspirator attached. The panel over the duct has been removed to reveal the duct opening under the laboratory bench.

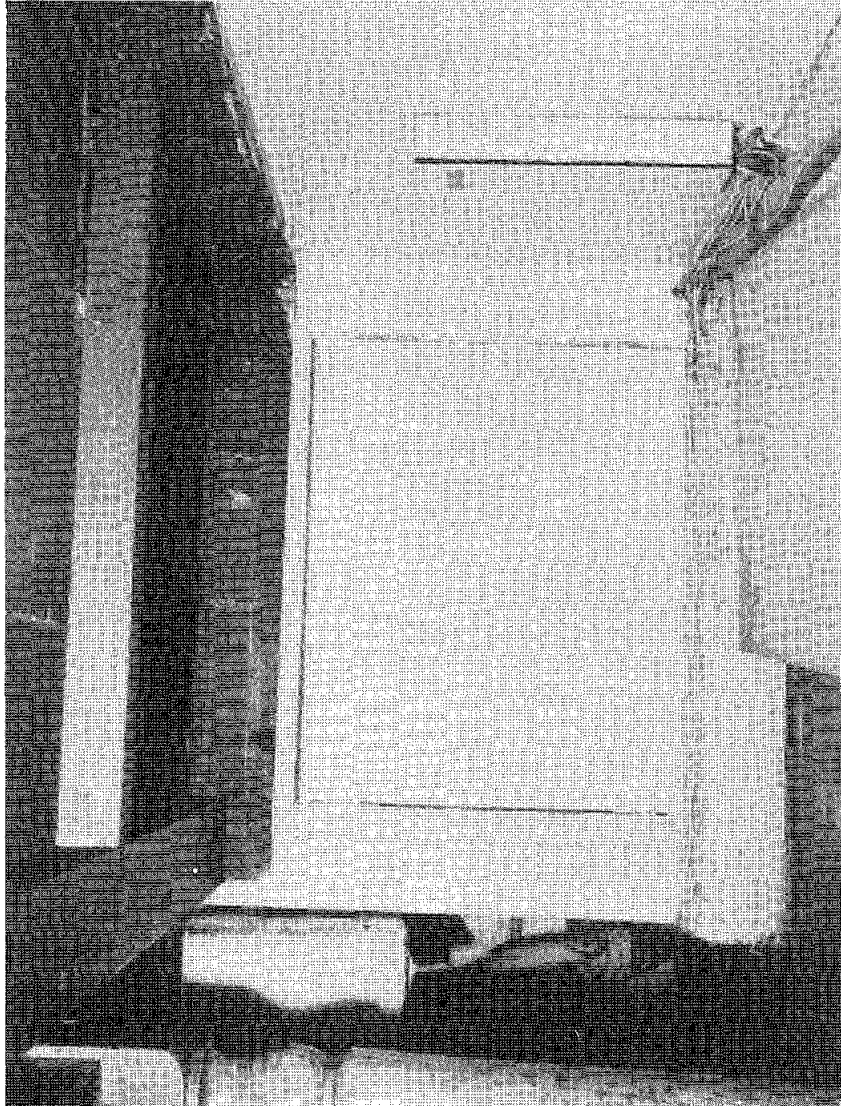


SEMINAR ROOM
Showing badly fitting panels on duct.



THE "TELEPHONE ROOM"

View under the table upon which lay the telephone, showing the badly fitting panel over the duct.



aspirator, was hand-operated. Other equipment on the bench included a hot water steriliser and a bath-type ultra sonicator. The floor was covered with parquet tiles. Under the bench there was a plywood covered inspection panel on a service duct (4) (Duct B), one of several which ran vertically through the building and which are shown diagrammatically in Fig. 2. The outer duct panel was only loosely held in place by screws, and there were obvious gaps between the panel and its frame. A sealed duct (30) passed overhead through the smallpox room from the window. This duct conveyed air to the inner tissue culture room. The door to the smallpox room had a louvered window, and we were told that the door remained locked except at times of entry and exit. Under a bio-hazard sign the door carried notices:

SMALLPOX LABORATORY

Smallpox Laboratory

ACCESS RESTRICTED TO THOSE WHO ARE LISTED BELOW OR WHO CARRY WRITTEN AUTHORISATION FROM PROFESSOR BEDSON OR DR. SKINNER.

H. S. BEDSON

G. R. B. SKINNER

L. HARPER

R. H. GEORGE

J. DURHAM

Outside the smallpox room door there was a 'Tacmat', a sticky doormat designed to trap dust particles from shoes, upon which anyone leaving the smallpox room was required to step with both feet. A visitors' book hung on the outside of the door.

30. The tissue culture room was used for uninoculated eggs and tissue culture. It was adjacent to the smallpox room but separate from it, was windowless and opened onto the animal pox room. High up on the wall adjacent to the smallpox room was an air-inlet grill (30) connected to the sealed duct which passed through the smallpox room and conveyed air in through a grill in the window. Within this duct was a fan, operated by a switch in the tissue culture room, which vented fresh air into the tissue culture room. It was not possible to reverse the air flow. The room contained a wooden laboratory bench (11) which ran along two sides of the room, two incubators (10), an ultra-violet light (9), and a sink (8). The door of this room was kept closed when tissue culture work was in progress.

31. The animal pox room, in which work with vaccinia and animal pox viruses was carried out, measured 24' × 18'. It had two windows facing the East Courtyard, both of which were meshed to keep out insects but which did not shut properly. A large amount of material and laboratory supplies were stored on open shelves around the room. There were two sinks, one with foot-operated taps. The room contained a range of laboratory equipment and supplies including a safety cabinet (25) on the bench by the windows, and an MSE Super Multex low-speed centrifuge (22) at the far end of the room from the smallpox room, adjacent to a plywood and asbestos-covered double panel in another of the service ducts (23) (Duct C) running vertically through the building. There were also gaps between this panel and its frame. Some of the gaps had been

sealed with putty. Along the inner wall were three incubators. One was for eggs infected with smallpox virus (18), one for tissue cultures infected with smallpox virus (19) and the third for work with animal pox viruses (20). The two incubators for use with smallpox virus had locks. Immediately inside the door leading from the main corridor to the animal pox room was a large lockable chest freezer (12) two-thirds full, containing the laboratory's stocks of smallpox and animal pox viruses. Some viruses used in other laboratories of the Department of Medical Microbiology were also stored in it. Other equipment included a second bath-type ultra sonicator. There were a number of discard buckets. The exit door to the corridor had three locks.

32. At each end of the main corridor running through the Department of Medical Microbiology there were swing barriers on which there were warning notices. These stated:

**REGIONAL SMALLPOX LABORATORY. NO ENTRY WITHOUT
AUTHORISATION. ENQUIRIES TO ROOM EG. 36.**

One of these barriers was 8' from the entrance door to the animal pox room. This door also had warning notices, as follows:

**NO ADMITTANCE
REGIONAL SMALLPOX LABORATORY
DEPARTMENT OF VIROLOGY
DANGER
HAZARDOUS PROCESS
DO NOT ENTER WITHOUT SPECIFIC PERMISSION FROM
HEAD OF DEPARTMENT OR HIS REPRESENTATIVE.
ALL ENQUIRIES TO SECRETARIES' OFFICE, EG. 36
OR TELEPHONE DR. H. S. BEDSON, MR. G. J. BARSON
(Office and Home Telephone Number given)**

Mr. Barson was one of the Departmental safety officers. Under the notice were conventional radio-active and bio-hazard warning notices. The second swing barrier was across the main corridor at the far end of the Department.

Staff

33. The persons who worked in or had access to the smallpox room were Professor Bedson; Dr. Linda Harper, his former PhD student and now a Research Fellow at the University; Mrs. Jennifer Durham, an experienced laboratory technician who had been with the Medical School for 11 years; and Miss Anita Dickerson, a new technician who had joined the team within the last year. In addition, Dr. Skinner, a senior lecturer in the Department, and Dr. George, a doctor from outside the University nominated by the Regional Health Authority (to diagnose smallpox), were permitted when required to enter the smallpox room to handle diagnostic smallpox specimens. If it became necessary for anyone else to enter the smallpox room, for example to carry out maintenance work, they were required to record their names in a special visitors' book that hung from the door, and their vaccination status was checked. Between the period January to August 1978, 20 visits were recorded in the book.

34. We were told that after he took charge of the Department in October 1975, Professor Bedson had become progressively more involved in his administrative work and teaching, and that recently he had done very little to supervise the laboratory work in the smallpox room. Work in the smallpox room was done by Dr. Linda Harper and Mrs. Durham.

35. A larger number of staff visited or had access to the animal pox room. In addition to the regular occupants, Dr. Harper, Mrs. Durham and Miss Dickerson, visitors included other staff from the Department of Medical Microbiology, the two cleaners and occasionally maintenance engineers. All of them were required to be vaccinated. We were told that casual visitors to the pox virus laboratory were challenged by the staff and were not admitted until their vaccination status had been checked. The entrance door from the main corridor was triple-locked and keys were held by the laboratory staff, the cleaners and a lecturer of the Department. Whenever smallpox work was in progress this outer door was locked from the inside.

Research on pox viruses

36. With the eradication from the world of human smallpox, there is concern that there may still exist unknown animal reservoirs of smallpox, and that viruses as yet confined to animals may begin to infect humans. The fairly recent discovery of these variola-like viruses has emphasised the limitations of present methods of identification, and has stimulated work around the world. Professor Bedson was a recognised international expert in this difficult field, and for the last few years his laboratory had been primarily engaged in attempting to improve methods of differentiation and identification of these viruses. He was supported by grants from the World Health Organisation and from the Medical Research Council.

37. Earlier work had been concerned with attempts to distinguish viruses by studies of the enzymes they produce. More recently increasing attention had been paid to pox virus identification by polyacrylamide gel electrophoresis of virus-induced polypeptides. Viruses may be distinguished from each other by their different proteins (or polypeptides). In recent years it has become usual to separate and partly identify these polypeptides by polyacrylamide gel electrophoresis (PAGE). For this, the virus is dissolved by heating in a strong solution of detergents and other reagents, and the solution is then placed on top of a slab of polyacrylamide gel. By passage of an electric current the various peptides move into the gel at different rates and thereby become separated. This method was being applied in Birmingham using techniques developed by other workers who had used it successfully, for instance with herpes virus.

38. This technique required the preparation of increased quantities of virus, and the staff estimated that by March 1977 the work with variola virus had tripled. The results were promising, and so that it could be extended Professor Bedson obtained from Professor Dumbell of St. Mary's Hospital, London, a further 22 variola strains in May 1978. From that time the pace and scale of work increased, perhaps by as much as tenfold. By the end of July all the new strains had been grown in eggs and inoculated into HeLa cell tissue cultures and harvested. There appears to have been a sense of urgency to complete the studies by the end of the year when the work was due to cease.

Safety

39. There were two Departmental Safety Officers, but we were told that the responsibility for safety in the pox virus laboratory rested with Professor Bedson. The typewritten instructions issued to each member of staff working in the pox virus laboratory (see Appendix 2) stated that safety depended upon:—

- i. Vaccination and regular re-vaccination of all concerned.
- ii. Restriction of access to protected individuals.
- iii. A check on illness occurring in departmental staff.
- iv. Containment of the virus while it is being handled.

40. Information about the first three items was contained in a Departmental Information Book. The fourth, according to the typewritten instructions, depended on careful forethought and planning in experimental work, the highest standards of technique, and strict attention to detail, particularly in the matter of disposal of infected items. We discuss in Chapter 12 the lack of strict observation of these regulations.

41. Vaccination of Departmental Staff: Vaccinations were performed and the inspections for “take” were made by Professor Bedson. Those working in the pox virus laboratory were vaccinated every year; all others in the Department, including the cleaners, were re-vaccinated at two-year intervals. Those who had access to the Department, including University maintenance staff, security staff, Medical School porters and service engineers of outside contractors, were also vaccinated at two-year intervals. Vaccination was also offered to the families of staff in the Department of Medical Microbiology. We are satisfied that this policy was rigorously maintained by Professor Bedson. Vaccination was not, however, offered to staff working in the other Departments elsewhere in the Medical School, and we have commented on this omission later on in our report.

42. Check on illness: All members of staff on the Medical Microbiology floor received a card indicating the nature of the work done, which was intended to be given to their General Practitioner and filed with their NHS records. In addition, they carried a card to be shown to their doctor in case of illness, and were required to notify their Department immediately of any absence through illness. We are satisfied that this policy was meticulously followed.

43. Containment: The list of safety instructions for the handling of smallpox virus was issued to all members of the pox virus laboratory staff. These restricted all “open work” with smallpox virus to the safety cabinet in the smallpox room, and open work included such operations as making dilutions, inoculating and harvesting eggs and tissue cultures, loading and unloading centrifuge vessels, and preparing diagnostic specimens. Separate rear-fastening gowns were provided for use in the smallpox room as distinct from the front fastening laboratory coats worn in the animal pox room and elsewhere in the building. After use, the rear-fastening gowns were intended to be placed in disposable plastic bags for disinfection by autoclaving within the smallpox room. All infected material was

to be autoclaved or disinfected by chemical means before removal. Our examination of the laboratory procedures actually followed showed several deviations from the rules laid down.

Cleaning

44. Cleaning of the animal pox room was undertaken once every fortnight by two very safety-conscious cleaners. They usually worked unsupervised, arriving early in the morning. They held keys to the laboratory. They were not permitted entry to the smallpox room, which was cleaned by the laboratory staff. The cleaners wiped down the benches in the animal pox room with a disposable duster which was discarded into a plastic bag in the laboratory. The floor was cleaned with a mop which was disinfected after use by the cleaners themselves. All cleaning equipment was kept in a cupboard on the Medical Microbiology floor. The cleaners were also responsible for cleaning the rest of the Medical Microbiology Department, but not the Anatomy Department.

The Department of Anatomy's Studio and Darkroom

45. The Department of Anatomy occupies the first floor of the East Wing of the Medical School building, above the Department of Medical Microbiology. The Department of Anatomy also used some rooms on the Medical Microbiology floor just outside the swing barriers that cordoned off the pox virus laboratory.

46. The Anatomy Department's photographic studio and darkroom, in which Mrs. Parker and an artist worked, were on the first floor of the East Wing, but not directly above the pox virus laboratory. The studio is a large room with windows opening on to the courtyard. Viewed from the courtyard, the distance between these windows and the windows in the pox laboratory on the floor below is 9 yards. We were told that the studio windows remained open in summer, as the room became very hot. The room contained drawing and photographic equipment; two typewriters, one with large type which was used by many people in the Anatomy Department; in the corner there was a sink, and above it a rack containing several mugs. A "coffee-club" consisting of Mrs. Parker and five friends was run from there, and, because the rules forbade the taking of food or drink in offices or laboratories, the practice was for cups to be filled in the studio with coffee or tea which was then drunk in a common room situated at the end of the corridor. In addition to the daily visits by the members of the "coffee-club", visitors to the studio were frequent, though nearly all were from the Anatomy Department itself and had no direct connection with the pox virus laboratory.

47. The studio had a connecting, windowless, darkroom. This contained the usual equipment associated with a photographic darkroom. Ventilation was provided by a two-way fan set high on one wall and into a service duct that ran vertically from the subway to the roof. The room also contained a self-exchange air conditioner.

48. The remaining rooms on the Anatomy floor are laboratories and offices and the vertical air ducts noted in the description of the Medical Microbiology Department pass through them. One such room is situated immediately above

the animal pox laboratory; this "telephone room" is referred to in detail below (paragraph 86).

49. Mrs. Parker's work mainly involved photo-micrography of fixed slides and photography for illustrations. Occasionally she was asked to take photographs of animals in the Department of Anatomy primate colony. We were told that she last visited the primate colony for this purpose on 2nd May 1978.

50. Mrs. Parker had the reputation of being a good photographer; she was described as being very level-headed and easy to work with. She had previously worked as a police photographer but left, because of the irregular working hours, to join the staff of the Medical School in 1975. Mrs. Parker had a small circle of friends among the staff in the Anatomy Department, but did not venture far from her studio. There is certainly no evidence that she visited the pox virus laboratory suite, though she might occasionally have visited a dark-room belonging to the Department of Anatomy on the same floor as the pox virus laboratory and about 15 yards distant from it. On one occasion she perhaps visited the enquiry office at the end of the Medical Microbiology corridor. She did, however, have occasion to visit the "telephone room".

CHAPTER 4

INVESTIGATION OF THE SOURCES OF MRS. PARKER'S INFECTION: THE SMALLPOX LABORATORY

51. No other case of smallpox was known to have occurred anywhere in the world since October 1977 and therefore the smallpox laboratory in the Medical School was the obvious source of Mrs. Parker's infection. In investigating the laboratory we felt that there were three questions to be answered:—

- i. Was the particular strain of virus that infected Mrs. Parker one of those being handled by the smallpox laboratory?
- ii. If so, how had the measures designed to contain smallpox failed?
- iii. If the virus escaped from the smallpox laboratory, how did it reach Mrs. Parker?

Examination of the Virus

52. Between 21st July 1978 and 3rd August 1978, a period during which, at some time, Mrs. Parker became infected, work was in progress in the smallpox laboratory with the following strains:—

Variola major: Taj I, Taj II, Abid, Jumma, Harvey, Kuwait 5.

Whitepox: 64/7255.

This strain was isolated in the Netherlands from a tissue culture of a kidney of a Malaysian monkey.

Hybrid strains: VC3, VC4, VC5, VC6, VC7, VC8.

These had been produced in 1963 by growing together *Variola major* (Harvey strain) and cowpox (Brighton strain). Descriptions of them were published by K. R. Dumbell and H. S. Bedson, "The use of ceiling temperature and reactivation in the isolation of pox virus hybrids." (Journal of Hygiene, Cambridge (1964) 62, 133), and H. S. Bedson and K. R. Dumbell, "Hybrids derived from the viruses of *Variola major* and Cowpox." (Journal of Hygiene, Cambridge (1964) 62, 147).

The strains were in use on the following dates:—

- | | |
|-----------|--|
| 21st July | Tissue cultures infected with Taj I, Taj II.
Eggs infected with Abid, Jumma. |
| 24th July | Tissue cultures of Taj I, Taj II harvested.
Eggs infected with Abid, Jumma harvested. |
| 25th July | Virus titrated in tissue culture Taj I, Taj II.
Tissue cultures infected with Abid, Jumma. |
| 28th July | Virus titrated in tissue culture Taj I, Taj II.
Tissue cultures infected with Abid, Jumma harvested.
Virus titrated in tissue culture Abid, Jumma. |

- 31st July Eggs infected with VC6, VC7, VC8.
Eggs infected with VC3, VC4, VC5, harvested.
- 1st August 35^s labelling of 64/7255, Taj I, Abid, Jumma.
Tissue cultures infected with Harvey, Kuwait 5.
- 3rd August Eggs infected with VC6, VC7, VC8 harvested.
Tissue culture infected with Kuwait 5 harvested.

53. Samples of vesicle fluid were obtained from Mrs. Parker and virus was isolated from them at Liverpool by Professor K. McCarthy; vesicle fluid from her mother, Mrs. Whitcomb, was examined at the Public Health Laboratory, Colindale, by Dr. M. Pereira, who isolated smallpox virus. These viruses were then examined in detail by Professor K. R. Dumbell at the smallpox laboratory in St. Mary's Hospital Medical School, London.

54. Professor Dumbell's examination (see Appendix 3) showed that both Mrs. Parker and her mother were infected by a strain of *Variola major* virus indistinguishable from one another and from the strain known as Abid. This indicated that Mrs. Parker was not infected by one of the hybrid or whitepox strains. Abid has the same origin and history as Taj. Both strains were isolated from smallpox patients in Pakistan in 1970; Abid was a 3 year old male and Taj an 18 year old male. The Abid strain was first received by the Birmingham laboratory on 26th May 1978, from the smallpox laboratory at St. Mary's Hospital Medical School, London, and work on the virus had taken place intermittently since that date.

55. No cases of smallpox have been identified in the United Kingdom in the last five years before Mrs. Parker's illness and the last recorded case of smallpox anywhere in the world was in October 1977 in Somalia. We were informed by the Area Medical Officer of the Birmingham Health Authority that there was no evidence that deaths occurring in his Area during the months of June and July 1978 might have been from smallpox. It is our opinion, therefore, that the smallpox laboratory in the Birmingham University Medical School was the source of Mrs. Parker's infection and that Mrs. Whitcomb contracted the disease through contact with Mrs. Parker.

Examination of the Pox Virus Laboratory, and Containment of Smallpox Virus in Material being Handled

56. We carried out a thorough investigation of the entire pox virus laboratory suite to check whether it was possible for smallpox virus to have escaped from it despite the containment and safety measures set out in the safety instructions. We commissioned a number of scientific tests, and examined the laboratory procedures and the work actually performed.

57. The safety measures for the handling of smallpox virus in this laboratory were designed to prevent the escape of smallpox virus from the material handled, and to restrict any virus that did escape to the confines of the smallpox room. To achieve this a policy of containment was laid down. All open smallpox work was to be carried out within the safety cabinet in the smallpox room. All infected material was to be disinfected before leaving this room; special gowns, retained

in the room and disinfected before leaving it, were to be worn for smallpox work. Entry to the smallpox room was to be restricted to nominated individuals. As the door to the smallpox room presented the only physical barrier between it and the animal pox room, the door was to be kept shut and the fan in the safety cabinet in the smallpox room was to be switched on 15 minutes before and after work with smallpox virus. In that way it was thought that a negative air pressure would be created in the smallpox room and so prevent the escape of any airborne virus to the outer animal pox room. These arrangements were not re-considered or modified when work began that required the production of large amounts of virus for biochemical analysis.

58. We commissioned tests on the safety cabinet in the smallpox room. As will be seen in Appendix 4 this safety cabinet was working well, with an air-flow that ensured that tracer substances released within the cabinet did not come back into the smallpox room. The exhaust air filter for the cabinet was also shown to be effective.

59. We examined the laboratory records and interviewed members of the laboratory staff who gave us step-by-step accounts of the way they carried out the various laboratory techniques employed by them while working with smallpox virus. We concluded that the policy of containment laid down in their instructions was not properly followed.

60. We learned that when virus was harvested the aspiration of culture fluid from Petri dishes containing infected tissue cultures took place on the bench in the smallpox room, outside the safety cabinet. We were told that this was done because of the lack of space inside the safety cabinet, and that on occasion as many as 90 Petri dishes in one session were handled on the very small amount of bench space available.

61. The aspirator used consisted of a rubber tube connected to a water pump attached to the tap in the sink. Between the tube and the water pump were two flasks containing formalin, linked in series. The first flask held the fluid aspirated from tissue culture plates, and the second trapped any carry-over of fluid from the first flask. There was no air filter installed between the second flask and the water pump. The flasks were emptied when full or at the end of work, into a separate container, and the fluid held over-night before discarding. We noticed that the inlet in the side of the safety cabinet, designed specifically to admit the rubber tubing of aspirators, burners, etc., was sealed with adhesive tape.

62. In our opinion, the use of the aspirator outside the safety hood to remove the culture fluid from the Petri dishes, was a dangerous practice. Apart from the risk of generating aerosols and splashes of virus that could result from the aspiration itself, the number of cultures being worked on could have increased the possibility of accident spills.

63. "Absorbed serum" was prepared for serological tests by adding serum to synthetic medium containing live variola virus and placing this in a dialysis sac within an anaerobic jar. Negative pressure was applied to the jar until the contents of the sac were reduced to the required volume. This process took place inside the smallpox room. However, we were told that the contents of the

sac, still containing live smallpox virus, were then removed to the animal pox room where they were centrifuged at low speed to remove the majority of live virus particles. The supernatant fluid was then bottled and stored in a +4°C refrigerator in the animal pox room as it was regarded as non-infective. It is our opinion that the supernatant would still have contained infective smallpox virus as centrifugation is not an effective method of clearing fluids of virus particles.

64. Inspection of discard buckets both inside and outside the smallpox room showed pipettes not fully immersed in disinfectant after use. In some cases pipettes were put into a container where full immersion was not possible and where complete disinfection could not take place.

65. The portable autoclave in the smallpox room, which was used for the disinfection of gowns, some glassware and infected eggs, was operated at 10 lbs pressure for 10 minutes as against the 15 minutes or more specified in the maker's instructions (displayed in the laboratory). We were told that screw cap bottles placed in it were autoclaved with their caps firmly screwed on. The size of the autoclave was inadequate for the sterilisation of all materials used in the smallpox room and was reserved for a minority of items including gowns which were autoclaved in a dressing drum one at a time. Gowns which, according to the safety instructions, should have been autoclaved after use were changed once weekly when they were autoclaved before leaving the laboratory.

66. Tests were carried out on the portable autoclave in the smallpox room and on a larger laboratory autoclave situated in a room on the floor below and which was used for a second sterilization process of items from the smallpox room (see Appendix 6). These tests were conducted on our behalf by Dr. G. Ayliffe and Mr. C. E. A. Deverill of the Hospital Infection Research Laboratory, Birmingham. Thermocouples and biological test pieces were placed in the centre of a typical load in each autoclave which was operated through its normal working cycle. The results of the tests indicated that temperatures far in excess of those required to kill smallpox and other viruses were reached in typical loads during two standard cycles with each machine. This was confirmed by biological tests.

67. When harvesting or preparation of virus cultures in the smallpox room it was usual, and often necessary, for the person carrying out this work to leave the smallpox room in the middle of the operation and enter the animal pox room. This was done in order to use the low-speed centrifuge, the incubators or the freezer situated in the outer pox laboratory, or to collect equipment. The staff on these occasions did not remove the special rear-fastening gowns they wore in the smallpox room neither did they remove or disinfect the gloves they had been wearing while working with smallpox virus. Anything they touched in the outer pox laboratory was therefore likely to become contaminated, and this practice presented considerable opportunity for contamination of the outer animal pox room.

68. We also learned that when inoculated eggs, virus cultures or bottles containing virus were placed in the freezer or incubators after they had been worked with in the smallpox room, they were not routinely disinfected on the

outside. In any event, they were carried by staff still wearing the nondisinfected gowns and gloves they had worn while working with the smallpox virus. Furthermore, we learned that sealed containers were not used to carry inoculated eggs and infected tissue cultures to and from the smallpox room and outer animal pox room.

69. Apart from the possibility of creating airborne and surface contamination of the outer animal pox room that we have already mentioned, contaminated objects placed in an incubator or freezer might present an additional hazard when retrieved at a later date.

70. We were concerned at the risk presented by contamination of the outer surfaces of the freezer (12 in Fig. 1) used for storing virus. This freezer stood in a corner just inside the entrance door to the animal pox room from the corridor. Those working in this room as well as visitors would have to pass within touching distance of it.

71. As the entire pox virus laboratory was closed immediately upon the diagnosis of smallpox in Mrs. Parker, we did not have an opportunity to observe the normal working practices, though we did talk to the staff who gave us detailed accounts of the way their work was performed. However, a team of World Health Organisation inspectors visited the laboratory on 4th May 1978 when it was functioning normally. They had considerable reservations about the physical facilities in the laboratory and made certain recommendations concerning the procedures they observed. Professor Bedson responded to these, agreeing to some of them and rejecting others. The WHO observations are discussed in detail later in this report.

Conclusions

72. Because of the poor laboratory procedures, the failure to use the safety cabinet for all open work with smallpox, the failure to use sealed containers to transport infected materials, and the practice of passing in and out of the smallpox room during work without changing gowns or gloves or washing hands, we believe that opportunities existed for virus particles to become airborne and to be transferred both in this way and by direct contact to surfaces. This would have happened in the animal pox room as well as in the smallpox room. The intention of the laboratory's safety measures was the containment of smallpox virus within the smallpox room itself. The result of the unsatisfactory procedures taking place was that the animal pox room could become heavily contaminated. This represented a major breach in containment policy.

CHAPTER 5

ROUTE OF TRANSFER OF VIRUS FROM THE SMALLPOX LABORATORY TO MRS. PARKER

73. There was no evidence to suggest that Mrs. Parker had ever been in the pox virus laboratory suite, and there was no reason for her to have done so in the course of her work. We feel that the transfer of virus from the laboratory to Mrs. Parker must therefore have occurred by one of three routes:—

- i. on an air current
- ii. by personal contact
- iii. by contact with contaminated equipment or apparatus leaving the laboratory.

An Aerial Route

74. The efficiency of the two safety cabinets in the pox virus laboratory was tested on our behalf by Mr. G. J. Harper of the Microbiological Research Establishment, Porton. The one in the smallpox room was intended, in the typewritten safety instructions issued to each member of the staff, to be used for all open work with smallpox virus. The one in the animal pox room was used only for work with animal pox viruses. The tests were done by measuring airflow and spraying an aqueous suspension of viable spores of *Bacillus subtilis var globigii* (BG) inside each of the safety cabinets. Air samples were collected near the outlets of the cabinets in the East Courtyard and in addition air samples were collected in the smallpox room and the animal pox room. Full details of the tests are contained in Appendix 4.

75. The results of the tests showed that the safety cabinet in the smallpox room was functioning efficiently. No tracer organisms were recovered from this cabinet's outlet and none was detected in either the smallpox room or the animal pox room when the cabinet was under test.

76. Other tests showed that when the fan in the safety cabinet in the smallpox room was switched on, and the door to the room closed with its louvres shut, the airflow was consistently into the smallpox room from the outer animal pox room, and that air in the smallpox room did not pass out to the animal pox room. There was no escape of air from the smallpox room into the duct running through the room (Duct B) by way of cracks round the duct hatch covers. In fact air was sucked from the duct into the smallpox room (see Appendix 7).

77. In these circumstances the extract fan in the safety cabinet in the smallpox room did create the negative pressure in the smallpox room that it was thought to do, and would have ensured that airborne virus in the room did not pass out to the animal pox room.

78. However, the airflow through the safety cabinet was sufficient to do this only when the door to the smallpox room was closed. Tests showed that when the door was open, whether the cabinet fan was switched on or not, air moved through the doorway from the smallpox room to the adjoining animal pox room.

79. We arranged for tests on the airflows within and from the pox virus suite to be carried out by Dr. O. M. Lidwell, and his detailed report is given in Appendix 8. He found that:

- i. When a tracer substance was liberated in the smallpox room it leaked out into the animal pox room when the door between the two was open, even if the safety cabinet was in operation. However, when the cabinet was in operation, the leakage of tracer was very much reduced.
- ii. There was a substantial leakage of tracer from the animal pox room to the corridor outside.
- iii. When the fan in the seminar room next door to the smallpox room was working on extract, there was a considerable transfer of tracer to the seminar room from the smallpox room by way of cracks round the sides of inspection panels of the service duct that lay between the two rooms (Duct B).
- iv. There was an indication of a small and irregular transfer to the room on the floor above next door to the "telephone room" via Duct B.
- v. There was some suggestion of a very small transfer to the subway via the bottom of the duct in the animal pox room (Duct C).
- vi. There was no indication of any measurable transfer to Mrs. Parker's darkroom via its service duct (Duct D) and the input ventilating fan.
- vii. There was an appreciable transfer of tracer from the animal pox room to the Anatomy Department "telephone room" on the floor above via the service duct (Duct C) between the two rooms; the inspection panels to this duct had cracks round them. There was also appreciable transfer of tracer to the "telephone room" when the tracer was liberated in the smallpox room with the safety cabinet fan not switched on, and the door open. When this was done with the safety cabinet fan switched on, tracer was still found in the "telephone room" but much reduced in amount.

80. The airflow tests thus showed that virus from the smallpox room could travel some distance within the East Wing of the Medical School. The tests were conducted in the smallpox room with its door open. It could be argued that this door remained closed while smallpox work was in progress and that the tests did not give a true picture of the actual situation. However, our examination of the laboratory procedures carried out by the staff showed that they passed several times in and out of the smallpox room in the course of their work with smallpox virus in order to use the low-speed centrifuge and to deposit or retrieve inoculated eggs, cell cultures or virus stocks from the incubators and freezer in the animal pox room. We have established that smallpox work was taking place

on the open bench in the smallpox room, outside the safety cabinet. The opening and closing of the smallpox room door and the passage in and out by whoever was conducting work on the virus would have created the opportunity for any airborne virus to escape into the animal pox room. The failure to take off and leave behind in the smallpox room gowns worn during work with smallpox virus also meant that if virus had contaminated the gowns during work outside the safety cabinet, or the sleeves of the gowns during work inside the safety cabinet, the virus could have been shaken off the gowns and become airborne.

81. The airflow into the safety cabinet situated in the animal pox room (see Appendix 4) was found to be about half the recommended value for Class 1 cabinets, and viable spores of the tracer organism were recovered from the cabinet's air outlet. On removal, the filters were subjected to further tests and themselves were found to be working satisfactorily. We also found very heavy airborne contamination in both the animal pox room and the smallpox room shortly after the start of spraying of the tracer organism inside this cabinet. This heavy contamination was still present 15 minutes after turning off the spray inside the cabinet. The tests demonstrated that aerosol particles generated in this safety cabinet could spread within the rest of the laboratory suite and to the courtyard outside. We were told, however, that this cabinet was not used for work with smallpox viruses. It was purchased in March 1966, its filters had not been changed nor had it been regularly tested or serviced since. We informed the Department of Health and Social Security about this so that other laboratories employing the same type of safety cabinet could be advised to carry out efficiency checks on them.

82. Tests were conducted on the two centrifuges in the pox virus laboratory by Mr. G. J. Harper of the Microbiological Research Establishment, Porton (see Appendix 9). These were the MSE 25 high speed centrifuge used in the smallpox room and the MSE Super Multex, referred to in our report as the low speed centrifuge, used in the animal pox room. The object of the tests was to measure aerosol generation by the centrifuges. The plastic tubes used in the MSE 25 high speed centrifuge and glass bottles used in the low speed centrifuge were filled with an aqueous suspension of viable spores of *Bacillus subtilis var globigii* (BG), they were placed in sealed buckets and centrifuged. Neither centrifuge produced an aerosol during the tests. Further examination of the low speed centrifuge is referred to in paragraph 91.

83. Given that the whole laboratory suite might have been contaminated with smallpox virus, we considered the possible exits by which virus could have escaped. These, we noted, were the door leading to the corridor; the two large windows in the animal pox room which opened on to the East Courtyard; a service duct in one corner of the animal pox room (Duct C), and a similar duct (Duct B) which ran through the smallpox room, next to the laboratory bench. Both ducts had inspection panels set into them, these were double-layered and though efforts had been made to make them as close fitting as possible, there were a number of gaps.

84. The duct in the smallpox room (Duct B) had its inspection panel situated just under the laboratory bench. The panel was not properly fixed in place. Pipette pots containing used pipettes were stored on the floor next to this panel.

The duct contained a large number of pipes of various sizes running through it. On an adjacent wall of the duct there was another inspection panel which faced into the Medical Microbiology Department seminar room. This room was used for weekly meetings of staff in the Department. Above the smallpox room, the duct entered a laboratory in the Anatomy Department, a distance of about 8', and finally vented to the outside through a grille facing the East Courtyard in the wall, above window height, on the Anatomy Department floor. Below the smallpox room the duct entered the lower ground floor.

85. The duct in the animal pox room (Duct C) was situated in the far corner, adjacent to the small office that led off the laboratory. A laboratory bench was positioned to one side of the duct, and the low speed centrifuge was situated and operated about four feet away. There were traces of putty sealing some of the gaps between the inspection panel and the duct, and we were told that this was intended to prevent steam issuing from the hot pipes inside the duct. On removing the inspection panel we saw that this duct had been sealed with cement at floor level and was therefore open only to the animal pox room and to a room on the floor above. It too had a ventilation grille fixed outside the building and above window level on the Anatomy Department floor.

86. This animal pox room service duct (Duct C) connected with a room in the Anatomy Department above that had not been occupied since June 1978 and which was being used as a repository for surplus laboratory furniture and materials. The duct in this room had inspection panels. The room also contained a telephone which could be used for calls outside the building. This telephone was used regularly by Mrs. Parker for ordering photographic supplies, since her telephone was only capable of internal calls. For ease of identification in this report we have called this room the "telephone room".

87. A further vertical duct (Duct D) ran through the darkroom where Mrs. Parker worked and the darkroom contained a two-way exhaust fan which was set into the duct. All the vertical ducts in the building connected with a large horizontal duct that ran through the basement. It was conceivable that if the fan was set to exhaust into the darkroom it would draw air from the other ducts, including Duct B in the smallpox room.

88. The tests had demonstrated that if airborne particles of virus were released within the smallpox room they might be able to travel a considerable distance beyond the confines of the pox virus laboratory suite. This could place any person using the corridor or the seminar room in the Medical Microbiology Department, or the "telephone room" in the Anatomy Department on the floor above at risk of infection from smallpox virus. Staff working in the Medical Microbiology Department and other members of staff who had regular contact with the pox virus laboratory were, however, protected by regular vaccination. This policy did not extend to all staff working in the Anatomy Department on the floor above the pox virus laboratory or to staff in the other Departments of the Medical School.

Mrs. Parker's Movements

89. Our enquiries into Mrs. Parker's movements about the Medical School showed that she had never been in the pox virus laboratory suite. However, we

believe that she visited another darkroom belonging to the Anatomy Department which was situated on the same corridor as the pox virus laboratory and with an entrance about 15 feet distant from it. This darkroom was for the use of students, and Mrs. Parker is thought to have visited it in connection with photographic assistance she was giving to an MSc student. It was also suggested to us that she might have visited an enquiry office, situated opposite the darkroom on this floor, in order to deliver some photographic prints, about the last week in July.

90. We have also established that Mrs. Parker was a very frequent user of the telephone in the "telephone room" which lay directly above the animal pox room and shared Duct C. As far as we know, two other persons in the Anatomy Department used this telephone besides Mrs. Parker, but only very occasionally. During the last two weeks in July and the first week in August we were told that Mrs. Parker used this telephone several times a day, every day. The Department's accounting year ended on the 31st of July, and Mrs. Parker was busy telephoning suppliers to order photographic materials. A check of the orders placed by Mrs. Parker during this period reveals that on 25th July she placed an unusually large number of orders. The relevant strain of smallpox virus, Abid, was being handled in the smallpox room on the 24th and 25th July.

91. Tests conducted in the pox laboratory showed that it was possible to recover inside this "telephone room" tracer particles liberated in the smallpox room outside the safety cabinet, or in the animal pox room, whether the safety cabinet was functioning or not. The telephone in this room is situated a few feet from the inspection panel on Duct C that links with the animal pox room. Anyone using the telephone would have been close to this panel and the tests also revealed a strong airflow emanating from it. We know that the centrifuge in the animal pox room was regularly used for work with smallpox virus. This centrifuge was situated a few feet from the hatch on the duct leading to the telephone room. Even though the smallpox virus was centrifuged in sealed containers, these containers and the centrifuge were being handled with potentially contaminated gloves and it is possible that the containers and the centrifuge itself were contaminated. Tests we conducted on this centrifuge (see Appendix 7) showed that shortly after it was switched on, a strong airflow escaped from under its lid and was drawn towards the hatch on the duct. The centrifuge operated at 3,000 r.p.m. and at this speed it seems possible that any virus clinging to the outside of the sealed cups or the frame of the centrifuge itself, would be dislodged into the atmosphere. The airflow from the centrifuge might also be powerful enough to dislodge any virus on the gown of the user.

92. It is possible that Mrs. Parker could have inhaled smallpox virus while visiting the main corridor outside the pox virus laboratory, but so could many others. If she was infected by airborne virus we feel it is more likely that she was infected while using the telephone in the "telephone room" just above the animal pox room and connected to it directly through Duct C. There are some experts who have worked with smallpox virus who would doubt whether airborne dissemination of the virus during laboratory work is a credible route for the transfer of infection, and it is true that we know of no proven case of airborne spread of smallpox from laboratory cultures. That such a route is possible for

the natural disease was demonstrated in 1970 in Meschede, West Germany*, where a smallpox patient admitted to the ground floor of a hospital infected patients on the first and second floors despite having no direct or even indirect contact with them. The pattern of the spread of the secondary cases pointed to airborne transmission of virus as the route by which they were infected, and this was confirmed by smoke tests.

Personal Contact

93. We also investigated the possibility of virus being transferred from the pox virus laboratory to Mrs. Parker by direct contact with a member of staff. Our enquiries among all the members of staff in both the Medical Microbiology and the Anatomy Departments revealed only one known direct link between the pox virus laboratory and Mrs. Parker.

94. The contact was a member of the Medical Microbiology Department who visited the animal pox room on most days to give advice on experimental work being undertaken, but who never entered the smallpox room. On these visits a laboratory coat was not always worn, and the hands were not washed when leaving.

95. The visitor had consulted Mrs. Parker in her studio and darkroom at least once, and perhaps twice, during the last week in July. The purpose of the visit was to discuss with Mrs. Parker the technical details of a photographic process she used for making contact prints which might be applied to some work then going on in the Medical Microbiology Department. With the lapse of time it was not possible to establish if the visit to Mrs. Parker took place immediately after leaving the animal pox room or not.

96. As a member of the staff of Medical Microbiology Department, the visitor was regularly vaccinated every two years and would therefore run little risk of contracting smallpox. There is, however, the possibility that the visitor's hands or clothes were contaminated in the animal pox room from smallpox virus deposited on surfaces or perhaps airborne, and that in this way virus was carried to Mrs. Parker.

97. It is, perhaps, possible that no close contact between Mrs. Parker and the visitor was needed for transfer of the virus. Experiments with foot and mouth disease virus have shown that following the examination of infected animals, some virus was present in the examiner's nose. Sellers, Herniman and Mann (1971)† carried out work to see if those who had examined infected animals could transfer the virus to other animals by artificially coughing near them, and with one animal were successful. We are not aware that a similar route has been demonstrated for smallpox, or if it is possible, and we consider this an unlikely path.

98. Our enquiries also revealed a more tenuous human connection between Mrs. Parker and the pox virus laboratory. Two of Mrs. Parker's friends with

*WHO Weekly Epidemiological Record 1970, 249-256.

†R. F. Sellers, K. A. J. Herniman and J. A. Mann. "Transfer of Foot and Mouth Disease Virus in the Nose of Man from Infected to Non-infected Animals." *The Veterinary Record* (1971) 447.

whom she regularly took her coffee, also occasionally visited the Medical Microbiology corridor and made contact with the staff working there. However, they had never been in the pox virus laboratory. It is just possible that on one of these visits smallpox virus was deposited on their hands or clothing and subsequently transferred to Mrs. Parker. This, however, seems to us to be highly unlikely. Neither of Mrs. Parker's friends had been vaccinated against smallpox and would therefore have run a greater risk of contracting the disease themselves.

99. We also established that Mrs. Parker occasionally undertook private photographic work, mainly taking passport photographs, among the staff in the Medical School. As far as we are aware, and examination of the negatives appears to confirm this, she did not take any photographs of the staff in the pox virus laboratory or of the Medical Microbiology Department in the last fortnight of July and the first week of August 1978.

100. Mrs. Parker's visitor, who had regular contact with the pox virus laboratory, establishes a direct contact link between her and the laboratory during the relevant period. If the visitor was contaminated in the course of visiting the laboratory, it is possible for this contamination to have been carried to Mrs. Parker via clothes or hands.

Contact with Infected Equipment

101. Mrs. Parker did not undertake any photographic work for the Medical Microbiology Department. However, we made enquiries to trace any equipment or apparatus which may have originated from the pox virus laboratory and with which Mrs. Parker may have come in contact.

102. We found that an item of apparatus used for gel electrophoresis, which might occasionally have been used in the animal pox room, was borrowed regularly from the Medical Microbiology Department by a PhD student in the Anatomy Department, who used it to study the changes in cytosol proteins. His laboratory was situated across the corridor from Mrs. Parker's studio and she was known to have visited it on occasion.

103. However, our enquiries reveal that the student had not borrowed the apparatus from the Department of Medical Microbiology after June, as he had arranged for an apparatus of his own to be constructed. We were also told that the apparatus was always at the back of his laboratory, furthest from the door, and there was no evidence that Mrs. Parker had ever made contact with it.

104. It is unlikely that this piece of apparatus was a source of Mrs. Parker's infection because it was not in use in the Anatomy Department after June, it was not used with live virus samples, and there was no evidence that Mrs. Parker made contact with it.

Conclusions

105. The evidence points to two possible routes by which smallpox virus was transmitted from the pox laboratory to Mrs. Parker: by the airborne route, either through the duct in the "telephone room" or while visiting the Medical

Microbiology corridor; or by the personal contact route, transfer being by the visitor from the Medical Microbiology Department who regularly entered the animal pox room. We are unable to say with certainty which of these two routes might have led to Mrs. Parker contracting smallpox. Both are possible though neither seems capable of delivering a large dose of virus unless an accident occurred involving the liberation of virus, which was not recognised or recalled. Nevertheless, from what we know small doses of virus could have been liberated from time to time which could have been responsible for Mrs. Parker's infection. We believe that the airborne route through the duct to the "telephone room" is the most probable way by which Mrs. Parker was infected because this seems to be the one route that could have selectively affected her.

CHAPTER 6

INVESTIGATION OF THE SOURCE OF MRS. PARKER'S INFECTION— THE 1966 OUTBREAK OF SMALLPOX

106. In 1966 there was an outbreak of smallpox in the West Midlands in which seventy-three people were infected. The disease was due to *Variola minor*, a less virulent form of smallpox virus. Its clinical presentation was in general mild and many of the early cases were at first diagnosed as chicken pox or influenza. By the time the diagnosis of smallpox had been made, in April 1966, the disease had already progressed into at least a fourth generation of cases. The last patient suffering from smallpox in this outbreak was discharged from hospital on 1st August 1966. There were no deaths.

107. Epidemiological analysis showed that probably the first person affected in the outbreak developed the disease in February 1966 and was a photographer employed at the Birmingham University Medical School in the studio and dark room of the Anatomy Department. This was the identical studio and darkroom in which Mrs. Parker subsequently worked. In view of the similarity of the events in 1966 with those in 1978 we considered it was important to re-examine the events of 1966.

108. In 1966 the outbreak of smallpox caused less public concern than the recent one. There were other cases of smallpox occurring in the United Kingdom in 1966 that had no apparent connection with the West Midlands cases. At that time, the WHO smallpox eradication programme was in its infancy and the disease was still endemic in many parts of the world. Birmingham and the West Midlands had a growing immigrant population, and the common reaction to the outbreak was that it originated among travellers from overseas rather than to suspect an escape of virus from a smallpox research laboratory. In this particular instance, by the time it was confirmed that the outbreak was of smallpox, the Medical School photographer had already returned to work.

109. The feeling at the time is summed up in the following extract from a press notice issued on 1st May 1966, by the Birmingham Regional Hospital Board: "It is obvious that the risk to the public is quite minute and certainly does not warrant any clamour and anxiety for vaccination. Supplies of vaccine are adequate to protect those who are at definite risk and those who have been in contact with infection. This policy of vaccination will be adequate to prevent the spread of this mild disease."

110. We searched with care for records of the 1966 outbreak. A clinical account of the epidemic was published in the *Lancet* in June 1966 and we also obtained a detailed report that had been prepared by the National Communicable Diseases Center, Atlanta, U.S.A., and a report published in 1966 by the Chief Medical Officer of the Ministry of Health. One might have expected a formal enquiry to trace the source of the outbreak to have been held by the Medical Officer of Health in Birmingham. We were told that no such enquiry

had been held. We did obtain a record of a meeting held by the health authority in May 1966, the purpose of which was to study the smallpox outbreak. Present at the meeting were representatives of the Ministry of Health, the University of Birmingham, and the Regional Hospital Boards in the area. The Department of Virology of the University of Birmingham had played a valuable part in the control of the outbreak and the diagnosis of cases. We obtained from the University and from Professor Bedson's files detailed clinical records of the cases that had occurred and of the epidemiological analysis that had taken place. We also spoke to a number of members of staff who had been working in the Medical School at the time.

111. We went to considerable trouble to ascertain exactly what enquiry, if any, took place in the University at that time, but there is no evidence to suggest that the University held any formal enquiry into the source of the photographer's infection. On this point we have the assurance of the present Vice-Chancellor of the University, confirmed to him by his predecessor. We also traced and interviewed the photographer, and he cannot recall a formal enquiry being held. This is also the recollection of all who were there at the time, to whom we have spoken. Furthermore, we have not found any record or mention of a formal enquiry in documents we have seen from the files of the Department of Health and Social Security, or from the files of the Department of Virology (now Medical Microbiology) of the University.

112. In May 1966 as an observer from the National Communicable Diseases Center, Atlanta, U.S.A. was in this country, he was invited by the Ministry of Health to observe the investigation and containment procedures being conducted by the Medical Officer of Health in Birmingham. Their report was not intended to be definitive or comprehensive, but rather to provide information to the United States Health Authorities. The following extract from the observer's report describes what took place:

"The earliest case identified occurred in J.A.M., a 23-year-old male photographer employed in the anatomy department of the University of Birmingham Medical School. He fell ill on February 18 with fever, headache, backache, and vomiting, and developed a generalized rash four days later. During the first week of illness he remained at home; when the rash appeared he felt better and returned to work a few days later. He was seen by a physician while the rash was evolving and was thought to have drug eruption. He denied contact with chickenpox, with persons exhibiting a rash similar to his, and with recently arrived immigrants or travellers from foreign countries; he had never been outside the United Kingdom.

During the weeks prior to his illness he had photographed monkeys from India in the course of experiments in the Anatomy Department. Before his illness was recognized in late April all of these monkeys had been sacrificed and were not available for examination. None had appeared ill to their lab handlers.

The Department of Anatomy is situated on the floor immediately above the virology department. At the time of the outbreak, experiments with strains of *Variola major* and *minor* were in progress. However, detailed investigations did not disclose any link between the virology department

and the photographer. None of the virology personnel knew or had any association with J.A.M., and he denied having visited the department. There was no investigation of possible connections between the ventilating system of the two laboratories.”

113. We learned that following the outbreak of smallpox, those working in the Department of Virology of the Medical School felt that it would be wise to have somebody from outside to examine the safety measures in the smallpox laboratory. The head of the Department at that time, Professor P. Wildy, has told us that: “There was no official enquiry into the means by which the photographer in 1966 became infected but naturally as head of a department in which smallpox virus was being investigated I was concerned that his infection might have originated from our work.” (See Appendix 10).

114. Professor Wildy accordingly asked Professor A. W. Downie, then Professor of Bacteriology in the University of Liverpool and a leading international smallpox expert, and Dr. A. D. Macrae, then in charge of the Virus Reference Laboratory of the Central Public Health Laboratory at Colindale, to visit the smallpox laboratory. Both their reports (see Appendix 10) showed they were satisfied with the safety measures in force in the laboratory. A query in Professor Downie’s report about disinfection of an ultra-centrifuge was answered to his satisfaction in a later letter by Professor Bedson. A copy of the report was sent to the Medical Officer of Health of the City of Birmingham.

115. In 1966, the layout of the pox virus laboratory differed from that in 1978. What in 1978 was the smallpox room was then being used as an office and all smallpox work was done on open benches in the main outer laboratory. At that time, safety cabinets had not yet been installed. The windows in the outer laboratory were not sealed. Although the laboratory would not qualify by present day standards as a secure containment area, its facilities were no different from those to be found in a number of other smallpox laboratories in the U.K. and abroad in 1966.

116. We interviewed the photographer concerned in the 1966 outbreak. He had been employed in the Medical School for about a year, and had left in June 1966 to take up other employment. His work in the Anatomy Department included the photography of diagrams and occasionally of human and primate specimens. Some of his work was conducted in the Anatomy Department primate colony. He said that his job was a busy one and he spent about seventy-five per cent of his time in the darkroom. He shared his studio with an artist, who was also employed by the Anatomy Department.

117. Questioned about his movements around the Medical School, he said that he had never been into the pox virus laboratory and had never ventured through the swing-barriers that cordoned off the pox virus laboratory on the Medical Microbiology Department corridor. He had daily contact with members of the Medical Microbiology Department and also staff from other departments through meeting them in the canteen in the basement of the East Wing. He also visited friends of his who worked in a histology laboratory (not the “telephone room”) which was situated a few doors down from his studio. Our enquiries established that this histology laboratory lay next door to what is now the

“telephone room” and was directly above a room connected to the pox virus laboratory which was then an office and which has since been converted to the present smallpox room. A service duct (Duct B) ran through both the office and the histology laboratory.

118. The photographer enjoyed a full and varied social life and said that he had frequent contact with immigrant communities through visits to parties and public houses. In 1966 this was considered to be the likely source of his illness. He could not, however, recall any of his immigrant friends having been ill with smallpox. He described his general state of health just prior to his infection from smallpox as good, and said that he was not at that time undergoing any medical treatment. He had never been vaccinated against smallpox. He stated that as far as he could recall, there had been no University investigation into how he contracted the disease and that the only person to contact him for such a purpose was a doctor acting, he thought, for the World Health Organisation.

119. There were several routes by which smallpox virus could have escaped from the smallpox laboratory in 1966, particularly as work with smallpox virus was carried out on the open bench, without the use of a safety cabinet, and the photographer had regular contact with staff from the Virology Department. Our interview with the photographer established that he was occasionally present in the histology laboratory situated directly above an office that is now the smallpox room with a service duct (Duct B) running through both rooms. We therefore enquired further into the state of the service ducts in 1966 and were assisted in this by the recollections of Professor Wildy who said, “When I arrived in Birmingham in 1963 the present pox virus laboratory was in use as a medium room. It was in a bad state; in particular the plywood panels were rotten and steam actually leaked into the room. I saw at once that the only thing to do was to move the medium making and completely renovate that room. This was done early in 1964. Curiously the one item left off the plan of alterations was the need to replace panels and seal them. Henry Bedson arrived in the early summer of 1964 and we held up all work on smallpox virus until the panels had been made good. Unfortunately I have no record of when the smallpox work actually began, but I remember that work was confined to vaccinia virus until we were satisfied. The plywood panels were replaced with asbestos sheet which I believe was embedded in mastic. Because mastic is apt to crack we had flexible adhesive tape put over the outside of the joints. Until this was done I remember that the small room (then used as an office by Henry Bedson and Ian Cruickshank) had been hot and steamy, and since this was cured I conclude that the panels in the small room were satisfactorily sealed as well as those in the larger outer laboratory.”

120. As we have indicated, there were several other routes to consider. It was impracticable for us to trace and question all the members of the Anatomy and Virology Department staff who were working in the Medical School in 1966 about personal contact, movements of staff and equipment or of any possible accident that might have occurred in the pox virus laboratory. However, our air tests on the laboratory under the present containment conditions, have shown that if virus did escape it could have travelled a considerable distance in the Medical School.

121. The photographer fell ill on 18th February 1966. We have a note in Professor Bedson's handwriting, saying that on 7th February 1966 thirty tissue culture dishes were inoculated with a strain of *Variola minor*, and that on 10th February 1966 these cultures were harvested. This information is confirmed by the entry in the laboratory day book. Both dates are within the probable period of exposure of the photographer. Confirmation that the laboratory was working with *Variola minor* is also given in the report by the National Communicable Diseases Center, Atlanta.

122. The *Variola minor* strains isolated in the 1966 outbreak still exist as does the strain being worked on in the laboratory at that time. We have sought advice as to whether it would be practicable to distinguish these strains from each other, but we have been told that with present techniques this could not be done.

123. Mrs. Parker could not have been infected by contact with virus lying dormant in her studio or darkroom since 1966 as her infection was *Variola major*; the 1966 strain was *Variola minor*.

Conclusions

124. A lot of emphasis has been placed on the coincidence that two photographers working in the identical darkroom but twelve years apart were both primary cases in an infection of smallpox. It is our opinion that after twelve years it is impossible to say if the photographer was infected from the smallpox laboratory. Nevertheless we believe it to have been likely since our own recent enquiries into the working conditions of the pox virus laboratory have shown that it would have been possible for the photographer to have been infected from this source.

125. There is no evidence that a formal enquiry was held by the University into how the photographer became infected with smallpox. Although, in retrospect, we think an enquiry might have revealed the source of the infection, it is understandable that no such enquiry was held in view of the epidemiological situation and the climate of opinion regarding safety at that time, and the fact that the techniques in use in the smallpox laboratory were similar to those in use in laboratories elsewhere and were considered to be safe.

126. It is considered impossible that Mrs. Parker was infected from the same source as the photographer who was ill in 1966 through virus lying dormant in her studio or darkroom since that time. It is, however, possible that virus reached both of them by similar routes. Each photographer shared the studio with an artist. Neither artist contracted the disease and, as far as we know, neither was vaccinated against smallpox. Others may have been exposed too but it is known that smallpox attacks capriciously those exposed to it.

CHAPTER 7

INVESTIGATION OF THE SOURCES OF MRS PARKER'S INFECTION: VARIOLA SINE ERUPTIONE, CONTACT WITH PRIMATES, DELIBERATE REMOVAL OF VIRUS FROM THE LABORATORY.

127. When our enquiry began, we determined that there were five possible sources of Mrs. Parker's infection (see paragraph 12). The investigation into two of these possibilities has already been detailed in this report, and this Chapter records our investigations into the remaining three.

The Possibility that Mrs. Parker became infected by Contact with a Case of Variola Sine Eruptione Occurring in a Vaccinated Member of the Medical School Staff.

128. Clinical diagnosis of smallpox may be difficult when it occurs in a mild form or when the course of the disease is modified by previous vaccination. Few of the characteristic skin lesions may be seen, and in the extreme form, known as *Variola sine eruptione*, a febrile illness occurs but no rash follows the onset of illness. Even these patients may very rarely transmit the infection by droplets from the mouth.

129. We considered the possibility that a member of the staff of the Department of Medical Microbiology had developed smallpox modified by vaccination and had then infected Mrs. Parker. Questioning of the 28 members of the staff of the department showed no evidence of febrile illness in the latter half of July.

130. Successful vaccination against smallpox induces antibodies in the recipient's blood stream, but commonly at a lower level than those induced by the disease itself. We therefore asked Dr. M. S. Pereira of the Central Public Health Laboratories of the Public Health Laboratory Service to examine 90 blood samples provided voluntarily by the staff of the Department of Medical Microbiology, and the adjacent Department of Anatomy (Appendix 11). Tests were made for antibody to vaccinia by haemagglutination inhibition. 86 of these individuals had antibody titres ranging from less than 10 to 80, which fall well within the range of a normal response to vaccination. Four members of staff, all working in the Department of Anatomy, had antibody titres of 160 which could be considered to lie within the range following smallpox. However, on interview we learned that all four had been re-vaccinated in August 1978, which probably accounted for the high titres, and none had had a febrile illness late in July. They did not have contact with the pox virus laboratory.

131. We took advice from experts in this country, WHO in Geneva, and the Communicable Diseases Center, Atlanta, as to the possibility of distinguishing between antibody produced by vaccination against smallpox, and that produced by the disease. We were told that at present this would not be possible.

132. We have, therefore, found no evidence to support the possibility that Mrs. Parker was infected from a member of the staff suffering from smallpox modified by vaccination and do not consider this a likely source.

The Possibility that Mrs. Parker Derived her Infection from a Monkey in the Department of Anatomy's Primate Colony.

133. In the course of her work as departmental photographer, Mrs. Parker was asked to take photographs of animals in the Department of Anatomy's primate colony. On these occasions she would enter the colony with her equipment, do what was necessary and then go away. She was not thought to visit the colony other than for professional reasons. The last occasion she was known to have visited the colony was on 2nd May 1978. Since that date she was not thought to have photographed dead tissues or tissue cultures from the primate colony.

134. Blood samples from all the 200 primates in the colony have been examined for antibody to vaccinia by haemagglutination-inhibition tests (Appendix 12). All had titres of <10 except for one, which had a titre of 40. This animal had been in the colony for 3 years. It was healthy on arrival and had remained so. We have been advised that in the circumstances the blood antibody titre was probably due to an old infection, almost certainly with an animal pox virus.

135. We consider that Mrs. Parker had not derived her infection from the primate colony.

The Possibility that Mrs. Parker was Infected through Virus Removed from the Laboratory.

136. Since we set out to investigate all the possible sources by which Mrs. Parker could have become infected with smallpox, we thought it necessary to consider whether there could have been deliberate or accidental removal of the virus from the pox virus laboratory.

137. We did not find any evidence that work with smallpox virus had been conducted in the Medical School other than in the pox virus laboratory itself. Neither did we obtain any evidence to suggest that the virus had been deliberately removed from the laboratory. Smallpox virus was stored together with other viruses (being used elsewhere in the Department of Medical Microbiology) in the freezer in the animal pox room. We have described how it was the practice to place smallpox virus stocks in this freezer without disinfecting the outsides of the containers after they had been in the smallpox room and this, in our opinion, could have led to contamination of the outside surfaces of other containers in the freezer. Anyone subsequently removing virus stocks from the freezer for use elsewhere in the Department could therefore have accidentally removed smallpox virus from the pox virus laboratory via contamination on the outside of containers. Furthermore, the storage of other viruses along with smallpox virus was an unsatisfactory practice because it could have also led to the wrong container being accidentally removed from the laboratory.

138. We were told by a member of staff that on one occasion the laboratory was found to be unoccupied with the entrance door unlocked despite the fact that the keys of the laboratory were held only by a few selected persons and

a policy of restricted access to the laboratory was in force. In our view, such a lapse of security could have provided an opportunity for unauthorised entry to the laboratory, but we have no evidence that such entry occurred.

139. We concluded that smallpox virus could have been accidentally removed from the pox virus laboratory, either by taking a wrong container or on the outside of a contaminated container, there was however no evidence that this occurred or that Mrs. Parker came into contact with such material.

CHAPTER 8

CONCLUSIONS ON THE SOURCE OF MRS. PARKER'S INFECTION

140. We have no doubt that Mrs. Parker was infected with a strain of smallpox virus used in the smallpox laboratory, probably in the last week in July. Working conditions were such that it could have become airborne or could have been deposited on surfaces in both the smallpox room and the outer animal pox room. We cannot be certain by what route she was infected.

141. It is possible that Mrs. Parker became infected by the airborne route. The most probable route was through the duct in the outer animal pox room to the "telephone room" immediately above, as this was the shortest in distance and time. The distance through the duct (Duct C) of the animal pox room from the "telephone room" was about 8 feet. Mrs. Parker made almost exclusive use of the "telephone room" and during the relevant period she was using the telephone there several times a day every day. When seated at the telephone she would have been close to the ill-fitting inspection panel of the duct.

142. Tests also showed that tracers liberated outside the safety cabinet in the smallpox room also reached the main corridor outside the pox virus laboratory suite and if Mrs. Parker visited the enquiry office or the darkroom at the end of this corridor, and we believe she may have done, she might have inhaled smallpox virus while there. This is a less likely route and furthermore this corridor was also used by many other persons, some of them unvaccinated.

143. We cannot be certain the airborne route was involved. Indeed some experts who have worked with smallpox virus are of the opinion that normal working conditions would not be likely to generate sufficient amounts of airborne virus for infection to occur. However, very large quantities of virus were being used in this laboratory and the procedures being employed were far from satisfactory. That airborne spread of smallpox virus from an infected patient is possible was demonstrated by the outbreak in 1970 of smallpox among the patients in a hospital in Meschede, West Germany (see paragraph 92).

144. It is also possible that Mrs. Parker became infected by direct or indirect contact transfer. One member of the Microbiology Department who was a frequent visitor to the outer animal pox room visited Mrs. Parker at least once during the relevant period, and it is possible that this visitor picked up the virus on hands or clothes from the outer animal pox room and carried it in this way to Mrs. Parker.

PART II
THE LESSONS TO BE LEARNED

CHAPTER 9

**ADMINISTRATIVE ARRANGEMENTS FOR THE CONTROL OF WORK
WITH SMALLPOX VIRUS IN LABORATORIES**

145. The recent history of the containment of smallpox in laboratories in the United Kingdom is an unhappy one. In 1973, again in 1978, and possibly also in 1966, there have been escapes of virus which on two occasions have resulted in the death of affected individuals.

146. In 1974 the Cox Committee reported on the outbreak of smallpox that had followed the escape of smallpox virus from a laboratory in the London School of Hygiene and Tropical Medicine in 1973. The Committee's recommendations included the setting up of a permanent group of experts who would designate a list of dangerous pathogens, including smallpox virus, and formulate a code of practice for working with them. The Committee also recommended a number of requirements for inclusion in such a code and in addition set out an Interim Code (see Appendix 13) for laboratory work with smallpox virus. This interim code was agreed by virologists from a number of establishments, including Birmingham University. Copies of the Code were sent to Directors of Departments of Microbiology in Universities, Teaching Hospitals and Research Laboratories by the Chief Medical Officer (DHSS) on 8th June 1973. It should be noted that this Interim Code included the recommendation that regular vaccination and re-vaccination should be offered to members of Departments working in the same building in which a smallpox laboratory is situated. This was an important recommendation which, although implemented by the Birmingham Medical School in 1973, was not vigorously pursued.

147. Following the recommendations of the Cox Report, a Working Party was set up in November 1973 under Sir George Godber's chairmanship to report on the measures to be taken to ensure better laboratory safety in relation to the handling of dangerous pathogenic organisms. The Working Party covered a range of pathogens, against many of which vaccination was not possible and as a result more emphasis was placed on the requirements for containment.

148. In 1973 there was no recognised list of organisms that should formally be regarded as dangerous, and no complete list of laboratories holding or working with such organisms. The Working Party accordingly set out by means of a questionnaire to seek this information. They identified over seventy organisms that they thought should be handled with special precautions, and for good reason. Of these, they called thirty-nine Category A Pathogens because they were so dangerous as to present great risks to the health either of laboratory workers or of the human or animal communities such that material containing live organisms should not be accepted knowingly or held at all in this country

without authorisation. Five of these Category A Pathogens—herpes B virus of monkeys, Lassa fever virus, Marburg virus, rabies virus and smallpox virus, presented hazards primarily or significantly to the human community. The remainder presented hazards only to animals. The Working Party found that one hundred and fifteen of the establishments that answered their questionnaire held Category A Pathogens, and that nineteen held smallpox virus.

149. At the time of the survey, responsibility for safety in handling human Category A Pathogens rested entirely with establishments where pathogens were handled. The Working Party were aware that while in many places this responsibility had been taken seriously, and codes of practice drawn up and appropriate safeguards adopted, in some cases this had not happened. The agriculture departments had exercised rather more direct control over animal pathogens by a mixture of statutory power and voluntary controls but a number of important gaps still existed.

150. The Working Party therefore recommended* for Category A Pathogens that “a system of control for work with pathogens in this category should be set up as soon as possible. Such a system of control could only be voluntary in the first instance and in due course it would need to be reinforced by appropriate statutory powers. It involved the establishment of a confidential system whereby any laboratory holding or handling (or intending to hold or handle) pathogenic micro-organisms included in Category A would apply to the appropriate Department. The Department would then seek the advice of a Dangerous Pathogens Advisory Group on the desirability of that laboratory’s continuing with or undertaking the work proposed and on the conditions under which the work should be done. The Dangerous Pathogens Advisory Group would be a small independent body of experts consisting of individuals whose experience would command the confidence of those working in laboratories”. The Working Party also formulated a comprehensive Code of Practice for use by laboratories working with Category A pathogens (see Appendix 15) by which DPAG could exercise its system of control.

151. Following the recommendations of the Godber Working Party the Dangerous Pathogens Advisory Group was constituted, and held its first meeting on 14th November 1975. Its terms of reference were:

“To advise on the suitability of particular laboratories to work on the specified pathogenic organisms of the most dangerous kind indicating precautions they should observe, and on the advisability of particular work projects with such organisms in relation to hazards presented; and to advise generally, as appropriate, on questions of prevention of infection resulting from laboratory work with dangerous pathogens and on classification of pathogens according to the dangers they present.”

152. The group consisted of 18 members at whose meetings there were observers from the Health and Safety Executive, Ministry of Agriculture, Fisheries and Food, the Scottish Home and Health Department, the Welsh Office, the Northern Ireland Office and the Department of Health and Social Security.

*Cmnd 6054, May 1975.

153. At the same time WHO was engaged in an active programme for eradicating smallpox throughout the world and was recommending a reduction in the number of laboratories holding smallpox virus. In August 1977 they published a Workshop Report on Safety Measures in Laboratories Retaining Variola Virus which contained recommended safety procedures relating to the physical construction and administration of these laboratories. The Birmingham smallpox laboratory did not fully meet the conditions and was inspected by WHO in May 1978.

154. It is a matter of great public concern that the escape of virus in 1978 from the Birmingham laboratory should have occurred despite the expert advice on the control of laboratory safety that had been given since 1973 following the outbreak of smallpox originating from a laboratory in the London School of Hygiene and Tropical Medicine. The Cox Committee in 1973 made recommendations designed to prevent a recurrence of that incident, in 1974 the Godber Working Party made further recommendations on laboratory safety. In 1974 the Health and Safety at Work Act had imposed statutory obligations with regard to safety that would have applied to Birmingham University and to its employees, in 1976 the smallpox laboratory was inspected for DPAG and on its recommendation approved for smallpox work by DHSS, in 1977 WHO had produced its own recommendations on safety in laboratories holding variola virus and in May 1978 they had carried out an inspection of the smallpox laboratory. We therefore examined the circumstances in which the bodies most directly concerned, DPAG, WHO and Birmingham University, had failed to ensure that work with smallpox virus in the Birmingham laboratory was carried out in conditions of complete safety.

CHAPTER 10

DPAG's DECISION TO RECOMMEND THE APPROVAL OF THE BIRMINGHAM LABORATORY

155. One of the first tasks of DPAG when it was formed in November 1975 was to begin the inspection of laboratories notified to the Godber Working Party as holding Category A pathogens. It also began the formulation of the requirements and code of practice for laboratories holding Category A pathogens, basing its work on the recommendations of the Cox Committee and Godber Working Party. The Code of Practice was produced in October 1976.

156. The Birmingham smallpox laboratory was inspected on 4th February 1976. The inspection report (see Appendix 18) showed that the laboratory was carrying out research work to extend the basis of identification of unknown viruses related to smallpox, to compare smallpox viruses with animal pox isolated in Africa and to undertake research on whitepox and other viruses of the pox family. The laboratory also functioned as the Regional Smallpox Laboratory and examined twelve to thirty specimens a year from suspected smallpox patients. The facilities of the laboratory and the safety practices said to be in use were based on the recommendations of the Interim Code of Practice of the Cox Committee, with the exception of recommending smallpox vaccination of all those in the building where the laboratory was situated. However, it fell short of the full proposals of the Godber Working Party, particularly in the absence of an air-lock, shower, changing facilities and double-ended autoclave for sterilization of material from the smallpox room. The inspector reported that the safety precautions appeared to be very thorough and that there was a comprehensive programme of vaccination within the Department of Medical Microbiology which was said to be carried out conscientiously.

157. The inspector recommended that approval be given to the laboratory for continued work with smallpox virus for the following reasons, despite its being unable to comply in full with the requirements of the Godber safety code. First, Professor Bedson was a very reputable, experienced and safety-conscious virologist. Second, all smallpox work was restricted to a few named members of staff working under Professor Bedson's personal supervision. Third, a highly efficient vaccination programme was in force in the Department. Fourth, the safety procedures in use were very thorough. Finally, the laboratory served in its diagnostic capacity a large and important area in the Midlands with a constant flow of people to and from tropical and sub-tropical parts of the world where smallpox was not yet fully under control.

158. After discussion, DPAG decided that in view of the recommendations of its inspector and of the experts' view of the long history in this country and elsewhere of safe work with smallpox virus under conditions frequently less adequate than those in Birmingham, it would be safe for work with smallpox virus to continue in Birmingham despite the laboratory's inability to comply fully with the requirements of the Godber Safety Code. DPAG felt justified in

taking such a view since it involved the exercise of its discretionary power with regard to the conditions of the safety code along the lines recommended in the Godber Report.

159. The safety code was not intended according to the Godber Working Party to be implemented fully and absolutely in every case. An element of discretion was allowed in deciding whether selective application of the code would be more appropriate in relation to certain laboratories. The Godber Report stated that:

“The code we have drawn up is intended as appropriate to work on very dangerous pathogens presenting a hazard to humans, for example as Lassa fever or Marburg viruses. It is intended that it should be suitably amended to take account of the different properties of other Category A pathogens. The Dangerous Pathogens Advisory Group should have the unquestioned authority to advise the reinforcement or relaxation of the code as appropriate to the pathogens held and to the work proposed in any individual laboratory.”

and

“As Category A pathogens are not a homogenous group but display widely differing properties, it is not expected that the whole code would be applied in all circumstances.”

and

“The Dangerous Pathogens Advisory Group would be able to exercise discretion in advising Departments either if it were satisfied that the ends which the code sought to achieve were fully met by other means or if it decided that the hazards presented by a certain type of work on a specific pathogen in a particular laboratory required either reinforcement or relaxation of the barriers laid down in the code.”

160. In August 1976, DPAG recommended to the DHSS that work with smallpox virus should continue in the Birmingham smallpox laboratory. They added the following rider:

“Fresh clearance should be sought in the event of significant changes in staff, facilities or work programme.”

161. Professor Bedson was given formal approval by DHSS in September 1976 for his laboratory to continue to work on smallpox virus (see Appendix 18).

162. In October 1976 DPAG published a Handbook on the control of dangerous pathogens incorporating a Code of Practice which was almost identical to that of the Godber Working Party. It was distributed to all laboratories where pathogens of any kind were held or handled, including the Birmingham smallpox laboratory. In this Handbook it was stated that “The Ministers hope that the heads of all laboratories which as a matter of deliberate policy, hold or handle or might in future hold or handle Category A pathogens, and anyone else who may do so, will be able to co-operate in establishing the system of safeguards now described.” (See Appendix 16).

163. The 1978 escape of smallpox virus from the Birmingham laboratory resulting in the infection of someone outside the laboratory was the sort of event which DPAG was set up to prevent. We looked, therefore, into the circumstances by which DPAG arrived at the wrong recommendation.

164. The report on which DPAG based its recommendation was the outcome of a half day visit to the Birmingham laboratory by DPAG's inspector. During his visit no work was being done in the smallpox room (although subsequent examination of the laboratory day book showed that a considerable amount of work was done that day), and the time was spent inspecting it, and talking to Professor Bedson about the work in progress. The inspector was vaccinated by Professor Bedson at the start of the visit. The Inspector did not compare the facilities and procedures in the laboratory against the detailed list of requirements in the safety code contained in the Godber Report.

165. The airflow through the safety cabinet was tested with an anemometer and found to be satisfactory, but no other physical tests of airflow or apparatus were done. Attention was not drawn to the inspection panel covering the service duct in the corner of the smallpox room, and it was not noticed. No mention was made of the 1966 outbreak of smallpox or the possibility that it might have originated in the smallpox laboratory. Stress was laid on the fact that work with smallpox virus was done by four nominated people; Professor Bedson and his technician Mrs. Durham, with Dr. Skinner and Dr. George in reserve for diagnostic work. Professor Bedson had the reputation of a meticulous and careful worker and the inspector accepted his assurances about the safety precautions in use in the smallpox room; these included the use of the safety cabinet, the disinfection of the working surfaces in the room with formalin at the end of a session, the changing of gowns and the washing of hands in the laboratory sink before leaving the room.

166. In retrospect it is clear that what did not emerge from the interview was the range and extent of the work being done. In particular the inspector was not told, nor did he ask, about work with tissue cultures, and he thought, but again did not enquire, that the methods in use of harvesting smallpox virus did not require the use of a low speed centrifuge. These points seem to us to be of considerable importance since one of the unsatisfactory features in the practice of the laboratory as described to us, was the necessity to pass in and out of the smallpox room during the course of work with smallpox to place cultures in the incubators and to use the low speed centrifuge. Assurance should have been sought from Professor Bedson that it was not necessary to leave the smallpox room regularly during the course of work.

167. It will be clear from the earlier part of our Report that since the inspection in February 1976 changes in the practice of the laboratory had taken place that had not been notified to the Department of Health and Social Security or DPAG, despite the requirement that fresh clearance should be obtained in the event of significant changes in staff, facilities or work programme. In August 1976 Professor Bedson was appointed to the Chair of Medical Microbiology and from then on was heavily engaged in teaching and the administration of his department. Although directing the work on smallpox, Professor

Bedson delegated the actual experimentation to a PhD student who was not one of the four people he had originally specified should work on smallpox and who told us that since she had begun her work with smallpox viruses in the smallpox room she was on no occasion supervised at her work with live smallpox viruses by Professor Bedson. The development of unsafe practices, including the failure to use the safety cabinet for some open work with smallpox virus, and the handling of equipment outside the smallpox room with unwashed and undisinfected gloves, coincided with the introduction of new techniques necessitating the preparation of greater quantities of virus, and culminating in the early summer of 1978 with the examination, under conditions of urgency in view of the decision to cease smallpox work at the end of the year, of twenty-two additional strains of *Variola major*. It was one of these strains that we believe infected Mrs. Parker. DPAG were not informed of the transfer of these strains to Birmingham from St Mary's Hospital Medical School smallpox laboratory, as required by the Godber Working Party and by DPAG, nor was the rule observed which required the despatching laboratory to obtain confirmation from the receiving laboratory that worked with the particular material.

168. It is now clear that the inspection report on the Birmingham smallpox laboratory did not provide enough information for DPAG to obtain a complete picture of the laboratory and not enough questions were asked about the actual working of the laboratory. As DPAG was set up to implement the safety code recommendations in the Godber Report it should have insisted on an inspection report that listed the facilities and procedure in the laboratory against those contained in the Safety Code*. We feel that it is vital to obtain as much information as possible on which to base recommendations. WE RECOMMEND that DPAG should compile a detailed checklist to be followed by their inspector in carrying out his inspection of Category A laboratories; and that the inspector should also examine any laboratory records and interview the staff who are to undertake Category A pathogen work.

169. We endorse the recent decision of DPAG that the inspection of laboratories should be carried out in conjunction with the Health and Safety Executive and, where appropriate, the Ministry of Agriculture, Fisheries and Food who also inspect Category A laboratories in fulfilment of their statutory duties. These combined inspections will help to provide DPAG with much more detailed and diverse information on which to base their recommendations.

170. The DPAG recommendation reflected the firmly held belief of experts that work with smallpox virus could be carried out safely within the Interim Code of practice of the Cox Committee, and without all the provisions of the Godber Working Party, and it was on this basis that DPAG exercised their discretion. It is our opinion that if the safety recommendations of the Cox Committee and of the Department of Medical Microbiology itself had been adhered to, no escape of smallpox virus from the laboratory would have occurred. There is, however, no substitute for safe methods of working, and this episode has now emphasised that human skill and behaviour should not be relied on as a substitute for structural or mechanical barriers to the escape of a dangerous

*A comparison of the specifications of DPAG's Safety Code with facilities obtaining in the Birmingham laboratory is given in Appendix 17.

pathogen. If the Birmingham laboratory had had the facilities on which DPAG exercised its discretion, primarily the provision of an airlock, a shower, changing facilities and double-ended autoclave, these facilities would have made considerably more difficult to develop the bad practices that led to the escape of smallpox virus. WE RECOMMEND that in future, discretion should be exercised by DPAG only if alternative arrangements are in force in a Category A laboratory which are able to achieve a degree of safety equivalent to that specified in the Safety Code.

171. It is our opinion that the wrong guidance given by DPAG to the DHSS stemmed from three sources. The first was the lack of knowledge of the precise conditions in the Birmingham smallpox laboratory. The second was a failure to foresee the possible development of unsafe laboratory practices and unannounced changes of work after the inspection, and the third was the mistaken use of the Group's discretionary powers.

172. In view of the gap that has emerged between the findings of the inspection report presented to DPAG and the work actually taking place in the Birmingham smallpox laboratory, we think the public are entitled to be concerned whether DPAG's approval of the other laboratories holding Category A pathogens was based on less than adequate information. (A list of these is given in Appendix 19.) WE RECOMMEND that DPAG carry out an immediate and comprehensive inspection and review all of other laboratories holding and handling Category A pathogens. The Committee has noted the advice published by HSE for all establishments working with Category A pathogens.

173. At present, the Safety Code is observed by laboratories on a voluntary basis. It was always the intention of the Godber Working Party that the voluntary measures controlling laboratories holding dangerous pathogens would eventually be made compulsory under legislation. They said, "We hope and expect that improvements will be introduced as a result of close co-operation and constructive discussion between the laboratories and the Advisory Group. Nevertheless, we consider that the public has a right to expect powers of enforcement to exist." These powers already exist with the Health and Safety Executive who enforce the requirements of the Health and Safety at Work etc. Act 1974. The Act imposes duties on those at work to avoid endangering the health and safety of workpeople and the general public. Under the Act, the HSE Inspectorate have extensive powers to enforce these duties as well as any relevant precautions recommended by such bodies as the DPAG. We feel, however, that the present system of voluntary registration of laboratories is unsatisfactory. WE RECOMMEND that regulations be made to require laboratories to notify their intention to hold or handle Category A pathogens, together with details of their proposed work and other supporting information, to HSE, DPAG and the appropriate Health Departments and that reconsideration be given to the arrangements for approval of laboratories holding or handling Category A pathogens.

Regional Diagnostic Laboratories

174. DPAG was set up to advise laboratories holding and working with Category A pathogens. While we are recommending re-inspection and

arrangements for the compulsory registration of these laboratories, we realise that there will be some practical problems in relation to Category A pathogens where diagnostic laboratories are concerned.

175. In the normal course of its clinical work any diagnostic laboratory may receive a specimen containing a dangerous pathogen from a patient for whom the clinical diagnosis has not yet been made. For the examination of specimens from patients suspected of suffering from smallpox or Lassa fever, arrangements have been made by DHSS for them to be sent to designated laboratories. They are listed in Appendix 19.

176. Most of the specimens will be from patients with other infections and in whom the chance of the illness being due to a Category A pathogen is slight. It may be very necessary to determine the true nature of the patient's illness with as little delay as possible. In some forms of malaria there is, for example, great urgency to establish the diagnosis and to begin treatment if life is to be saved, and any appreciable delay in the examination of laboratory specimens would not be acceptable. We believe it will be inevitable that some specimens will initially have to be examined in certain diagnostic laboratories that lack full Category A facilities.

The Role of the Department of Health and Social Security (DHSS)

177. DPAG was set up to advise the Department of Health and Social Security on the suitability of particular laboratories to work with specified pathogenic organisms.

178. Following consideration of the inspection report on a laboratory, DPAG makes its recommendations to DHSS. The responsibility for accepting, rejecting or modifying, and in any event acting on, that advice is the Department's. It is clear that DHSS would not, other than in the most exceptional circumstances, act contrary to the advice given to it by a panel of independent experts set up for this purpose. The expected course for the DHSS is to accept and act on the advice given to it by DPAG in every normal case, DPAG's advice being qualified by:—"While the DPAG and those who assist in its work act of course to the best of their ability, responsibility for the precautions taken or omitted in any laboratory must rest with those concerned in its operation. This report is made only on the basis that neither the DPAG nor its inspecting officer has any legal liability for the advice given or the consequences of following it."

179. DHSS formally wrote to Professor Bedson on 10th September 1976 informing him that they had accepted DPAG's recommendations that his laboratory was suitable for work with smallpox virus and in addition for the examination of specimens from possible Lassa fever patients for bacterial and malarial infection. The letter also instructed Professor Bedson, along the lines suggested by DPAG, "It is requested fresh clearance should be sought if there is significant change in staff, facilities or work programme."

180. Approval for work with Category A pathogens is given at present by the DHSS, and in the short period that the voluntary system for control of Dangerous Pathogens had been working no action had been taken in respect of

monitoring or re-inspection of approved laboratories. Reliance had been placed on laboratories informing the Department of significant changes in people or work in the laboratories. Our examination of the Birmingham laboratory showed that in the two years since inspection considerable changes had taken place in staff, facilities and the work programme. Indeed it would be reasonable to assume that after a period of two years, changes would have occurred; we would have been surprised had they not. We therefore feel that frequent and regular reviews of laboratories should be carried out to ensure that they continue to operate within the Safety Code. WE RECOMMEND that Category A laboratories should be subject to annual review and should notify DHSS immediately of any significant changes in their staff, facilities or work programme.

The Future of Smallpox Work in the U.K.

181. Smallpox no longer exists anywhere in the world. Smallpox virus however is held in a very few laboratories; the only one in this country is St. Mary's Hospital Medical School, London. This laboratory was re-inspected by WHO and DHSS soon after the events in Birmingham and was found to be satisfactory. However, it seems to us that no matter how good the measures of containment may be in laboratories, it is impossible by these means alone to guarantee safety.

182. A choice must therefore be made—whether work with smallpox virus is to continue in this country or not. With the eradication from the world of human smallpox there is still concern that unknown animal reservoirs of smallpox may exist and that pox viruses as yet confined to animals may begin to infect humans. The recent discovery of variola-like viruses has emphasised the need to identify and differentiate them from other pox viruses and this has stimulated a great deal of research. This work is currently being done at St. Mary's Medical School and is important to the WHO smallpox eradication campaign.

183. If it is decided that work with smallpox virus must continue so as to monitor the occurrence of pox viruses following the apparent eradication of smallpox, we think it no longer makes sense to have the country's remaining smallpox laboratory in a densely populated part of London. Vaccination against smallpox is not without risk to those vaccinated, and for this reason too we believe that the laboratory should be moved to an isolated position where fewer people will require vaccination and where the control of visitors will be more practicable.* WE RECOMMEND that urgent consideration be given to re-siting this laboratory in a place where facilities for containment are stringent and which is situated where the number of staff who have to be regarded as potential contacts is smaller than in a Medical School.

*Examples of the complications that could arise as a result of vaccination against smallpox are recorded in the report on the 1966 outbreaks of smallpox by the Chief Medical Officer of the Ministry of Health—See Appendix 10.

CHAPTER 11

THE WORLD HEALTH ORGANISATION

184. With the eradication from the world of human smallpox, there is concern over the possibility that there may exist unknown animal reservoirs of smallpox and that viruses as yet confined to animals may begin to infect humans. Professor Bedson's laboratory was engaged in attempting to improve methods of differentiation and identification of recently discovered variola-like viruses of animal origin. His work was important to the World Health Organisation's smallpox eradication campaign and was supported by them through the provision of annual research grants.

185. In March 1977, Professor Bedson asked WHO to designate his laboratory as a Collaborating Centre. This followed a policy decision by WHO that variola virus should only be retained by designated WHO Collaborating Centres in order to minimise the danger of laboratory accidents by decreasing the number of laboratories holding the virus.

186. In August 1977, WHO produced a list of recommendations on safety measures to be taken by laboratories holding variola virus (see Appendix 20). The recommendations covered safety procedures, physical construction and the administration of these laboratories. We would suggest that DPAG consider these recommendations against those contained in their own Safety Code handbook.

187. In September 1977, WHO informed Professor Bedson that his laboratory was not to be made a Collaborating Centre. The inference from this would be that his work with smallpox virus would soon have to end. However, WHO emphasised that the laboratory's research work was important and ought to be supported and indicated that they were satisfied that the laboratory was suitably equipped for variola virus work. They offered Professor Bedson a research grant of \$7,500 for 1977.

188. The decision that the Birmingham laboratory should not become a Collaborating Centre came as a blow to Professor Bedson. In October 1977 he wrote to WHO saying that he had assumed that the work in his laboratory would end in 2 or 3 years and that then the laboratory at St. Mary's Hospital Medical School, London, would become the sole U.K. smallpox laboratory. He suggested that he should continue his smallpox work till the end of 1978. WHO, after consulting with their "International Commission for the Certification of Global Smallpox Eradication", confirmed that they were satisfied with this timetable and indicated that they had made it known to the U.K. Department of Health and Social Security.

189. Following a decision by WHO to inspect the smallpox laboratory in May 1978, Professor Bedson wrote to them on 31st March 1978 saying, "I hope that it is clearly understood that, while we are satisfied that what we are doing

is sensible and secure and has been approved by our National Bodies, our facilities in no way match those set out for the definitive smallpox labs in your workshop report SME 77/2. (See Appendix 20). It would be expensive and very costly in time if we were to try to establish such a laboratory and quite unjustified in view of our projected halt to the smallpox/whitepox work at the end of the year."

190. WHO replied to this letter on 14th April 1978, stating, "With regard to your laboratory safety, simply the expected benefit of your work far exceeds the minimal risk which is currently present in your laboratory and I believe your rationales will be well understood by the visiting team." They wrote again on 27th April saying that the inspection team had been fully briefed on "the circumstances concerning your situation." Professor Bedson was also asked whether he required WHO funding for 1978.

191. On 4th May 1978 WHO inspectors visited the Birmingham smallpox laboratory. On 15th May WHO wrote to Professor Bedson reporting the results. The inspection team had said, "Dr. Netter, Dr. Wahba and I (Dr. Richardson) have considerable reservations about Dr. Bedson's facility. While surveillance and immunisation practices are very good, the physical facilities clearly do not meet the WHO recommendations. Laboratory facility and practices do not meet with recommendations. Recommendations were made: Prohibiting all (WHO's underlining) mouth pipetting in lab; using back fastening gowns which will remain in laboratory; the use of chemical (hypochlorite solution) as permanent barrier in sinks, and gloves to be worn for all activities in BSC (biological safety cabinet) involving infectious materials. The use of tabletop hot water sterilisers was questioned." WHO went on to say in the letter that for the time being some of the safety measures could be applied and improved upon. They added, "Whilst your study is important, I would like to receive your assessment of the risks involved." Professor Bedson was advised by WHO that it would be difficult to invest additional funds to remodel his laboratory but WHO felt that "further modification in technical procedures and management in the laboratory will certainly lead to strengthening of the safety measures." The WHO inspectors did not comment on those aspects of technique which we have criticised in this report nor on the potentially hazardous service ducts.

192. Professor Bedson's reply dated 2nd June about the inspection team's comments said, "Their reservations about our physical facilities were of course expected. I have already told you of the respects in which they do not match the recommendations of WHO." He felt that the WHO criticisms were unfair and pointed out that they had not distinguished between practices affecting work on smallpox viruses and those affecting work with "ordinary" pox viruses. He pointed out that mouth-pipetting had not been used with smallpox for about 10 years. That observed by WHO was "in connection with an "ordinary" pox virus and was a temporary aberration which we will ensure does not recur." With regard to back fastening gowns, these were worn in the smallpox room but front fastening gowns were worn in the outer laboratory when dealing with ordinary pox viruses and elsewhere in the building, and the local Safety Committee had thought the distinction an important safety factor. About the use of hypochlorite solution and the wearing of gloves, he said that he was happy to adopt them "even though one could argue about the extent to which they affect the

safety of the work.” He defended the use of hot water tabletop sterilisers saying that there had been no evidence of cross contamination from them and that data showed that pox viruses were killed at temperatures lower than boiling.

193. Continuing his reply, Professor Bedson answered WHO’s request about his assessment of the risks involved in his laboratory saying, “the risks must be minimal. In support of this, I would cite 1) the long history of laboratory work with smallpox viruses, 2) the progressive decline in the scale and diversity of our operations, particularly since 1973, 3) the marked increase in the level of physical containment which has been introduced, again in the period since 1973 and 4) the maintained high level of our surveillance and immunisation practices.”

194. WHO replied to Professor Bedson’s letter on 1st August. However, he did not receive this letter until 24th August, when he returned from holiday, and by which time Mrs. Parker had been taken ill. WHO indicated that Professor Bedson’s comments had been passed to Dr. Richardson of their inspection team who had said: “I agree with Dr. Bedson’s assessment that the risks are probably minimal and feel that there is a reasonably effective surveillance system in effect. It is also apparent that actions to upgrade the containment capability of his laboratory have been minimal. I am still concerned over the following:

1. Absence of a shower for routine or emergency use.
2. The lack of secondary containment in the outer laboratory where the smallpox stock viruses are stored.
3. The performance capability and certification and maintenance of the biological safety cabinet in the isolation cubicle.

The laboratory falls short of the WHO Standard and should be upgraded to meet the Standard or should discontinue work with variola at the earliest possible date.” WHO added, “I believe you are making every effort to modify the safety procedures wherever possible.”

195. Professor Bedson replied on August 24th. (Mrs. Parker’s illness had not yet been identified as smallpox). He said that there was no question of his being able to upgrade his laboratory to meet WHO standards and he was therefore proceeding with his plan to complete his studies with variola/whitepox viruses by the end of the year. Should comparisons with smallpox/whitepox viruses be required after that, he was hoping to arrange to use the smallpox laboratory at St. Mary’s Hospital Medical School, Paddington. (That night, Professor Bedson examined specimens of vesicle fluid taken from Mrs. Parker and her illness was diagnosed as smallpox).

196. What is evident from this exchange of letters, covering the period March 1977 to August 1978 (reproduced in full in Appendix 21) is that the Birmingham laboratory did not comply with the safety standard laid down by WHO and had no plans to do so. Operating under such vulnerable conditions, we would have expected the staff in the laboratory to take especial care to observe the existing safety precautions, but, as the WHO inspection report discloses, unsatisfactory laboratory procedures were taking place. We are surprised at the statement made by Professor Bedson in his letter of 2nd June 1978 that there was a “progressive decline in the scale and diversity of our operations,

particularly since 1973.” Our findings do not support this. We also found that after this letter was written the pace of work increased still further because of work done on the 22 variola strains received from Professor Dumbell on 26th May 1978.

197. WHO should have advised DHSS after the visit in May 1978 that the laboratory did not come up to WHO standards and that they would not be prepared to support it as a collaborating laboratory. The decision not to request immediate cessation of smallpox work appears to have been influenced by the importance of the laboratory’s work for their smallpox eradication campaign and the fact that the laboratory was to cease work with smallpox virus at the end of 1978. This decision is all the more surprising because WHO were engaged in a policy of reducing the number of smallpox laboratories since the success of the smallpox eradication campaign meant that these laboratories were the only remaining sources for smallpox infection. Further the 1977 WHO recommendations provided that governments authorising smallpox work should assure WHO that safety standards were met, yet WHO accepted the Birmingham situation which did not meet their own standards.

198. It is anomalous that though WHO had decided the work could not be supported after the end of 1978 this was not communicated to DHSS or the University. Professor Bedson did not bring WHO’s findings to the notice of DPAG or DHSS, and he did not bring them to the attention of the Birmingham University until after Mrs. Parker had been diagnosed as having smallpox.

199. DHSS has a formal relationship with WHO and we feel that they ought to have had some way of finding out about WHO’s visit to inspect the Birmingham smallpox laboratory. They told us, “It is normal practice for the World Health Organisation to be in direct contact with many of the collaborating units and other establishments which it supports financially or otherwise in Member countries; there are in fact over 50 such establishments in this country. That is what happened in this case, and the Investigation should be aware that no copies of the World Health Organisation/Professor Bedson correspondence were sent to the Department at that time. When the Department became aware of their existence following receipt of the report of the local Source of Infection Committee which Dr. Nicol had set up under his auspices early on, the Department requested and obtained copies of the relevant documents from the World Health Organisation. The Department realises that there is here a source of weakness in our relationships with the World Health Organisation, and will take steps to remedy this.” WE RECOMMEND that in future WHO should maintain a closer liason with the responsible government authority regarding its dealings with Category A pathogen laboratories and in particular with regard to the safety of those laboratories.

CHAPTER 12

SAFETY IN BIRMINGHAM UNIVERSITY

200. The responsibility for the operation, maintenance and safety of the smallpox laboratory in the Medical School rested ultimately with the University of Birmingham. The University had established a structure of safety committees to monitor, advise and act on all aspects of safety within the University in order to ensure that high standards were achieved and maintained. In the course of our investigation we examined the workings of the safety structure, both in general and with particular reference to the Department of Medical Microbiology and the pox virus laboratory.

201. In April 1975, in fulfilment of its requirements under the Health and Safety at Work Act 1974, the University issued a document "Safety" setting out its safety policy and arrangements (see Appendix 22). The policy laid down in that document was still in operation in the University during the period of our enquiry. The document gave detailed guidance on the safety responsibilities of individuals, supervisors, Heads of Departments and also the various Safety Committees. In our examination of the University's safety structure we not only referred to the "Safety" document but were also given free access to the minutes of the various safety committees, going back over a period of some years, and received evidence from the University's administration and also from representatives of the staff.

202. Safety within the University rests with the University Safety and Environmental Health Committee (USEHC) which is a joint committee of the Finance and General Purposes Committee and the Senate. This Committee advises both the Finance and General Purposes Committee and the Senate on safety policy and is also responsible for ensuring that University safety policy is properly implemented. It must also ensure that an adequate safety structure is established, that safety information is circulated, and that advice on safety matters is available. More detailed consideration of specific safety problems is given by a number of other committees and sub-committees:

- a. Committee for the Control of Pathogenic Organisms and Infectious Materials—this is a sub-committee of USEHC.
- b. Committee for the Control of Radiation Exposure—this is also a sub-committee of USEHC.
- c. Faculty of Medicine and Dentistry Joint Services Board Safety Sub-Committee.
- d. Faculty of Science and Engineering Safety Committee.
- e. Works and Maintenance Committee—responsible for fire precautions, emergency lighting, safety of maintenance and grounds personnel, etc.

203. The Committee particularly relevant to our enquiry was the Committee for the Control of Pathogenic Organisms and Infectious Materials. The Committee was set up in 1966, and its terms of reference are:—

- a. Control of species of micro-organisms which might be studied in the University together with precautions needed for particular species.
- b. Safety measures in animal houses as well as laboratories.
- c. Prophylactic measures.
- d. Contact with general practitioners.
- e. Legal aspects.

The Committee is composed of members of the Academic staff and there are no representatives of other University staff. The University Safety Officer also attends its meetings.

204. The Committee required all departments to provide it with a list of the organisms they were working with and a register was compiled. In October 1974, Professor Bedson became a member of the Committee. In 1975 the Committee visited all the departments with micro-organisms on register so that their arrangements could be examined and appropriate recommendations made. Follow-up action was taken where necessary. In 1976 the Committee began preparing a document listing immunization requirements in the University although in the case of smallpox, immunization requirements had been recommended in 1973. The document was approved in 1977. Professor H. Smith was the first Chairman of the Committee in 1966 and remained Chairman until 1977 when Professor Bedson succeeded him. The Committee last met on 22nd February 1977, and before that on 20th October 1976.

205. We were told by the University that in their view safety in microbiological laboratories depended on:—

- i. Provision of proper facilities.
- ii. The design of safety codes of practice for particular micro-organisms.
- iii. Operating the codes efficiently.

The USEHC, or its appropriate sub-committee, was responsible for monitoring (i) and (ii), but Heads of Departments were responsible for (iii).

Safety in the Medical Microbiology Department

206. The University's document, "Safety", sets out the responsibilities of Heads of Departments:—

"The Head of Department has the duty to ensure that proper safety arrangements are made in conformity with University policy. This should not be taken to imply that the Head of Department is personally responsible for each and every detailed aspect of safety. However, included, for example, among his duties should be to ensure:—

- a. that a safety conscious attitude is encouraged, particularly with regard to technical operations;

- b. that safety information and instructions are adequately disseminated in his Department;
- c. that a proper mechanism exists within the Department for raising safety matters and that this is well publicised;
- d. that proper arrangements are made for the disposal of hazardous wastes.”

207. Professor Bedson became acting head of the Department of Medical Microbiology in October 1975. After his appointment, he continued to retain charge of the smallpox laboratory and remained responsible for the safety in it. We were told that there were two Departmental Safety Officers, Dr. G. R. B. Skinner, a senior lecturer, and Mr. G. J. Barson, Senior Chief Technician and Laboratory Superintendent, but their duties did not extend to the smallpox laboratory whose safety was under the personal supervision of Professor Bedson. We were told of an incident which we felt illustrates this division; in 1977 one of the smallpox laboratory staff dropped a tray containing dishes of vaccinia virus on the laboratory floor. The incident was reported to Professor Bedson but the Departmental Safety Officers had no knowledge of it and indeed we were unable to trace any record of the incident in the Department's accident records.

208. The Department also had a Staff Committee composed of representatives of academic, technical, clerical staff and students. The Committee was formally set up in 1974, but a Staff Committee had been meeting occasionally since at least 1972. In 1978, the Committee met on 21st June and before that on 25th April. At neither meeting was there any mention of WHO's inspection of the smallpox laboratory. Prior to the April 1978 meeting, the Committee had met in March 1977 and before that in October 1975.

209. A Departmental Information Book which contained details of safety procedures was distributed among staff. A separate set of safety instructions was distributed to staff working in the pox virus laboratory. The pox virus laboratory safety instructions (already discussed in Chapter 3) stated that safety depended upon:—

- i. Vaccination and regular re-vaccination of all concerned.
- ii. Restrictions of access to protected individuals.
- iii. A check on illness occurring in departmental staff.
- iv. Containment of the virus while it is being handled.

210. Vaccination: Staff working in the pox laboratory were vaccinated every year and all others in the Department, including staff in other Departments who had contact with the pox virus laboratory or who worked on the same floor within that wing, were vaccinated every two years. We are satisfied that this policy was meticulously maintained by Professor Bedson. Vaccination was not, however, extended to staff working in other Departments elsewhere in the building although a decision was taken to do so in 1973. This is discussed in detail later in this Chapter.

211. Restriction of access: We were told that both keys to the pox virus laboratory were available only to the staff working in the laboratory, the cleaners, and a lecturer in the Department. However, on one occasion the laboratory had been found unlocked, and empty. We also found that the cleaners were allowed to work unsupervised in the laboratory. They were responsible workers but we doubt if it was right that one of the keys they held was for the smallpox room.

212. We were told that despite swing barriers and warning notices restricting access to the Medical Microbiology Department corridor, there was an intermittent flow of people passing through. There was no procedure for stopping this unauthorised use, except dependence on the chance sighting of the visitor by a senior member of the departmental staff. Some visitors from inside and outside the University, on finding nobody on duty in the enquiry office at the head of the corridor, went through the swing barriers in search of the person they wished to see. Our tests showed that it was possible for this corridor to have been contaminated with smallpox virus and therefore these people, if unvaccinated, could have been at risk. Unauthorised persons who entered the animal pox laboratory were warned off by being shouted at by the laboratory staff.

213. A check on illness occurring in departmental staff: All staff working on the Medical Microbiology floor received a card for their general practitioner to be filed with their NHS records. In addition they carried a card to be shown to their doctor in case of illness; it notified him that they worked in close proximity to a laboratory handling dangerous organisms. Staff were also required to notify their Department immediately of any absence through illness. This was meticulously followed. This system, however, did not apply to others working in the East Wing of the building and thus Mrs. Parker's general practitioner had no way of knowing whether she worked close to a smallpox laboratory. We also examined the accident records of the department; these were properly and satisfactorily maintained only when they related to injuries to staff. There were no records of virus spillages and, as indicated earlier in this Chapter, there was no record of the major vaccinia spillage that took place. We considered that all laboratory accidents and not only those relating to staff injuries should be recorded because their effects may only become apparent after a period of time and because a regular examination of such records provides useful information on the efficiency of safety procedures and of the staff themselves.

214. Containment: According to the written instructions, containment depended on "careful forethought and planning in experimental work, the highest standards of technique, and strict attention to detail, particularly in the matter of disposal of infected items." This applied to all staff working in the pox virus laboratory, whether they were engaged on smallpox work or not. In our view, containment would also rely on the proper functioning of equipment and therefore requires regular checks on equipment. Containment also relies on good laboratory procedures, having well-trained staff and arranging proper supervision of those staff.

215. Our own check on the equipment revealed a safety cabinet in the outer pox laboratory that did not function efficiently. The filters in this cabinet had not been tested since it was purchased in 1966, nor was there a scheme of maintenance for it. We were told by the staff that they regularly checked the airflow through the safety cabinet in the smallpox room and we found it to be satisfactory. We also found that the laboratory made regular use of a type of low-speed centrifuge that was prone to structural failure of its casing. The DHSS had issued a circular in December 1975 warning laboratories of this fault and advising them to discontinue using this type of machine. This centrifuge was regularly used for smallpox work and was used outside the smallpox room in the main animal pox room. We found that the ultra-centrifuge, situated in the smallpox room, was regularly serviced and maintained.

216. It is a statutory responsibility of the University to ensure the proper training of its staff and we therefore enquired into the training and experience of the staff who undertook smallpox work. In our view it was inadequate. The most experienced member of staff was a technician who had been employed in the pox virus laboratory for about eleven years. She had been instructed in smallpox work by Professor Bedson. The next most experienced was a former PhD student who had joined the laboratory in 1974 and, as far as we know, although she started her work on animal pox viruses, she was never formally trained in the special precautions required for work with smallpox viruses. The third member of staff, a trainee technician, had joined the laboratory immediately after leaving school and had been working there for about a year. She was being trained by the other technician. We learned that only nine months after she had joined the laboratory she was allowed to work with smallpox virus and had access to the smallpox room.

217. We were told that since he became acting head of the Department at the end of 1975, Professor Bedson spent very little time in the pox virus laboratory because he was preoccupied with administration and teaching. The PhD student told us that from the time she began smallpox work in 1975 she was on no occasion supervised at work with live viruses by Professor Bedson. Thus it appeared that work in the smallpox laboratory had been inadequately supervised since 1975. Professor Bedson was responsible for the safety in the smallpox laboratory both as Head of Department and as the safety officer for that laboratory; the fact that he was not supervising the laboratory throughout this period is not recorded in any of the Committee minutes we have studied. Neither was this fact brought to the attention of DPAG and WHO yet both these bodies had been heavily influenced in their decisions concerning the safety of the laboratory by the assurance that all smallpox virus work would be conducted under Professor Bedson's personal supervision.

218. We examined the financial records relating to the pox virus laboratory, and also the minutes of the appropriate University Committees to see if adequate funds were made available for safety equipment or for maintenance of the pox laboratory or whether there had been any delays in either because of financial constraints. There was no evidence that applications for funding beyond the departmental budget were made or refused or that there had been delays in providing funds.

Vaccination Policy in the Medical School

219. We know that staff in the Department of Medical Microbiology and any staff having regular contact with that Department were regularly vaccinated against smallpox. However, from our interviews with staff in the Anatomy Department we found that they were not offered vaccination. The Minutes of the meeting of 16th July 1973 of the University Committee for the Control of Pathogenic Organisms and Hazardous Biological Substances show that following the smallpox outbreak at the London School of Hygiene and Tropical Medicine, the Committee considered a policy for smallpox vaccination. Vaccination was to be offered to staff in "all departments of the Medical School" and to their families. A circular was issued in the Medical School drawing attention to this. The Pathogenic Organisms Committee reported on its action to the USEHC on 5th November 1973. It appeared therefore that in 1973 it was decided to offer smallpox vaccination to all the Departments in the Medical School. This decision does not appear to have been vigorously pursued at the time. In June 1974 the Cox Report recommended in the Interim Code of Practice that vaccination should be offered to all members of departments in the same building in which the smallpox laboratory was situated. This recommendation was agreed to by Birmingham but does not appear to have been implemented fully. Evidence that the policy had lapsed was given by members of the staff of the Anatomy Department who could not recall being offered vaccination. In September 1977 the USEHC presented a new set of immunization requirements for the University and these do not contain any requirements for smallpox vaccination to be offered to staff in other departments in the Medical School.

Conclusions

220. In our examination of the University of Birmingham's safety policy, we have concentrated on its operation with regard to the Medical Microbiology Department and its smallpox laboratory. The University had received reassurance from the DHSS, on the advice of DPAG, about continuation of work with smallpox, but our enquiries have shown that there was no effective system of determining whether both the University's and the Department of Medical Microbiology's own safety policies were being regularly implemented.

221. We appreciate the difficulty facing a university or similar institution in monitoring from a central committee the activities of a specialised department accustomed to act as an independent unit. But the safety of those working in such a department and those outside is too important to allow the central committee to obtain its information on a voluntary basis from individual departments.

222. The University told us that they considered that safety in microbiological laboratories depended on the USEHC or its appropriate sub-committee providing the proper facilities to carry out such work and devising a suitable safety code. The responsibility for operating the safety code efficiently lay with the Head of Department. Nowhere in this structure is there mention of the need for the Committee to make regular inspections to determine whether the facilities it had provided were adequate and the safety code was being correctly implemented. We were told that in 1975 the University Committee for the Control of Pathogenic Organisms and Infectious Materials arranged inspections

of all Departments working with micro-organisms to examine their arrangements. The inspections were carried out by Professor Bedson, Mr. Bush the University Safety Officer, and Dr. P. Brown. The Department of Virology (now Medical Microbiology) was also inspected and, with regard to the pox virus laboratory, they recommended that the arrangements whereby undisinfected materials such as smallpox-infected egg membranes were being removed to the basement for autoclaving should be discontinued. Since 1975 no further inspections of these Departments have been carried out by the University's Safety Committees. The inspections in 1975 did make a valuable contribution to safety in the Departments visited and we feel that they should have been continued on a regular basis. WE RECOMMEND that the University carry out regular expert safety inspections of facilities and working methods of Departments handling micro-organisms.

223. We also feel that the independent nature of the inspections is an important feature, and the University should ensure that the Head of Department should not be a member of the team that inspects his own Department. We appreciate that Professor Bedson was included in the 1975 inspection team because of his particular expertise in microbiology, but it should not be difficult, given the expertise available in the University of Birmingham, to find others capable of undertaking the task.

224. At present the University Committee for the Control of Pathogenic Organisms and Infectious Materials is composed solely of the Academic staff but it ought to have representatives of the other University staff to give it the widest possible perspective on safety. This Committee is a sub-Committee of the USEHC, which is composed of representatives of both Academic and other University staff, and it should reflect this basic composition. WE RECOMMEND that the University reconstitute the composition of their Committee for the Control of Pathogenic Organisms and Infectious Materials to include representatives of other University staff.

225. We were disturbed to learn that the University did not appear to have been told about, or to have known of, the WHO inspection in May 1978, or the arrival in the smallpox laboratory of the twenty-two strains of *Variola major* at the end of the same month. We learned that the details of WHO's inspection were only made known to the University after Mrs. Parker had been diagnosed as having smallpox. The responsible Safety Committee, the Committee for Control of Pathogenic Organisms and Infectious Materials, had not met since 22nd February 1977. We also noted that the Medical Microbiology Department's Staff Committee met on 21st June 1978, and there was no record in the minutes of that meeting of these items being raised. The University should take steps to ensure that in future they are fully aware of any reservations on safety that may be expressed with regard to any of their Departments. Other institutions may also wish to follow this advice and therefore WE RECOMMEND that in future institutions should ensure that all dealings with outside bodies concerning work with safety implications in their Departments are monitored by the central administration of the institution rather than handled on a private basis by the Heads of the Departments concerned or by other individuals.

226. The training of the staff working in the pox virus laboratory was inadequate. WE RECOMMEND that the University reviews its policy for ensuring that proper instruction in laboratory techniques and safety precautions is given to all laboratory staff before they are allowed to begin work on pathogenic organisms and to ensure that the staff are not permitted to carry out such work without appropriate arrangements for supervision.

227. We received representations that there was inadequate consultation on safety matters within the University. Under the Health and Safety at Work Act etc. 1974, the Safety Representatives and Safety Committee Regulations 1978 came into effect on 1st October 1978, giving recognised trade unions the right to appoint safety representatives who, among other things, will be entitled to make regular inspections of the place of work. We understand that discussions along these lines are currently taking place in the University of Birmingham, and we sincerely hope that they will contribute to improving the monitoring and implementation of safety procedures within the University.

The conflict of responsibility on Professor Bedson

228. Our investigation has revealed the conflict of responsibility that lay on Professor Bedson. He was a member of DPAG and one of the expert advisers who played a major role in formulating the code of practice for handling pox viruses. He was in charge of a laboratory which was carrying out work of international significance and which formed part of the programme of WHO for eradicating smallpox throughout the world. He had teaching and administrative duties within his own department. At the same time, he was responsible for safety within that department and he was Chairman of the Committee responsible for supervising safety in respect of dangerous pathogens throughout the University of Birmingham. It is a matter of deep regret to the Committee that this train of events probably contributed to the tragic death of Professor Bedson.

229. Equally, we sympathise with the Parker and Whitcomb families for the tragedy and suffering that came to them with the sequence of events described here.

CHAPTER 13

GENERAL OBSERVATIONS

230. The Report has dealt with the charge given to the Investigation under its Terms of Reference and the way in which it approached this task; the scientific evidence on the Birmingham incident has been recorded and the relevant activities of various organisations critically reviewed.

231. We believe that Mrs. Parker was infected with smallpox virus that was in use in the Medical Microbiology Department of the Birmingham University Medical School.

232. The smallpox virus escaped because measures designed to contain it while it was being handled were not fully carried out.

233. We do not know how the virus reached Mrs. Parker, but we believe one of two routes to have been the most probable. The first involved airborne spread, the virus travelling in a service duct to a room immediately above the pox virus laboratory suite. This room contained a telephone that was frequently used by Mrs. Parker. The second was by direct or indirect contact transfer from a visitor from the Department of Medical Microbiology to Mrs. Parker in her darkroom.

234. We have considered at some length the administrative arrangements concerned with the escape of smallpox virus from the laboratory. These have included:—

- i. the steps taken in the Department of Medical Microbiology for supervising work and the prevention of hazardous practices (Chapter 12).
- ii. the exercise of discretion by DPAG in respect of parts of the Safety Code (Chapter 10).
- iii. the part played by WHO following their inspection of the laboratory (Chapter 11).
- iv. the role of the DHSS in respect of a laboratory recognised as handling a dangerous pathogen (Chapter 10).
- v. the arrangements within the University of Birmingham by which they coordinated and monitored the safety arrangements for which they were responsible (Chapter 12).

235. We have made recommendations that we trust will remedy the weaknesses in the various arrangements we have described.

236. We think the main lesson to be learnt for the future is that containment of dangerous pathogens within laboratories working with them depends on adopting safe methods of working with adequate training and supervision and the correct use of physical containment facilities. Even so, no written code of practice, no matter how comprehensive and rigid, can in itself guarantee complete safety. Safety depends on people, and on the conscientious behaviour of both those working in laboratories with dangerous pathogens and those making the administrative arrangements in support of the work.

237. Although the facts speak for themselves, the Committee considers it right to express a general opinion on the situation revealed by the Investigation. We wish to record our deep concern at the failure to follow the agreed safety rules of the Department of Medical Microbiology. In addition, WHO failed to appreciate the extent of the hazard, which was not also recognised by the visiting inspector of the Dangerous Pathogens Advisory Group, and was unchecked by DPAG, by DHSS or by the University. The Committee gained a sense of a lack of information or consideration within and between the various bodies concerned. Only chance and the efficient control measures of the preventive safety authorities prevented a wider spread of infection. The report does not deal in detail with the statutory aspects of the Health and Safety at Work etc Act.

238. Our Report has not conveyed the unhappiness and disruption that followed in the wake of the escape of smallpox virus. It brought tragedy and loss of life to the Parker and Bedson families, disrupted the daily lives of over 300 people who were quarantined, affecting general and hospital practice in the area, placed an enormous burden on the Area Health Authority and caused widespread concern both in this country and abroad. A consequence of this was that travellers going abroad, many of them for their summer holidays, were required to be vaccinated against smallpox often at very short notice.

239. Finally, we feel that if the situation like that found at Birmingham exists elsewhere, the need for identification and remedy is urgent.

Summary of Recommendations

The Dangerous Pathogens Advisory Group

1. DPAG should compile a detailed checklist to be followed by their inspector in carrying out the inspection of Category A laboratories. The inspector should also examine any laboratory records and interview staff who are to undertake Category A pathogen work (paragraph 168).

2. In future discretion should be exercised by DPAG only if alternative arrangements are in force in a Category A laboratory which are able to achieve a degree of safety equivalent to that specified in the Safety Code (paragraph 170).

3. DPAG should carry out an immediate and comprehensive inspection and review of all laboratories holding and handling Category A pathogens (paragraph 172).

4. Regulations should be made that require laboratories to notify their intention to hold or handle Category A pathogens, together with details of

their proposed work and other supporting information, to HSE, DPAG and the appropriate Health Departments. Reconsideration should be given to the arrangements for approval of laboratories holding or handling Category A pathogens (paragraph 173).

5. Category A laboratories should be subject to annual review and should notify DHSS immediately of any significant changes in their staff, facilities or work programmes (paragraph 180).

The World Health Organisation

6. WHO should maintain a close liaison with the responsible government authority regarding its dealings with Category A pathogen laboratories, and in particular with regard to the safety of those laboratories (paragraph 199).

The University of Birmingham

7. Birmingham University should carry out regular safety inspections of Departments handling micro-organisms (paragraph 222).

8. Birmingham University should reconstitute the composition of their Committee for the Control of Pathogenic Organisms and Inspection Materials to include representatives of other University staff (paragraph 224).

9. Birmingham University (and other institutions) should ensure that all dealings with outside bodies concerning work with safety implications in their Departments are monitored by the central administration of the institution rather than handled on a private basis by the Heads of the Departments concerned or by other individuals (paragraph 225).

10. The University should review its policy for ensuring that proper instruction in laboratory techniques and safety precautions is given to all laboratory staff before they are allowed to begin work on pathogenic organisms and to ensure that the staff are not permitted to carry out such work without appropriate arrangements for supervision (paragraph 226).

The holding of Smallpox Virus

11. The remaining smallpox laboratory in the United Kingdom, at St. Mary's Hospital Medical School, London, should no longer remain in a densely populated part of London. It should be re-sited in a place where facilities for containment are stringent and where the number of staff who have to be regarded as potential contacts would be smaller than in a Medical School (paragraph 183).

We would like to put on record our appreciation of the work done for this investigation by our two Secretaries, Dr. Desmond Robinson and Mr. Owen Thorpe. Their sustained labours and unfailing good humour have been much appreciated by all of us. It is only by their total commitment that the Committee has been able to deal with the very large amount of information that had to be collected and studied in the short time since it was constituted.

We would also like to record our thanks to Mrs. Mary Moorat who throughout the investigation has dealt most expeditiously with the considerable amount of paper work it generated.

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C. C. Booth
David Evans
J. R. McDonald
D. A. J. Tyrrell
Robert Williams
E. J. Morris
R. Owen*

18th December 1978

*(Secretaries)
D. L. H. Robinson
O. C. L. Thorpe*

APPENDIX 1

BIRMINGHAM SOURCE OF INFECTION COMMITTEE

The first and only meeting of the Committee was held on 28th August 1978, shortly before the Ministerial Investigation was set up. The Committee's information is given below.

I. Source of Infection Committee

Preliminary Report

The Source of Infection Committee held its first meeting on Monday, 28th August 1978, at 10.30 hours. The members were: Professor H. S. Bedson, Professor M. R. W. Brown, Dr. A. B. Christie (Chairman), Dr. E. Lowbury and Dr. G. Skinner.

The purpose of the committee was to enquire into and try to establish the source of infection of the patient Mrs. Janet Parker.

Members felt there were three main possibilities:

1. That virus spread from the smallpox laboratory to the Anatomy Department either—
 - (a) on an air current from the smallpox laboratory to the photography section of the Anatomy Department, or
 - (b) by direct physical spread on persons.
2. That Mrs. Parker was infected by a missed case in either the Anatomy Department or the Microbiology Department. Such a missed case would have been a patient ill during the last few days of July.
3. That Mrs. Parker might in her photography work have handled material (e.g. slides) from the Medical Microbiology Department.

The committee understood that Mrs. Parker had not been abroad and they assumed that the possibility of contact with people from abroad had been investigated thoroughly and that there was no such contact.

The Medical Microbiology Department

1. Professor Bedson answered many questions regarding the work of the department. Work on smallpox virus had been done on most days during July. During the last week of July Professor Bedson was working with *variola major* virus. There had been no change in the nature of the work and no change in personnel for several months, nor was any unusual incident known to have occurred.

Because the question of photographic procedures had been raised, Professor Bedson described in some detail the process of disrupting virus particles into their constituent polypeptides and subsequent autoradiography. Professor Brown suggested that there is a very slight risk that not all particles would be rendered non-infectious and that therefore infectious aerosol conditions might be caused. Professor Bedson agreed and the committee accepted that there were

other procedures which could result in aerosols of infectious particles. But this was a hazard of every laboratory and this was one of the reasons for special precautions.

The pox laboratory consists of two rooms: an outer, where various pox viruses are handled and used smallpox virus is stored or incubated, and an inner room where smallpox virus is handled and where all processes other than storage or incubation are carried out. There are strict security measures in both rooms.

The smallpox laboratory is ventilated through vents in the door between the inner and outer room. There is no ventilation through windows. The safety cabinet connects through a filter with the outside air and there is negative pressure from the room to the cabinet. The air-flow has been intermittently checked and is adequate. The safety cabinet is not in operation all day or for prolonged periods, but only when work is in progress. Surfaces in the inner room have been intermittently checked for virus contamination and these tests have always been negative. The air-flow as checked by anemometer was 150 linear feet per minute.

There is a portable Baird & Tatlock autoclave in the inner room for materials and articles contaminated or liable to be contaminated—for example white coats, towels, waste paper, etc. Glassware, pipettes, petri dishes and the like are chemically treated.

When smallpox virus is taken from the inner to the outer room for incubation or storage the door of the outer room is locked.

The laboratory was visited by the Inspectorate of the Dangerous Pathogens Advisory Committee in 1976 and subsequently approved by the DHSS for continued work with variola viruses.

The laboratory was visited in May 1978 by the WHO Inspectorate. A first letter from WHO contained certain recommendations and those have been adopted by Professor Bedson. A second letter was received by Professor Bedson only on 23rd August—it refers to the lack of provision of showering, to the lack of containment in the outer room and also asks for further information about the safety cabinet.

When asked if he considered the safety procedures in the laboratory to be adequate, Professor Bedson replied that had he been asked the question one week earlier (i.e. before the diagnosis of smallpox on 24th August) he would have said that he regarded them as adequate.

Ideally of course a purpose-built unit would have been desirable but there was no question of providing this as the decision to cease variola work at the end of 1978 had already been taken.

For comment on physical contact between the anatomy and microbiology departments see afternoon session.

2. A register of all illness is kept of the staff of the department. Five members of staff had been off duty through illness at the end of July. Three of these had had "colds", one had menopausal symptoms and the fifth was suffering from the vomiting of pregnancy. These illnesses had occurred between 21st July and 1st August. The committee felt that these five members of staff should be interviewed and examined as soon as possible.

Two cleaners are employed in the department. They enter the outer but not the inner smallpox room. They work only in the Microbiology Department.

3. Mrs. Parker did no photographic work for the department. Professor Bedson said that there were doubtless slides of smallpox virus in the department but that they did not leave the department under any circumstances.

The committee discussed the possibility of aerial spread from the inner room, through the vent of the safety cabinet and into the photography room of the Anatomy Department.

The committee were aware that in the 1966 outbreak of *variola minor* a photographer working in the same room as Mrs. Parker had caught the disease and that he may indeed have been the first case. They considered the possibility of virus persisting in the room from 1966 to 1978. Dr. Skinner said he understood that there had been some "spring-cleaning" in the Department of Anatomy and wondered whether dust from books etc. containing virus might have been disturbed. The committee was of course aware that the outbreak in 1966 was of *variola minor*, this of 1978 is of *variola major*. Professor Downie and Dr. A. K. MacRae visited the laboratory by invitation at this time and made proposals about centrifuging procedures which were adopted and suggested no major changes in the way in which the work was carried out.

This ended the discussion of the morning session. The second meeting would be held at 14.30 hours at the University, when Professor Kevin McCarthy of Liverpool would be present.

II. The second meeting of the Source of Infection Committee was held at the University at 14.30 hours when Professor Bedson, Professor Brown, Dr. Christie, Dr. Lowbury and Professor McCarthy were present. The afternoon was spent studying the courtyard, the photography section of the Anatomy Department and the smallpox laboratory. Mr. Steer, the Safety Officer of the Anatomy Department, accompanied us.

1. The Courtyard

On the external wall of the smallpox laboratory there is a short extract duct—a blue metal tube about 18" long. This is on the first floor of the building housing the Medical Microbiology and Anatomy Departments, and is the third room from the near end of the building. The window of the photography section of the anatomy room is on the second floor of the building at the far end of the wall where there is a right-angled corner. ("Near" and "far" as applied to us as spectators.) The distance might be about 15 yards.

The inner room of the smallpox laboratory has no opening window: it is ventilated through the door from the outer room. Above the false ceiling of the inner smallpox room there is provision via a vent duct and from the ventilation from outside the tissue culture room which opens off the outer room. The outer room of the pox laboratory is ventilated by windows which open but are protected by fine gauge mesh against the ingress of insects etc.

The photography section of the Anatomy Department has windows which open and which are often wide open. The windows of the rooms on the anatomy floor, except the photography room and the one next to it, have two-way

ventilators. On a platform on the "near" side of the laboratory extract duct there is a very large ventilation extract duct, which extracts air from the Anatomy/Microbiology Building and pumps it with considerable force into the courtyard.

We observed pieces of fluff floating in the air of the courtyard. They drifted away from the Anatomy/Microbiology Department diagonally across the courtyard, i.e. away from the photography window. We noticed however a small green plant on a platform lower than this big duct and a short distance on the far side from the laboratory duct: it was fluttering in a different breeze and there was obviously some turbulence in the courtyard.

The only opening into this square courtyard is through a relatively narrow gateway. The courtyard might therefore not be greatly influenced directly by the wind outside, but wind blowing across the top of the courtyard would probably suck air out of the courtyard, or cause wind currents in the courtyard. Whether this would draw air towards the photography window we do not know.

One point may be important, as will be related later, air is intentionally sucked into the photography room in order to ventilate the dark room.

2. The Photography Section of the Anatomy Department

This consists of two rooms: an outer room which has windows which open to the courtyard but which has no fan ventilation; and an inner dark room which has no windows at all. There is a fan ventilator in this room high up on the far wall; this expels air into a duct in the far corridor. This is a two-way fan but we were told it was always operated as an extractor fan. In its action it sucks air from the outer room. By using a piece of fluff we were able to see that there is a fairly strong current of air from the outer to the inner room and some turbulence in the inner room. There is also an air conditioner in this room, but it is a self-contained air-exchange unit not connecting with the outside air in any way. It may add to currents and turbulence.

The room did not look as if it had recently undergone major "spring-cleaning" and this may not have taken place in this part of the Anatomy Department.

3a. The Medical Microbiology Department

The inner and the outer rooms of the pox virus section are as already described. We saw the incubators and the freezer and we looked through the window of the door into the inner room. Professor McCarthy suggested that the temperatures of the incubators should be checked: there is a difference of only 0.8°C between criteria temperature for *variola minor* and *major*. We discussed the possibility of "typing" strains of *variola major*. Professor Bedson and Professor McCarthy agreed that this was at present a difficult area technically. The strain isolated from Mrs. Parker can be kept frozen and, if necessary, this matter could be discussed later.

We discussed the efficiency of the filter of the safety cabinet and we decided that a test should be carried out. Dr. Hutchison was contacted and he agreed to carry out a test with phage on Wednesday morning, 30th August. The phage used will have a diameter half that of *variola* virus. If it does not pass through

then *variola* virus certainly could not. If it passes, then we would have to stage further tests.

3b. Physical contact between the Departments

During the afternoon we interviewed Dr. A. Buchan of the Medical Microbiology Department. He informed us that he frequently visited the Anatomy Department. He works in the Herpes section of the Microbiology Department and has access to the outer but not the inner room of the pox virus Department. He said that in connection with autoradiography work he visited the Anatomy Department and took with him some apparatus used in the Medical Microbiology Department. There is a 1 in 5 chance that one piece of apparatus could have been used in the Pox Laboratory. Mrs. Parker was interested in this work but there would have been no need for her to come in contact with the equipment from the Medical Microbiology Department. Material would have been taken to her from it for photography. The equipment taken from the Medical Microbiology Department had been treated with SDS, a powerful detergent, and Professor Bedson and Professor McCarthy agreed that there was little chance of virus surviving this treatment. Professor Bedson later went into detail about this procedure and the Committee accepted his view that this was a highly unlikely source of infection.

This concluded the afternoon session. We agreed to meet on Tuesday 29th August. Professor McCarthy would not be able to attend but could be contacted by telephone.

Statements given to Source of Infection Committee and previous emergency committee meetings.

STATEMENT BY DR. GEDDES

At 7.30 p.m. on Thursday, 24th August 1978 I was telephoned by Professor H. V. Morgan, Duty Consultant Physician, Department of Communicable and Tropical Disease, East Birmingham Hospital, who invited me to come to East Birmingham Hospital to see a case of suspected smallpox. The patient, Mrs. Janet Parker, a 40-year-old married lady who works as a Medical Photographer in the Department of Anatomy at the Medical School, University of Birmingham, had been admitted to a single isolation cubicle in Ward 32 at East Birmingham Hospital at 3.00 p.m. on the afternoon of Thursday, 24th August. Her illness had started 12 days previously with influenzal symptoms, notably headache and myalgia. She went to work at the Medical School on the first day of her illness and thereafter remained either at her home or at that of her parents, to which she was transferred in her father's car on 21st August. On the third day of her illness she developed "spots" on her limbs, trunk and face and was visited on 15th August by her GP, Dr. L. E. Arundel, who prescribed an antibiotic. Two days later she was seen at home by Dr. Arundel's partner, Dr. G. M. Horry, who altered the medication. She remained unwell with further lesions developing on trunk, face and limbs and on the afternoon of Thursday 24th was visited by her parents' GP, Dr. A. R. Price, who referred her to hospital with a diagnosis of Rash and Fever.

Mrs. Parker was last vaccinated against smallpox in 1966 and gave a history of chicken pox in childhood. Her occupation as a Medical Photographer in the

Anatomy Department at the Medical School principally involves micro-photography of fixed slides and during the past two months she has not been in contact with unfixed tissue or with primates. She had not travelled abroad during the past year.

On examination the patient was febrile and complaining of aching in her limbs but fully conscious and lucid. Her temperature was 101°F. There was a generalised vesicular/pustular eruption on all areas of skin including palms of hands and soles of feet. Lesions were principally round with surrounding erythema. The rash was semi-confluent on the face.

I took specimens of fluid from three vesicles and took them to the Smallpox Laboratory at the Medical School where Professor Bedson undertook virological examination of the specimens.

Under electron microscopy he demonstrated brick-shaped particles which were highly suggestive of pox viruses. I immediately telephoned Dr. W. Nicol, Area Medical Officer, Birmingham Area Health Authority (Teaching) and arranged to meet him at East Birmingham Hospital. I also spoke on the telephone to Professor Morgan, who had already made provisional arrangements for the opening of the smallpox hospital at Catherine-de-Barnes.

On return to East Birmingham Hospital I met Dr. Nicol and we were joined by Dr. S. Bakhshi, Medical Officer of Environmental Health together with Professor Morgan, Dr. J. G. P. Hutchison, Director, Public Health Laboratory and Mr. R. B. Payne, Hospital Administrator, East Birmingham Hospital. Arrangements were made to set up an Emergency Committee comprising Mr. Payne, Dr. J. A. Innes, Consultant in Communicable Diseases, a Senior Nursing Officer and Dr. Bakhshi, who was designated Outbreaks Liaison Officer.

At approximately 10.00 p.m. Mrs. Parker was transferred by Smallpox Ambulance to Catherine-de-Barnes Hospital. She was accompanied in the ambulance by the bedding from her cubicle in Ward 32 and terminal disinfection of the room and ward lift with formaldehyde was arranged by Dr. Ian Farrell. Discussions then took place regarding contact listing and vaccination (see Attached List). The husband of Mrs. Parker was telephoned by Dr. Nicol, who made arrangements for him to remain at his wife's parents' house. Dr. M. J. Khetani, Clinical Medical Officer, Birmingham AHA(T), went to the house at 11.00 p.m. on the evening of Thursday, 24th August and vaccinated Mr. Parker and his wife's parents. He placed these three contacts in quarantine and obtained a detailed history regarding visits to the two houses during Mrs. Parker's illness. She had been visited by two neighbours, Mr. and Mrs. Rowley of 11 Burford Park Road and also Mrs. Allen, Mrs. Parker's mother's sister. Other visitors to the house were Mrs. Parker's GP, Dr. Arundel (16th Aug.) and his partner Dr. Horry (18th Aug.). The parents' GP, Dr. Price, visited once on the day of the patient's admission to East Birmingham Hospital.*

At 10.00 p.m. on Thursday 24th August Dr. Nicol decided to close East Birmingham Hospital to all admissions and to minimise any movement to or from the two-ward block containing wards 31 and 32. The Emergency Committee was instructed to obtain a list of the names of all patients, staff and patients' visitors who had at any time been in Ward 32 and also Ward 31 during the period of approximately seven hours when Mrs. Parker was in East Birmingham Hospital

The Committee was requested to offer immunisation to all of those people, making sure that parents' permission was obtained in the case of children (Ward 31 is a children's ward and is immediately below Ward 32).

Dr. J. G. P. Hutchison confirmed that his laboratory had 60,000 vials of smallpox vaccine sufficient to immunise 180,000 people.

On the morning of Friday 25th August the Emergency Committee met at 9.00 a.m. at East Birmingham Hospital and interviewed the medical and nursing staff directly concerned with Mrs. Parker's admission to East Birmingham Hospital. They were instructed to ascertain that all the guidelines laid down in the Memorandum on the Control of Outbreaks of Smallpox were adhered to.

At 10.00 a.m. on Thursday, 25th August a meeting took place in Dr. Nicol's office between Professor H. S. Bedson, Mr. H. T. Mitchell, Mr. R. Redgate, Dr. Geddes and Dr. Nicol and was followed by a Press Conference in the Conference Room where the press were given all available information regarding the case.

This was followed by a further meeting in Dr. Nicol's office where a discussion took place regarding details of tracing contacts and vaccination including contacts at Mrs. Parker's place of work, her home and that of her parents including the visiting GP's and also East Birmingham Hospital contacts. Dr. Arundel and Dr. Horry were placed in quarantine at home to be visited by members of staff of the Public Health Department.

Hyperimmune anti-vaccinal gamma-globulin and methisazone was given on the afternoon of Thursday 24th August to all close contacts (see Attached List*).

MOVEMENTS OF PATIENT

10th August (first day of symptoms)	A. MEDICAL SCHOOL own car
	B. HOME (1) (own) father's car
21st August	HOME (2) (parents') ordinary ambulance
24th August	C. EBH WARD 32 smallpox ambulance
24th August	D. CATHERINE-DE-BARNES HOSPITAL

At 2.00 p.m. on Friday, 25th August, Dr. W. Nicol and myself met the Dean of the Faculty of Medicine, Professor Brodie Hughes, at the Medical School. The Dean was informed of the events to date and agreed to vaccination of all members of the staff of the Department of Anatomy. Close contacts of the patient would be identified and given gamma-globulin and possibly also methisazone. The Dean agreed that all work should cease in the Smallpox Laboratory and, after discussion with Professor Bedson who had joined the meeting, it was agreed that further specimens for smallpox diagnosis should be sent to the Central Public Health Laboratory at Colindale, London.

Accompanied by Professor Bedson and the Dean, together with Mr. Hill, Administrator of the Department of Anatomy, we visited the area of the Department in which Mrs. Parker worked. This proved to be a room at the end of the corridor in the corner of the block, facing a courtyard. Leading off this room was a dark room with an Xpelair fan and other piece of equipment which appeared to be an air-conditioning unit. The dark room itself had no windows. We then visited the courtyard and noted an extract duct—a blue piece of metal tubing approximately 18" long, which was situated a third of the way up the wall of the building at approximately 40' from the room in which the patient worked. Adjacent to this duct, which came from the smallpox laboratory and distal to the aforementioned room, was a large, extremely powerful ventilation extract duct, pumping air into the quadrangle.

The two rooms in which Mrs. Parker worked were then locked and arrangements made for them to be fumigated.

All available members of the staff of the Department of Anatomy were to be vaccinated later on the afternoon of 25th August and arrangements made to trace several members not on duty. Particular care would be taken to trace a close contact of Mrs. Parker's who was said to be on holiday with his parents in Ilkeston, Derbyshire.

Dr. Nicol discussed with the Dean the matter of setting up a Committee of Inquiry into the possible origin of this infection. This committee will look into the siting of the Smallpox Reference Laboratory and its relationship to the Department of Anatomy.

** = not reproduced.*

Proposed Action

1. Classification of Contacts—as given in the Memorandum on the Control of Outbreaks of Smallpox—pages 12 and 13.
2. Human antivaccinial immuno-globulin and methisazone to be given to all household contacts including GPs (Dr. Arundel and Dr. Horry) by Dr. Bakhshi. Also to close contacts at East Birmingham Hospital not vaccinated in previous five years. Methisazone should be given *after vaccination*.
3. If contacts develop pyrexia, headache, sore throat, nausea, vomiting or skin rash while in quarantine, urgent consideration must be given to their admission to Catherine-de-Barnes Hospital.
4. Surveillance of Category A contacts including medical, ambulance and public health staff—16 clear days after last possible date of exposure.
5. Quarantine—household contacts only.
6. Terminal disinfection of cubicle in hospital, ambulances and homes—Environmental Health Department to arrange.
7. East Birmingham Hospital—re-open on morning of Friday 25th August but keep wards 31 and 32 closed.
8. Laboratory at East Birmingham Hospital—specimens sent on 24th August 1978. Dr. Flewett to investigate and vaccinate contacts.
9. Action at the University of Birmingham. Dr. Nicol and Dr. Geddes to visit.

10. Further meeting 11.00 a.m. at AHA(T) on Saturday 26th August—check lists to be arranged.

A meeting took place at 11.00 a.m. on Saturday, 26th August 1978, at the headquarters of Birmingham Area Health Authority (Teaching). The meeting was chaired by Dr. W. Nicol. Others present included: Dr. S. Bakhshi, Dr. A. M. Geddes, Professor H. S. Bedson, Dr. J. A. Innes, Dr. N. S. Galbraith (representing the Public Health Laboratory Service), Mr. J. Clayton (PRO), Mr. H. T. Mitchell (Environmental Department), Mr. R. Redgate (Environmental Department) and Dr. P. Walker (RHA).

Dr. Geddes started by giving a detailed account of the present position regarding the case of smallpox. A discussion took place on tracing contacts, their surveillance and quarantine, if indicated, and vaccination. The matter was discussed under three headings:

1. The Medical School.
2. The two houses in which the patient had lived during her illness.
3. East Birmingham Hospital.

Dr. Bakhshi spoke on items 1 and 2 and Dr. Innes on item 3. Information was exchanged regarding uncontacted or unvaccinated contacts and it was agreed to establish a Central Records Department with full clerical support to maintain a record of contacts and their vaccination. Anxiety was expressed about two contacts from the Department of Anatomy who are at present abroad, one in the USA and another in West Germany. Dr. Galbraith undertook to pass the information to the appropriate overseas authorities.

With regard to wards 31 and 32 at East Birmingham Hospital, the following decisions were made:

Ward 31

- (a) discharges to proceed in a normal manner
- (b) all children to be vaccinated apart from two in whom it is medically contra-indicated (one eczema and one on steroids)
- (c) normal visiting to be allowed
- (d) ward to be re-opened for admission on Monday 28th August.

Ward 32

- (a) all patients to be vaccinated, including two compromised hosts, who will also be given gamma globulin.
- (b) discharges to be allowed—patients to return on Wednesday 31st August, to have vaccinations read.
- (c) ward to re-open for admissions on Friday 1st September.
- (d) infected cubicle to remain closed and sealed (has been fumigated twice).

All discharges from both wards to be notified to Dr. Bakhshi.

Professor Bedson stated that he hoped to have final virological confirmation of diagnosis on the morning of Sunday, 27th August.

Dr. Galbraith offered to arrange for 2 or 3 community physicians to be seconded to BAHA(T) to assist with epidemiology. He also confirmed that the Central Public Health Laboratory at Colindale would provide facilities for virological confirmation of diagnosis.

A further meeting has been arranged for 11.00 a.m. on Sunday, 27th August.

APPENDIX 2

SAFETY IN THE SMALLPOX LABORATORY

Safety recommendations pertaining to the Department of Medical Microbiology at Birmingham University were contained in a "Departmental Information Book". The special precautions involved in the handling of smallpox viruses were the subject of a document drawn up for the information and guidance of the staff of the smallpox laboratory.

THE HANDLING OF SMALLPOX VIRUSES IN THE DEPARTMENT OF VIROLOGY, UNIVERSITY OF BIRMINGHAM

Smallpox viruses and related poxviruses are worked with in EG. 34 and EG. 34(b) for diagnosis and reference and for research directed at extending the basis of identification of unknown viruses related to smallpox virus. Work with smallpox virus itself is restricted to EG. 34(b). The outer laboratory (EG. 34) is used for work relating to poxviruses and for servicing the inner smallpox laboratory.

The safety of this work depends upon:—

1. Vaccination and regular revaccination of all concerned.
2. Restriction of access to protected individuals.
3. A check on illness occurring in Departmental staff.
4. Containment of the virus while it is being handled.

Information about the first three of these is contained in the Departmental Information Book and only repeated here in outline. The fourth requires careful forethought and planning in experimental work, the highest standards of technique and strict attention to detail, particularly in the matter of disposal of infected items. This applies to *all* those working in EG. 34 whether or not they are working with smallpox virus.

1. Vaccination

Vaccinations and the results of inspection for "take" are recorded by Dr. Bedson. Those working in EG. 34 and EG. 34(b) are revaccinated each year, all others in the Department, including special cleaners, are revaccinated at 2-year intervals. The University Maintenance Staff, Security Staff, Medical School porters and service engineers of outside contractors are likewise revaccinated at 2-year intervals. Vaccination is offered to those working in departments elsewhere in the Medical School and to the families of the staff of the Department of Virology.

2. Restriction of access

Only those *successfully* vaccinated in the last 2 years are admitted to EG. 34. The vaccination status of visitors must be checked with Dr. Bedson or another

medical member of staff *before* they are allowed into the laboratory. The names and addresses of casual visitors are recorded in the Visitors' Book.

Entrance to EG. 34(b) is restricted to those listed on its door or to those who have express permission from Dr. Bedson or, in his absence, a medical member of staff.

EG. 34(b) is kept locked both in and out of use. EG. 34 and its refrigerators are locked when the room is not in use.

3. Check on illness

At the time of starting work in the Department, all members of staff receive a card for their general practitioner which is intended to be filed with their N.H.S. records. In addition, they carry a card to be shown to their doctor in case of illness and are told of their duty to notify the Department immediately of any absence through illness. A record of the doctors with whom members of the Department are registered is kept in the Departmental Office.

4. Containment

Routine practice for working with pathogenic micro-organisms applies to *all* working within EG. 34 and 34(b), *i.e.*, no mouth pipetting, no eating, drinking or smoking, no licking of labels, immediate attention to spillage and breakage, disinfection of working surfaces after use, wearing of protective clothing properly fastened, washing of hands after practical operations, adequate labelling of experimental material—particularly in incubators and refrigerators, strict adherence to the laboratory drills for discard of infective material.

I. Work with smallpox virus

(a) All open work with smallpox virus is restricted to the safety cabinet within EG. 34(b), *i.e.*, operations such as making dilutions, inoculating and harvesting eggs and tissue cultures, loading and unloading centrifuge vessels, preparing diagnostic specimens. The operation of the safety cabinet ensures that this room is at negative pressure with respect to EG. 34 and the extract fan must be left on for 15 minutes after any period of use.

(b) Those working with smallpox virus within EG. 34(b) wear rear-fastening white gowns quite separate from those worn for work within EG. 34. These are supplemented by disposable plastic "overgowns" and rubber gloves as appropriate. After use disposable clothing and white gowns are placed in separate disposal bags for disinfection by autoclaving.

(c) Infective material is disinfected either by chemical means or by heat before removal from EG. 34(b) to EG. 34. The only exceptions are discarded white gowns which are placed within a disposal bag, removed to EG. 34 and placed in a disposal bag before being autoclaved.

(d) Centrifuge operations with smallpox virus are made in the MSE 25 ultracentrifuge within EG. 34(b). The MSE 25 log book is kept in EG. 34(b) and must not be removed. Centrifuge buckets are disinfected after use by immersion in 10% formaldehyde. Certain low-speed centrifuge operations may be made in EG. 34 using the MSE sealed buckets when these are available.

The operations of loading and sealing and unsealing and unloading must be done only within the safety cabinet in EG. 34(b).

(e) People leaving EG. 34(b) must step with both feet on the tacmat at the entrance to the room.

(f) Notes made within EG. 34(b) must not be removed from the room; where necessary, results can be dictated on the phone to Dr. Bedson's office.

(g) Specimens for storage and incubation are taken to incubators and refrigerators within EG. 34 but not outside this room. The only exception is material to be stored at -70° within the special locked rack in the Cliffco cabinet (EG. 27).

(h) Cleaning within EG. 34(b) is the responsibility of those working in this laboratory.

II. *Work with poxviruses other than smallpox*

(a) This is carried out on the open wall benches in EG.34. The safety cabinet should be used where appropriate and particularly for operations involving ultrasonic disintegration. The centre bench in EG. 34 must not be used for virus work; it is reserved for clean operations such as writing up records, etc.

(b) Those working in EG. 34 must wear white coats. When not in use these are left on pegs in EG. 34(c). Outdoor clothing, etc., may be placed on the pegs in Dr. Bedson's office or kept in lockers outside EG. 34. White coats are changed regularly each Monday, discarded coats being placed in a black disposal bag and autoclaved.

(c) Wastepaper basket contents from EG. 34 are collected daily into a large brown paper bag. Each Friday this is closed by stapling, put in a plastic lining bag and taken to the East Courtyard outside the animal room, whence it is collected and incinerated by the University Services Department.

(d) *Disposal procedures*

Infected pipettes: 10 ml and 1 ml—tall canisters—1% chlorox. 0.2 ml and Pasteur pipettes—separate short canisters—1% stericol (*N.B.* Special care is necessary to see that immersion is total and that the containers are emptied and recharged with disinfectant first thing each day before freshly-infected pipettes are added).

Infected glassware: small bottles in "front" autoclave bucket. Burrells and 500 ml bottles are autoclaved direct. Petri dishes are immersed in 1% chlorox bucket.

Infected disposable material: in "rear" autoclave bucket (these items include papers, plastic syringes, plastic Petri dishes, wee bottles).

Infected tissue culture media and protein-containing fluids: small amounts are aspirated into a reservoir containing neat formalin (sufficient for final dilution 1:20) and held overnight. Suction is applied to the reservoir through a second "trap-vessel" containing 10% formaldehyde. Large amounts are collected directly into a bucket containing formaldehyde and held overnight before disposal via the sink. (*N.B.* Protein-containing fluids must never be put into chlorox for disinfection).

Eggs: Collect in double layer black bags in autoclave bucket and remove to autoclave. Final discard is to the refuse container in East Courtyard.

Clean tissue culture glassware: pipettes are dealt with as if infected; 200 ml medical flats to water + Quix bucket and McCartneys to chlorox bucket in wash-up trolley. Burettes and 500 ml flats are filled with dilute chlorox and placed in the wash-up trolley.

III. *Accident drill*

Coping with accidental spillage or breakage requires the active co-operation of *all* using EG. 34 and its connecting rooms. The area of the accident should be covered with paper towels soaked in disinfectant and time given (30 minutes) for aerosols to settle. During this time, traffic in and out of the room concerned must cease and the door should be kept locked. The area of spillage is then cleaned as described in the Information Book. Dr. Bedson or the Deputy Safety Officer should be informed as soon as possible. It may be necessary temporarily to close the East Ground corridor to traffic. Decisions will also have to be made about total disinfection of the premises, about action in respect of clothing, etc., and about surveillance of individuals for subsequent illness.

APPENDIX 3

In order to identify the virus and establish that the causative organism of Mrs. Parker's infection originated in the Smallpox Laboratory Professor Keith Dumbell of St. Mary's Hospital Medical School London conducted extensive tests.

Report on investigation of viruses isolated from Mrs. Parker by Prof. McCarthy and from Mrs. Whitcomb by Dr. M. S. Pereira

The viruses isolated from Mrs. Parker and Mrs. Whitcomb have, so far, shown no differences in behaviour from each other. For the sake of brevity, they will be referred to in the rest of this report as the "Parker" virus, although all tests have been applied also to the virus isolated from Mrs. Whitcomb.

The Parker virus is a pox virus, antigenically in the vaccinia, variola sub group. On the chick chorioallantois it produces small, white, non-ulcerated pocks, indistinguishable from those produced by variola viruses. Pocks are readily produced at an incubator temperature of 38.25°, and this property excludes alastrim virus. Small doses of Parker virus do not give pocks at 39° and this together with the pock appearance, excludes monkeypox and vaccinia. The Parker virus does show certain properties which the majority of variola major viruses do not share and the next stage in the investigation was to compare Parker virus with various groups of viruses in use in Prof. Bedson's laboratory between 21st July and 2nd August.

The first group taken for comparison was the six hybrids VC 3, 4, 5, 6, 7 and 8. These viruses have been well characterized (Bedson & Dumbell 1964. J. Hyg. Vol. 62 table 1 on p. 149) but their human pathogenicity is, of course, unknown. Parker virus does not produce large, acidophilic cytoplasmic inclusions in CAM. This would exclude VC 3, 4, 6 and 7. Parker virus has a diffusible LS antigen, demonstrated easily by precipitation in gel. This would exclude VC 3, 4, 5, 6 and 7. The failure of Parker virus to produce pocks at 40°C would exclude VC 3, 4, 6 and 7. The pock type of Parker virus would exclude VC 3, 4, 5, 7 and 8. Thus all the VC viruses in use are different from Parker virus by at least one property. This comparison could be extended, but to get a second difference from VC 8 would require either animal inoculation or the co-operation of Dr. Linda Harper.

The next stage was to characterize Parker virus by the tests that I have used for intra species typing of variola strains. Three of these could be applied under the present circumstances of my laboratory. These are:—

- i. the difference in pock titre of virus at 35° and 38.25° expressed logarithmically.*
- ii. the ability of the virus to produce haemadsorption at supra optimal temperature in human diploid cells (MRC 5) expressed as A (complete) B (partial) or C (absent).*
- iii. the ability of the virus to adapt from egg-passed stock to growth in HEp2 cells on the first passage: this ability assessed by the amount of haemagglutinin produced.*

I was informed that the viruses to be considered in the first instance were: Butler and the Harvey, Kuwait 5, Abid, Taj, Jumma, strains of variola major and the whitepox 7255.

Results are shown in tabular form below:—

Virus	titre $\left[\frac{35}{38.3} \right]$	H:Ads group	HEp2 growth
Parker	0.5	A	< 4
Harvey	0.4	A	16
Kuwait 5	N.D	N.D	< 4
Abid	0.3	A	< 4
Jumma	N.D	A	16
Butler	> 3.0	C	< 4
7255	0.2	B	8

Kuwait 5 can be excluded because it lacks the LS antigen and Parker shows this by gel diffusion. Taj has not been included in the tests so far, because it has the same origin and history as Abid. Abid is the only virus in the group examined where no difference from Parker has been detected.

Parker virus was not typical of the majority of variola strains in two respects:—

- i. Its effect on HeLa cell cultures includes significant areas of syncytium though plaques are also produced. The plaques, though, lacked the rounded refractile cells seen with other variola strains and contained, instead, small, flat, clumps of dead, fused cells. The initial effect of most variola strains on HeLa cells is to produce small, hyperplastic foci, which rise above the plane of the monolayer. Plaques are produced at a later stage as central holes within these hyperplastic foci. Two strains of variola are known to give syncytia in HeLa cells. One such was reported by Tsuchiya and Tagaya Arch. Viron. 1972, 59, 292, the other falls within my own experience. In both instances the virus concerned had been passed a large number of times (35, 73) on the CAM.
- ii. Most strains of variola major will produce some pocks on the CAM at 38.5° but none at 39° even when inoculated in large doses. Parker virus, however, has shown some definite pocks on the CAM of eggs incubated at 39°, though this effect was not shown in all eggs.

These two peculiarities of Parker virus are both shown also by Abid virus. It is pertinent at this point to give some account of the origin and history of this strain Abid. Henry Bedson received it from me for inclusion in his tests of the polypeptide spectrum of variola and whitepox viruses. I received it from the smallpox reference laboratory in Moscow, at the same time as Taj. They were said to have been isolated from smallpox patients in Pakistan. Abid being a 3 year old male and Taj, 18 years old, who developed smallpox in February 1970. The material I received was labelled 4th egg pass. I made two egg passes and this material, 6th egg passage was that which was transferred to Birmingham in May 1978. The Abid virus that I have used for the tests described above has been taken from my own stock and from the stock of Abid in the Birmingham laboratory's deep freeze.

These results make it seem reasonable to consider the identification of Parker with Abid (or, possibly Taj), but this interpretation must be taken with some caution. Failure to find differences does not amount to proof of identity, and I do not know how much weight to put on the tests showing similar peculiarities of Abid and Parker. If further assurance of identity between Parker and Abid were required, this could be obtained by polypeptide analysis, using the expertise developed by Dr. Harper at Birmingham or by DNA analysis, using the resources of my own department. Both of these techniques are affected by nearly all or all of the total genetic complement of the virus, whereas biological markers may represent the effects of only a very small fraction of the total virus potential. Each of these investigations would be expensive and time-consuming and I do not propose to undertake them unless compelling reasons develop.

In summary, I can say with confidence that the 'Parker' virus is not vaccinia, monkeypox nor any of the VC hybrids; it is a variola virus.

Within the family of variola viruses, I can say that it is neither the standard alastrim virus strain Butler, nor the alastrim virus which was isolated from the 1966 outbreak in Birmingham and the Midlands. I have also found differences between Parker virus and the Whitepox virus 7255, and between Parker virus and the variola strains Harvey, Kuwait 5 and Jumma. I have found no difference in properties between Parker virus and Abid virus, and in addition, these two viruses share a property which is very uncommon among variola viruses. Thus, of the viruses (excluding Taj) which I understand were in use in the laboratory during the relevant period, Abid is the only one which matches the characters of the virus isolated from Mrs. Parker. The evidence falls short of proof, but in my opinion it is highly likely that Parker and Abid are the same strain of variola virus.

Keith Dumbell

23.XI.78

APPENDIX 4

SAFETY CABINETS

Tests Conducted by Mr. G. J. Harper of MRE Porton

1. The request to carry out these tests was received from Dr. D. L. H. Robinson, Professional Secretary to Professor Shooter's Committee.

2. Tests were limited to measuring the efficiency of the two safety cabinets installed in the Smallpox Reference Laboratory, Birmingham University Medical School. These were done by measuring airflow and by spraying with a Collison atomiser an aqueous suspension of viable spores of *Bacillus globigii* (BG) inside each of the safety cabinets. Air samples were collected near the outlets of the cabinets in the East Courtyard. In addition air samples were collected in the small room (34(b)) referred to in this report as the Smallpox laboratory, used for handling smallpox virus, and in the Main laboratory (see Figure 1).

3. Two air sampling devices, an automatic stepping slit sampler collecting at a rate of 25 litres per minute, and an all-glass cyclone collecting at a rate of ca. 800 litres per minute were used at each sampling station.

4. Control tests to measure any background contamination with BG were carried out by sampling for 10 minutes with the spray in position but not operating before each main test. Each main test lasted 30 minutes. No spraying took place during the first 5 minutes of the test, the spray was then operated for 10 minutes and sampling was continued for 15 minutes after turning off the spray.

5. For the first test the spray was operated in the LEEC cabinet in the Smallpox laboratory, in the second test the spray was operated in the Microflow cabinet in the Main laboratory. During both the tests the air supply to the small room used for handling tissue culture was switched on, and both safety cabinets were switched on. The windows in the Main laboratory were closed as far as was possible. (Note: The windows in this room could not be closed completely). The door between the Smallpox room and the Main laboratory was kept closed except for brief openings when the sampler operator passed from one room to the other. The louvres in the door to the Smallpox laboratory were in the closed position.

6. Air flow measurements were made using an Electronic Direct Reading Anemometer (Airflow Developments Ltd.) at the inlets to both safety cabinets and at the air outlet in the tissue culture room.

7. During both main tests the sampler operator moved freely about in and between both rooms and during the test with the Microflow cabinet in the Main laboratory he deliberately walked across the front of the cabinet whilst the spray was operating. No simulated operations were carried out inside the cabinets during the tests.

8. The arrangement of sampling stations is shown in Figure 1.

Results

9. (a) *Air flow measurements*

- i. *LEEC cabinet.* Type WL2 Serial No. 663 fitted with Microflow Grade HA filter No. HGC-118 200 c.f.m. NaCl penetration less than 0.003%. Size of working aperture $8\frac{1}{2}'' \times 28\frac{1}{2}'' = 1.68 \text{ ft}^2$.

	<i>Air flow ft. per minute</i>		
	<i>Left</i>	<i>Centre</i>	<i>Right</i>
<i>Top</i>	180/185	160/170	175/180
<i>Bottom</i>	170/180	155/160	165/170

- ii. *Microflow cabinet.* No details of type, serial number or filter marked on cabinet. Size of working aperture $11'' \times 31\frac{1}{2}'' = 2.41 \text{ ft}^2$. This cabinet was fitted with an inclined manometer graduated from 0 to 1.0 inches but with the cabinet fan off showed a reading of 0.35 inches. With the fan on the manometer reading was 0.85 inches.

	<i>Air flow ft. per minute</i>		
	<i>Left</i>	<i>Centre</i>	<i>Right</i>
<i>Top</i>	75	70	75
<i>Bottom</i>	80	70	70

- iii. *Air inlet to tissue culture room.* Measured close to the face of the inlet grille near the ceiling. Grille size $8\frac{1}{4}'' \times 14'' = 0.80 \text{ ft}^2$.

	<i>Air flow ft. per minute</i>		
	<i>Left</i>	<i>Centre</i>	<i>Right</i>
<i>Top</i>	210	300	210
<i>Bottom</i>	210	300	210

(b) *Smoke tests*

Smoke liberated in the centre of the floor area of the cabinets flowed strongly towards the air outlets in the ceilings of both cabinets. Brisk movements in front of the Microflow cabinet resulted in smoke being pulled into the room.

(c) *Recoveries of viable BG*

These are summarised in Table 1. Values of <3 colonies for cyclone samplers are based on the absence of BG colonies from plating out 2 ml of a 5 ml sample.

Figures 2 and 3 show the slit sampler plates and the clear association between spraying inside the Microflow cabinet (Test 2) and the recovery of viable BG at the cabinet outlet and inside both the Main laboratory and the Smallpox laboratory.

10. The recovery of, or the failure to recover viable BG from samples collected at the air outlets from the safety cabinets cannot be expressed in terms of percentage penetration because air samples could not be collected directly from the extract trunking. Due to the physical locations of the safety cabinet outlets, approximately 30 feet above ground level, the only access was from scaffolding specially erected for these tests. This arrangement allowed air samples to be collected as close as was practical to the air outlets. A few inches separated the air sampler inlets from the open ends of the safety cabinet outlets. Nevertheless

the emergent air from the cabinets could have been diluted with unknown volumes of outside air. The provision of air sampling ports as recommended in para. 9.3 of the Draft British Standard Specification for Microbiological Safety Cabinets would have saved considerable effort, time and expense and would have yielded more quantifiable results.

Comments on results

11. The air flow through the working aperture of the LEEC cabinet in the Smallpox laboratory was in excess of the minimum recommended by both the Draft British Standard and the Howie Committee*. No viable BG was recovered from the cabinet air outlet when approximately 10^{10} spores were liberated inside the cabinet. No tracer organisms were detected in either the Smallpox laboratory or the Main laboratory when this cabinet was under test.

12. The air flow through the working aperture of the Microflow cabinet in the Main laboratory was about half the minimum recommended value for Class 1 cabinets and viable BG were recovered from the air outlet by two sampling devices. Very heavy contamination of the air in both the Main laboratory and the Smallpox laboratory was found shortly after the start of spraying inside the cabinet and this heavy contamination was still present 15 minutes after turning off the spray inside the cabinet.

13. The recovery of viable BG from the Microflow cabinet outlet could have arisen by penetration through the filter or around the filter, or both. The possibility of leakage from the ill-fitting windows of the Main laboratory (which was heavily contaminated with airborne BG) to the outside air can be discounted. Figure 3 shows that the recovery of viable BG from the cabinet outlet ceased shortly after turning off the spray whereas it was still present inside the Main laboratory at the end of the air sampling some 15 minutes after turning off the spray.

14. Although many variations in ventilation conditions were possible the one tested was decided upon as a result of questioning a member of the Smallpox laboratory staff (Dr. L. Harper), and represented the maximum air movement that could be created in the laboratory suite *i.e.* air flow into the tissue culture room and air flow out, *via* safety cabinets from the Smallpox and the Main laboratories.

15. It is clearly demonstrated that an aerosol generated in the Microflow safety cabinet in the Main laboratory could readily spread within the rest of the laboratory suite. How much further such an aerosol could spread was not investigated. It was intended to carry out air sampling in other areas in the East Wing of the Birmingham University Medical School but such tests were not considered desirable by Professor Shooter's Committee at this stage of their investigations. If further tests on air movements from the Smallpox laboratory to other parts of the East Wing are required these could be similarly carried out.

*Working party to formulate a code of practice for the prevention of infection in clinical laboratories. Jan. 1978.

16. The tests described in this report were carried out on 15th September 1978 by Messrs. G. J. Harper, F. A. Dark and K. Crowe of M.R.E. Porton and were witnessed by Mr. E. J. Morris of the Health and Safety Executive. This report was compiled by G. J. Harper.

G. J. Harper
Aerobiology Section
M.R.E. Porton

Table 1

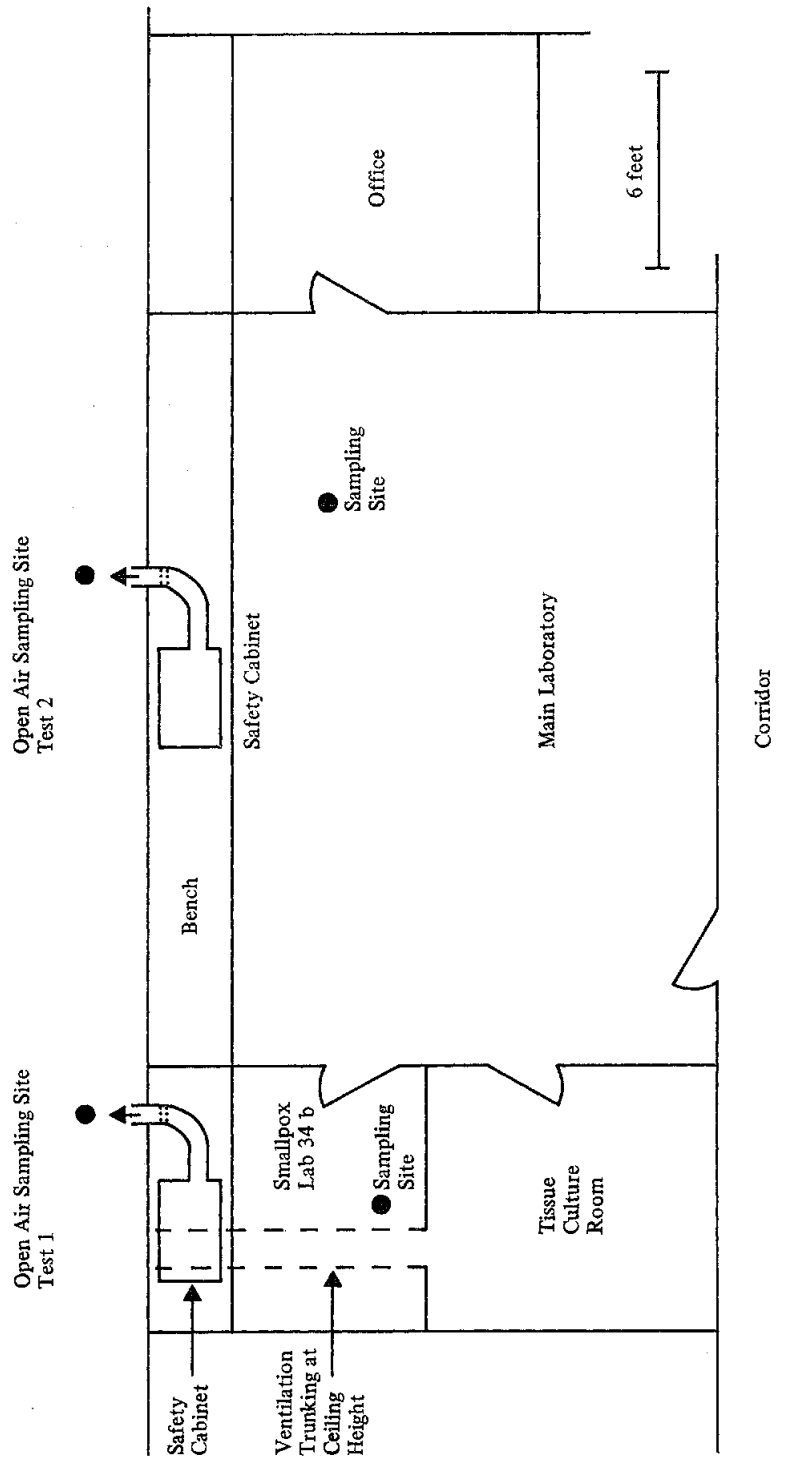
Recovery of viable BG after spraying ca. 1×10^{10} spores into safety cabinets over a 10 minute period

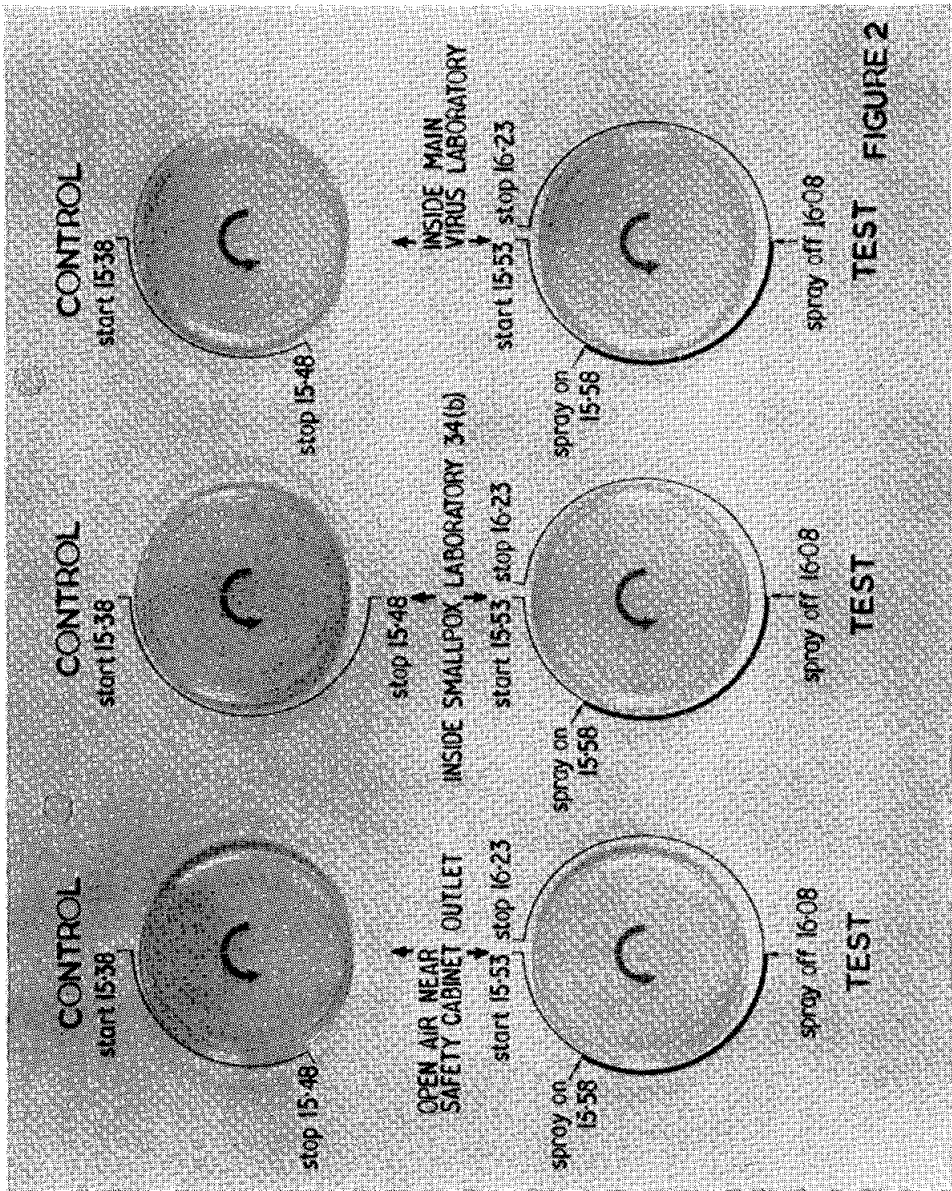
Site of spray	Test	Total BG colonies on slit-sampler plates collecting at 25 litres/minute			Total BG colonies recovered by cyclone samplers collecting at ca. 800 l/minute		
		Cabinet outlet	Smallpox laboratory	Main laboratory	Cabinet outlet	Smallpox laboratory	Main laboratory
LEEC cabinet in Smallpox laboratory	<i>Control 1</i> No spray 10 minutes sampling	0	1	0	<3	<3	<3
	<i>Test 1</i> Spray on 10 minutes 30 minutes sampling	0	1	0	<3	<3	<3
MICRO-FLOW cabinet in Main laboratory	<i>Control 2</i> No spray 10 minutes sampling	0	0	0	3	8	3
	<i>Test 2</i> Spray on 10 minutes 30 minutes sampling	81	TNTC*	TNTC*	9.6×10^2	2.50×10^5	5.25×10^5
Dosages Test 2 Colonies minutes per litre	**	3.2	TNTC*	TNTC*	1.2	313	673

*Colonies too numerous to count.

**Dosage = $\frac{\text{Total colonies recovered}}{\text{Flow rate of sampler in litres per minute}}$

Figure 1. Floor plan of Smallpox Reference Laboratory Birmingham Medical School





TEST FIGURE 2

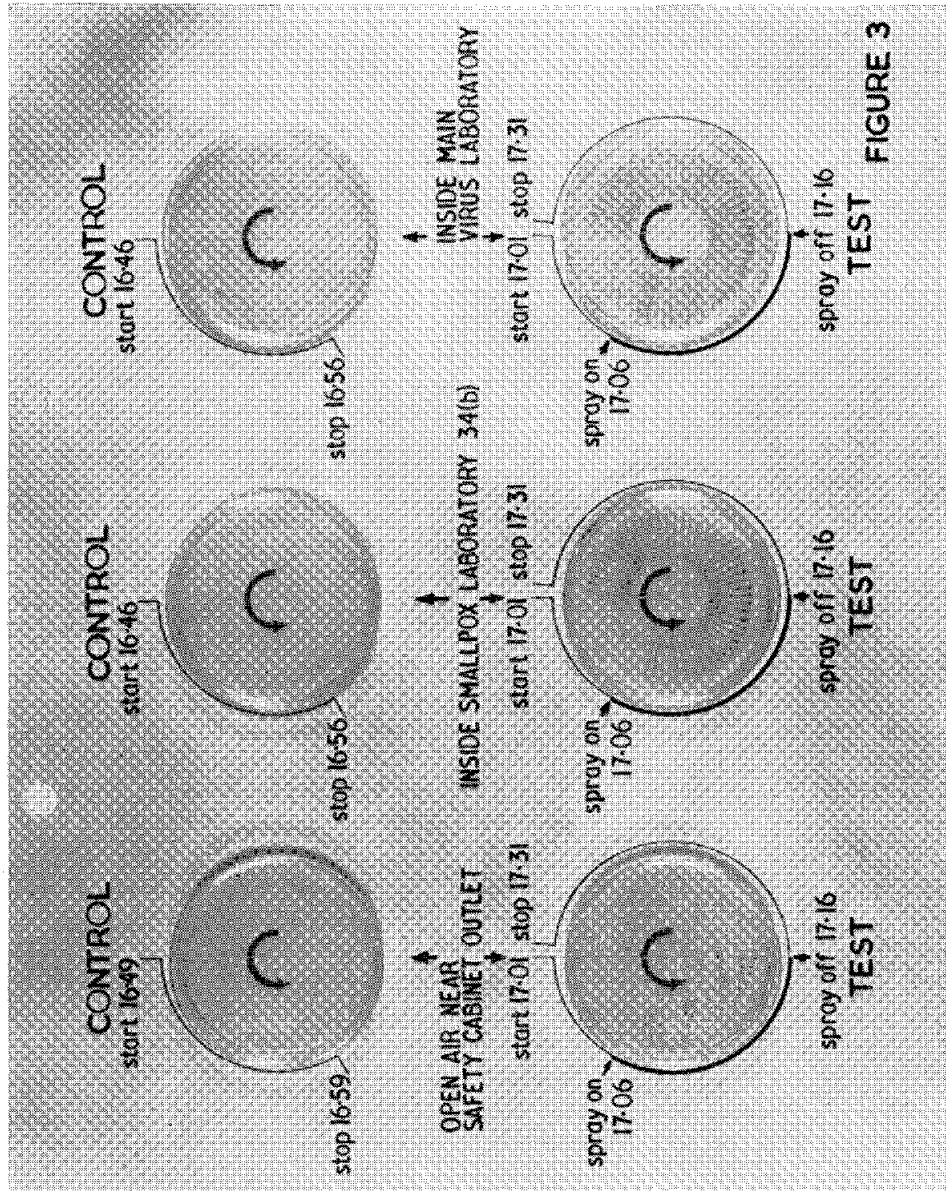


FIGURE 3

APPENDIX 5

Report by M.R.E. Porton on test of two filters removed from microflow cabinet in animal pox laboratory.

TEST CERTIFICATE

These are the test results for the two filters submitted by you to M.R.E. Safety Section for penetration tests.

Filters. Two twelve inch microflow filters both flanged top and bottom.

Origin. A microflow exhaust protective cabinet in Birmingham University Medical School.

Test procedure. The filters were positioned on a test-tunnel and challenged with a monodispersed cloud of bacterial spores whilst air was passed through the filter at the manufacturers' rated flow.

<i>Filter</i>	<i>Test flow rate</i>	<i>Res. (in W.G.)</i>	<i>Upstream Concn.</i>	<i>Downstream Concn.</i>	<i>% Pen.</i>
S569/2	100 CFM	1.00	$2.49 \times 10^6/\text{ft}^3$	4/ft ³	0.00016
S568/2	100 CFM	1.00	$1.94 \times 10^6/\text{ft}^3$	0.3/ft ³	0.000015

Test organism. 1 μm bacterial spores of *B. pumilus*.

Filter gaskets. This test procedure would not show leakage of particles around filter gaskets, and depending on how the filters were installed upon the Cabinet, for instance in a duct, this may occur. We would strongly recommend bedding all gaskets in a silicone rubber sealant upon installation, and if a flanged filter must be used, sealing the joint between the flange and the filter case. We also seal the corner joints on filter cases using the same technique.

Filters should ideally be positioned directly upon the cabinet carcass and not in ductwork allowing the possibility of air by-passing the filter.

S. W. F. Restall
M.R.E. Safety and Hygiene Section

Dr. R. J. C. Harris
Director M.R.E.

APPENDIX 6

As part of the tests on all equipment used by the Smallpox Laboratory an independent test was requested of the efficiency of two autoclaves.

Tests on Autoclaves in Birmingham Medical School

17.10.78

G. Ayliffe and C. E. A. Deverill

Hospital Infection Research Laboratory, Birmingham

Tests were made on two autoclaves to determine their effectiveness in decontaminating typical loads. The cycles were those normally used by laboratory staff.

Tests were made by Mr. C. E. A. Deverill in collaboration with Mr. K. Davies, Quality Control Pharmacist, Regional Sterile Fluids Unit, Mr. J. Barson, Mr. J. England and Mrs. J. Durham of the Birmingham Medical School.

Methods

Temperatures were recorded by thermocouples attached to a Chessell 301 pen recorder No. 051070. Chart speed was two minutes per cm. The accuracy of the system was checked the previous day.

Test Pieces

1. *B. subtilis var globigii* spore—strips (approximately 10^6 spores), produced by Steriseal Ltd.

2. *B. stearothermophilus* spore—strips (approximately 10^6 spores) provided by Southern Group Laboratories.

3. An overnight broth culture of *Str. faecalis* dried in serum on aluminium foil (approx. 10^6 organisms per strip).

B. subtilis spore-strips, tests and controls, were incubated in tryptone soya broth for five days at 37°C and the *B. stearothermophilus* spore strips for five days at 56°C .

Tests on Autoclave 1

A small portable Baird & Tatlock electric autoclave used for decontaminating gowns and other materials in Smallpox laboratory.

Cycle— 117°C (12 psi) for ten minutes.

Load—Two cotton gowns inside a dressings drum.

Tests

Thermocouples and biological test pieces were placed in gowns in the centre of the drum, outside of the drum, and on the base of the drum. Tests were made during two cycles.

Results

Although the load took six minutes of the ten minute cycle to reach 114°C (Chart 1, lead 2), decontamination was obviously effective. The irregularity shown by thermocouple 1 was due to temperature variations at the water air interface during heating. No growth after five days was obtained from four *B. subtilis* spore strips or six *Str. faecalis* exposed during two cycles. The *B. stearothermophilus* spore strips all showed growth in broth at 56°C.

Tests on Autoclave 2

A static laboratory autoclave (item 298) with piped steam supply in room ELG 7. This was used for a second decontamination process of items from the Smallpox laboratory.

Cycle—126°C (20 psi) for thirty minutes.

Load—A winchester and about 80 bijou bottles in a bucket, and a bowl of used culture plates.

Tests

Thermocouples and biological test pieces were placed in the centre of the load, in the chamber drain, and in the steam exhaust.

Results

The temperature of the load rapidly reached sterilizing temperatures (Chart 2, lead 3) in two cycles. No growth after five days incubation was obtained from eight spore strips (four *B. subtilis* and four *B. stearothermophilus*) or six *Str. faecalis* strips.

Comments

Str. faecalis is more resistant to heat than most vegetative organisms and viruses. The smallpox virus is known to be poorly resistant to heat. The killing of *B. subtilis* spores indicated an extra margin of safety in the processes, although a sporidal process was not required. Heat resistant spores (*B. stearothermophilus*) were not killed in the small autoclave, but these are normally used to determine sterilizing efficiency and have no relevance to the killing of smallpox virus. The tests on these two autoclaves indicate that temperatures far in excess of those required to kill smallpox and other viruses were reached in typical loads during two standard cycles with each machine. This was confirmed by biological tests.

Signed G. Ayliffe M.D. F.R.C.Path.

Consultant Microbiologist

APPENDIX 7

*Further tests on Centrifuge and Ventilation in smallpox laboratory complex
carried out by Dr. D. L. H. Robinson*

TEST OF CENTRIFUGE AT SMALLPOX LABORATORY, BIRMINGHAM 27th OCTOBER 1978

Centrifuge

MSE Serial No. 961170 04A 3.64 MkIII Multex. The centrifuge was fitted with a 4 position swing-out rotor. Two 50 ml buckets with 25 ml inserts were fitted.

Smoke Test

Titanium tetrachloride was placed on the rotor. When the centrifuge was operated there was no observable emission of smoke from the hole at the rear of the lid. The lid was opened before the centrifuge had come to a stop. There was no smoke seen in the outer part of the centrifuge. When the lid of the inner casing was removed no smoke was seen in the centrifuge.

Titanium tetrachloride was placed on the top (outside) of the lid of the inner casing.

When the centrifuge was operated, considerable smoke was generated before the centrifuge reached 1,000 rpm and all smoke had been emitted within 15 seconds and before 2,000 rpm had been reached.

The smoke drifted towards the duct and some was drawn up the duct.

The test was done with the office door open or closed. In both cases smoke drifted towards and up the duct. The only real difference was that it was easier to see the smoke with the door open.

Titanium tetrachloride placed on centre knob of inside casing. Smoke was emitted but was not as concentrated as when placed on lid.

VENTILATION TESTS IN SMALLPOX LABORATORY 8th NOVEMBER 1978

1. The LEEC Cabinet

The aperture in the cabinet was 72 cm × 21 cm (28 $\frac{3}{8}$ " × 8 $\frac{1}{2}$ "). Flow rates were measured with an ETA 3,000 anemometer. Fluctuations in flow rates were great and ranged from 20–180 linear feet per minute with the door open and 20–160 linear feet per minute with the door closed.

2. Air flows in the room

(a) Cabinet fan on

Smoke tests in the open doorway revealed a movement of air into the smallpox room at the top and bottom third of the door but across the middle third there was a considerable amount of turbulence. Air movement was in to the duct.

When the door was closed air was drawn into the room via all the apertures around the door and via the covered window. There was a marked positive outflow of air from the duct.

(b) Cabinet fan off

With the door open a flow of air into the room could still be detected. Air was drawn into the duct. With the door closed air was drawn into the room around the edges of the door and there was a marked flow through the louvered window. Air was drawn into the duct.

DR. D. L. H. ROBINSON

13th November 1978

APPENDIX 8

REPORT ON THE TRANSFER OF AIR-BORNE PARTICLES WITHIN THE EAST WING OF THE MEDICAL SCHOOL AT BIRMINGHAM FROM THE SMALLPOX LABORATORY ON THE GROUND FLOOR

By Dr. O. M. Lidwell, with the assistance of Dr. R. P. Clark
and C. A. Mackintosh

General Description

The apparent escape of smallpox virus from the smallpox laboratory leading to an infection in a worker on the floor above raises the question as to whether this could have occurred by transfer of air-borne particles carrying the virus.

The smallpox laboratory is situated on the ground floor in the East Wing of the Medical School. A sketch plan of this part of the building is shown in the figure. The building is naturally ventilated and air movements within it are consequently irregular, dependent on weather conditions and the degree of opening of doors and windows.

Safety Cabinets

There are extract safety cabinets in the Pox Laboratory EG34 and in the Smallpox Laboratory EG34b, which is a small room approximately 2.4×2.7 m opening off the pox laboratory. Tests on these cabinets (1) have shown that the one in EG34b was in good order with adequate extract volume and effective filtration. The safety cabinet in the outer laboratory EG34 was defective in both respects. The small room EG34a adjacent to EG34b has some mechanical input ventilation. There is no air-lock or lobby between EG34b and EG34 and no special sealing arrangements for this door or interlock with the safety cabinet in EG34b. It must therefore be assumed that it is possible for air to be exchanged between EG34b and the outer laboratory and for this air to carry any infected air-borne particles with it. Such particles could also be dispersed in the outer laboratory from clothing, including gowns, contaminated within EG34b as well as from any manipulations in the outer laboratory if these occurred. It is therefore necessary to consider both rooms EG34b and EG34 as possible sources for air-borne dispersal within the building.

There are, of course, innumerable routes by which such transfer might take place. The object of this investigation was to discover if there were any routes capable of transferring significant amounts of dispersed material to places where there might be a risk of infection for susceptible individuals.

Service Ducts

There are four service ducts running vertically through the relevant parts of the building labelled A, B, C, and D on the figure. These run upwards from the roof of the subway carrying the steam supplies to the Medical School and the hospital and pass through the lower-ground, ground and first floors to terminate

in grilles open to the atmosphere in the face of the building within the East Court. At each level there are access panels which make no pretence to be air-tight. Duct A runs through the office EG36 on the ground floor and the laboratory EF30 on the first floor. Duct B has access panels on the ground floor from both the Smallpox laboratory EG34b and from the seminar room EG35 and passes through room EF27 on the first floor. Both these ducts rise from a common subsidiary duct running horizontally out of a corner of the subway just under the roof, the entrance to this duct is blocked with what appears to be a plug of glass wool. Duct C is similarly blocked where it rises from the roof of the subway and is also said to be blocked by a concrete panel across it between the lower-ground and ground floors through which various service pipes pass. The seal is therefore unlikely to be completely effective; this duct then passes through the Pox laboratory EG34. The access panel at this level had been sealed with putty which was broken when the room was examined at an earlier date. However, cracks around the access panels are said to have been present before this took place. Above this the duct passes through room EF26 on the first floor, this room contains a telephone with connection for outside calls. It was not in use as a laboratory and was crammed with equipment and furniture. The only place where it was possible to use the telephone was immediately adjacent to Duct C. Duct D has a larger cross section than the other three ducts. It is not obstructed in any way at its lower end. There are no accessible access panels on the ground floor, on the first floor it passes behind the wall of the dark room EF23a. A ventilation fan is mounted in this wall by means of which air from this duct may be blown into the dark room or, alternatively, air may be extracted from the dark room and discharged into the duct.

Transfer Routes

Air from the smallpox laboratory carrying infected particles could reach the first floor by one or all of four ways. First it could leak out from the laboratory into the corridor and hence, via the stair wells, penetrate into all parts of the building. In the absence of any form of isolation ventilation in the smallpox laboratory group this must happen to some extent. The dilution of any escape will become progressively greater as the distance travelled increases. Second it could pass out through the windows of the Pox laboratory EG34 or be discharged via the safety cabinet in this room through the defective filter. It might then be carried through the air of the East Court and enter open windows on the first floor. Such a mechanism has been postulated as a factor in the spread of smallpox in the Meerschede outbreak in West Germany in 1970 (2). The dilution by such a route is likely to be very great except in unusual circumstances. Third it might pass down one of the service ducts B or C into the subway, pass up duct D and be discharged into the dark room EF23a. This route also would be subject to a very high dilution factor and involves the passage of contaminated air down ducts B and C contrary to the normal uprising air flow caused by the stack effect in a warm building, accentuated in this situation by the large collection of hot steam pipes in the subway and duct. However, momentary, or even frequent, reversal of air flow due to wind gusts, especially at a time when warm weather had minimised the stack effect, is not too improbable.

Fourth, air might be sucked from room EG34 or EG34b into ducts B or C through the cracks or openings in the access panels to these ducts and be

discharged into the room immediately above on the first floor, namely the laboratory EF27 or the room containing the telephone, EF26. Such a route would be short and direct if sufficient air did indeed entrain through the gaps on the ground floor and leak out into these rooms on the first floor. In addition there is a fan in the seminar room EG35, which shares duct C with the smallpox laboratory EG34b. The reduction in pressure caused by running this on extract with the doors closed could suck air into this room directly from EG34b.

Techniques

The possibilities discussed above were explored in two ways, concentrating attention on the third and fourth group of possible routes since it seemed more probable that if a significant transfer did take place in any of these ways it would be greater and occur more consistently than the other possibilities would allow.

The access panels to the ducts and the entry into them from the subway were examined on three separate days, 21st September, 3rd October and 4th October, using titanium chloride smoke to reveal the direction and strength of any air movements. To make a quantitative estimate of the extent of transfer due to the air movement that these smoke tests demonstrated, tracer particles were generated within the smallpox laboratory EG34b and the Pox laboratory EG34 and air samples taken at a variety of sites within the building. These positions are listed in Table 1 and shown in the illustrations. The tracer used was potassium iodide in particles approximately $7 \mu\text{m}$ in diameter generated from an alcoholic solution of the salt by means of a spinning disc (3), (4). The generators could disperse about 3×10^7 such particles per minute and the sampling devices could collect the particles from up to 100 litres of air per minute i.e. about ten times more than the breathing rate of a resting person.

The particles were collected on millipore filters and developed into visible spots, approximately 0.1 mm in diameter, by placing in a 0.1% acid solution of palladium chloride. Development takes only a few seconds and preliminary estimates of the numbers collected can be made immediately and the records are permanent. In order to avoid the possibility that the investigators themselves might transfer smaller or larger numbers of particles on their clothing or in other ways from the smallpox laboratory to the subway or first floors a different person was stationed on each of the three floors and the samples were developed on the floor where they had been collected. Because the air flows are variable in time, dispersal took place over at least 10 minutes, which resulted in challenge doses exceeding 10^8 particles. Experiments in other buildings (4) have shown that transfers over distances up to at least 100 m during periods up to 40–60 minutes can be followed by this method. Since the distances involved in the building did not exceed some tens of metres a total sampling time of 30 minutes was judged adequate. In an investigation of this kind it is sufficient if a positive transfer can be demonstrated, there is no need to find the conditions which inhibit this or to attempt a precise estimate of the magnitude of the transfer, which will, in any case, vary with the circumstances of the day.

Results

A. Smoke tests

Air was drawn into ducts B and C from the smallpox laboratory EG34b and from room EG34 respectively consistently on all three days.

Air was drawn strongly *out* of duct B into the seminar room EG35 when the extract fan in this room was on and the doors closed.

The air flow between duct B and laboratory EF27 on the first floor was irregular. Only on 5th October was any outflow from this duct into the room observed, when outflow and inflow alternated. There was a consistent *outflow* of air from duct C into the lab./telephone room EF26, especially from a hole in the corner at floor level. Occasional reversals of flow were noted and these only on 5th October. No significant air flows could be detected around the entry to ducts A, B and C in the subway. There was a vigorous inflow of outdoor air into this area from grilles at ground level, generated partly by an extract fan and partly by a very vigorous updraught of air into duct D.

B. Particle dispersal tests

The conditions pertaining during the three tests carried out on 4th October are given in Table 1b and the results of the sampling in Table 2.

A number of facts are immediately apparent from an inspection of this table.

1. Dispersal in the smallpox laboratory EG34b leaks out into the Pox laboratory EG34 when the door between the two is open even if the extract safety cabinet is in operation, (experiments I and II).

2. There is substantial leakage from the Pox laboratory EG34 into the corridor outside.

3. When the fan in the seminar room EG35 is working on extract with the doors closed there is considerable transfer into this room. When the fan is off there is only a small amount of transfer which could well have taken place via the corridor.

4. There is appreciable and unequivocal transfer to the lab./telephone room EF26 on the first floor.

5. There is some indication of a small and irregular transfer to laboratory EF27 on the first floor.

6. There is no indication of any measurable transfer to the dark room EF23a via duct D and the input fan to the room.

7. There is some suggestion of a very small transfer to the bottom of duct C in the subway.

It is perhaps useful to express the above results in terms of the inhaled dose for a specified dispersal and this has been done in Table 3. The dose in the seminar room EG35 was of the order of one particle for every 10^6 dispersed if the extract fan was on. That in the corridor on the same floor was about 1/4 of this but was much less when the safety cabinet in the smallpox laboratory EG34b (where dispersal was taking place) was in operation.

The dose in the lab./telephone room EF26 reached about one particle for every 10^7 dispersed when dispersal took place in the Pox laboratory EG34. Elsewhere the doses did not exceed one particle for every 10^9 dispersed.

The figures can alternatively be expressed as a fraction of that in the probable source room, Table 4.

This fraction reached as high as 7,000 ppm in the corridor, relative to the Pox laboratory EG34. It reached as high as 500 ppm in the lab./telephone room EF26 on the first floor, relative to the same source. The same figure was reached in the seminar room EG35 relative to the smallpox laboratory EG34b.

Finally, it is possible, by making a number of assumptions, to deduce the volumes of air transferred between the different rooms. The details of the calculations are given in the appendix. The outflow from the smallpox laboratory EG34b through the open door into the Pox laboratory EG34 was about 100 l.p.m. which fell to 30 l.p.m. when the safety cabinet was in operation. Both these figures are in fact much lower than would be expected for exchange of air across an open door (5). Presumably the very still conditions under which the tests were carried out reduced the exchange. Transfer from the smallpox laboratory EG34b to the seminar room when the extract fan there was in operation and the doors were closed was about 5–10 l.p.m. and that to the lab./telephone room EF26 from the Pox laboratory EF34 between 2 and 5 l.p.m. These figures are the effective transfer. Since there was undoubtedly a great deal of dilution in the ducts the actual flows through the cracks and apertures in the access panels must have been much greater.

Conclusions

These experiments have demonstrated without any doubt that airborne particles can and do escape from the smallpox laboratory and could reach sensitive unrestricted areas. In addition to transfer to the corridor in the Medical Microbiology laboratory and to the seminar room near the entrance to this, there was also readily demonstrable and consistent transfer to the lab./telephone room EF26 on the first floor.

The particles used for the investigation had a settling rate of about 30 cm/min. This is of the same order as that found for many naturally dispersed micro-organisms, both bacteria and viruses. However it is quite possible that dispersal of much smaller particles may occur in some circumstances, especially from cultured materials. In this case the losses by sedimentation would be less and the potential dose transferred for a given dispersal greater. In the calculations, the effects of sedimentation have been taken as $3\times$ those due to ventilation, and this would apply to both the source and receiving rooms. With very small particles the potential dose transferred could then be as much as $10\times$ greater than the values observed with the tracer particles. This difference is comparable to that found in a previous hospital study (4), where the difference between the transfer of gas and the tracer particles varied between 8 and 45 times according to the distance between the source and receiving rooms.

In addition if the person exposed were breathing more heavily the dose received might be two–three times greater again.

The magnitude of these transfers is not large in absolute terms, between about 1 particle per million and 1 per hundred thousand of those dispersed likely to be inhaled by any individual in these places. However, the episode under investigation represents an unusual event and a chance of this order,

which increases in proportion to the numbers dispersed, could easily reach 1 in 100 or more if there was substantial dispersal on any or several occasions.

O. M. Lidwell

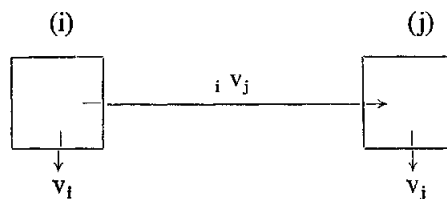
The experimental work necessary for this report was carried out on October 4th and 5th 1978 by Dr. O. M. Lidwell, with the assistance of Dr. R. P. Clark and C. A. Mackintosh. Dr. Clark was also responsible for the illustrations.

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Annex

Calculation of volume transfers



If two spaces, *i* and *j*, are connected so that there is an air flow ${}_i v_j$ from *i* to *j* and there are ventilation losses of v_i and v_j respectively, then the following relationships hold when *n* particles are dispersed in *i* and sampling is continued to completion in both spaces at a rate *r*, assuming that the air within the spaces is effectively mixed.

$$\text{Total particles collected in (i), } n_i = nr / (v_i + {}_i v_j)$$

$$\text{Total particles collected in (j), } n_j = nr \, {}_i v_j / v_j (v_i + {}_i v_j)$$

$$\begin{aligned} \text{Whence } n_j/n_i &= {}_i v_j/v_j \\ \text{or } {}_i v_j &= n_j v_j/n_i \end{aligned} \quad \text{—————(1)}$$

$$\begin{aligned} \text{Also } n_j v_j (v_i + {}_i v_j) &= nr \, {}_i v_j \\ \text{or } {}_i v_j &= n_j v_j v_j / (nr - n_j v_j) \end{aligned} \quad \text{—————(2)}$$

From these two equations it is possible to evaluate n_i and ${}_i v_j$ if *nr*, n_j , v_i and v_j are known or to evaluate ${}_i v_j$ when n_i , n_j and v_j are known.

The values of v_i and v_j in these equations must include sedimentation losses if these are relevant. If the horizontal surfaces within the spaces are A_i and A_j and the particles have a sedimentation velocity *s* then the contribution of sedimentation to the "ventilation" losses is $A_i s$ and $A_j s$.

In the East Wing the ventilation rates were in general unknown, but certainly small, and a value of 2 air changes per hour has been assumed throughout. Since the contribution of sedimentation, at 5 mm/sec, is equivalent to about 6 air changes per hour the exact value assumed for the ventilation rate has only a small effect on the values of v_i and v_j .

The results of this calculation applied to the data are given in Table 5. In this table the values for n_1 are calculated values as are those for ${}_1v_2$, ${}_1v_3$ and ${}_2v_4$. The calculated value for n_2 in experiment III is 3×10^6 which agrees fairly well with the observed value of $>1.7 \times 10^6$.

The calculated ${}_i v_j$ values represent the effective transfer. Since in the East Wing transfer was via ducts with unknown internal air flows there must have been considerable dilution in these and substantially greater volumes passing into and out of the ducts through cracks and gaps in the access panels.

TABLE 1a

Sampling positions, see illustrations, and experimental conditions

Sampling Position

Medical Microbiology Department

Pox Lab. EG34	On bench under window, to left (1) and right (2) of Safety Cabinet.
Corridor	24" above floor level by side of swing barrier close to wall between doors to Pox Lab and Seminar Room.
Seminar Room EG35	(1) ca. 4' above floor near to duct B, (2) on bench to left of this, below extract fan.

Anatomy Department

Laboratory EF27	(1) on bench under window near to duct B, (2) on the bench near to junction with window bench.
Lab./Telephone EF26	(1) on floor under bench near hole in duct C, (2) on bench by telephone above (1).
Studio EF23	On work bench along wall of Dark Room.
Dark Room EF23(a)	On work bench below fan in duct D.

Subway

Entry to duct A and B:	Just below roof in corner
Entry to duct C:	Within 12-18" of duct opening in roof
Entry to duct D:	Below duct opening.

TABLE 1b

<i>Experimental Conditions</i>	<i>Experiment</i>		
	I	II	III
Particle dispersal in:	Smallpox lab EG34b	EG34b	EG34b & EG34
Duration of dispersal	10 minutes	10 minutes	15 minutes
Duration of sampling from start of dispersal	30 minutes	30 minutes	30 minutes
Number of particles dispersed	3×10^8	3×10^8	$5 \times 10^8 + 5 \times 10^8$
Door to Smallpox lab EG34b	Open	Open	Open
Safety Cabinet in Smallpox lab EG34b	Off	On	Off
Extract fan in Seminar Room EG35	On	On	Off
Fan in Dark Room EF23a	Input	Input	Input

All other doors and windows were closed and all other fans, including safety cabinet in EG34, were off throughout.

TABLE 2

Numbers of air-borne tracer particles recovered at various sampling positions

POSITION	<i>Experiment</i>		
	I	II	III
<i>Medical Microbiology Department</i>			
Pox Lab. EG34 (1)	4,890	620	>100,000
(2)	3,800	400	>100,000
Corridor by barrier	540	14	2,920
Seminar Room EG35 (1)	2,774	2,160	20
(2)	3,504	1,782	30
<i>Anatomy Department</i>			
Laboratory EF27 (1)	1	0	18
(2)	0	0	0
Lab./Telephone EF26 (1)	40	5	890
(2)	43	2	760
Studio EF23	0	0	3
Dark Room EF23(a)	0	0	0
<i>Subway</i>			
Entry to ducts A and B	0	0	0
Entry to duct C	7	0	2
Entry to duct D	2	0	0

All samples were taken at 100 l.p.m. except for those in the Pox lab. EG34, which were taken at 6 l.p.m. only.

TABLE 3
Potential Dose received for 10^9 particles dispersed
 (Breathing 10 l.p.m.)

POSITION	<i>Experiment</i>		
	I	II	III
<i>Medical Microbiology Department</i>			
Pox Lab, EG34	2×10^4	2,500	$>1.7 \times 10^5$
Corridor by barrier	280	5	290
Seminar Room, EG35	1,050	660	2.5
<i>Anatomy Department</i>			
Laboratory EF27	<0.5	<0.5	1?
Lab./Telephone EF26	14	1	82
Studio	<0.5	<0.5	0.2?
<i>Subway</i>			
Entry ducts A and B	<0.5	<0.5	<0.2
Entry to duct C	2	<0.5	0.2?
Entry to duct D	1?	<0.5	<0.2

The values given as < represent those corresponding to 1 particle recovered, those marked with a ? are those where 1 or 2 particles only were recovered in the samples.

TABLE 4
Particles recovered as fraction of those in probable source room (p.p.m.)

POSITION	<i>Experiment</i>		
	I	II	III
<i>Medical Microbiology Department</i>			
Pox Lab. EG34	6,800	2,200	—
Corridor by barrier	7,500	1,600	<1,700
Seminar Room EG35	290	510	2
<i>Anatomy Department</i>			
Lab./Telephone EF26	580	410	<480

The figures given for the Pox Lab. EG34 and the Seminar Room EG35 assume that the Smallpox Lab. EG34b was the probable source, those for the Corridor and the Lab./Telephone room EF26 assume the Pox lab. EG34 as the source. The values taken for the Smallpox Lab. EG34b, as a source, are calculated from the numbers of particles dispersed, the floor area of the room and an assumed ventilation rate, see appendix.

TABLE 5.

Calculation of volume transfers (m³/min)

Quantity	<i>Experiment</i>		
	I	II	III
n	3×10^8	3×10^8	$5 \times 10^8 + 5 \times 10^8$
nr	3×10^7	3×10^7	$5 \times 10^7 + 5 \times 10^7$
v_1	2.7	7.6	2.7
v_2	15	15	15
n_2	72,400	8,550	1.7×10^6
n_1	1.07×10^7	3.9×10^6	1.07×10^7
${}_1v_2$	9.8×10^{-2}	3.3×10^{-2}	—
n_3	3,140	1,970	25
v_3	20	20	12
${}_1v_3$	5.9×10^{-3}	10×10^{-3}	3×10^{-5}
n_4	42	3.5	820
v_4	8	8	8
${}_2v_4$	4.6×10^{-3}	3.3×10^{-3}	2.2×10^{-3}

The notation used is that described in the Annex. The subscripts refer as follows:—

1. the Smallpox Lab, EG34b
2. the Pox Lab EG34
3. the Seminar Room EG35
4. the Lab./Telephone Room EF26

Air change rates have been assumed as ca. 2/hr. except for v_1 in experiment II when the safety cabinet extract has been taken as 5.6 m³/min (ca 200 cfm) and for v_3 in experiment I and II when the fan extract in the Seminar room EF35 has been taken as 11 m³/min (350–400 cfm). Loss by sedimentation has been taken as $0.3 \times$ floor area, assuming a particle sedimentation rate of 5 mm/sec.

Figure

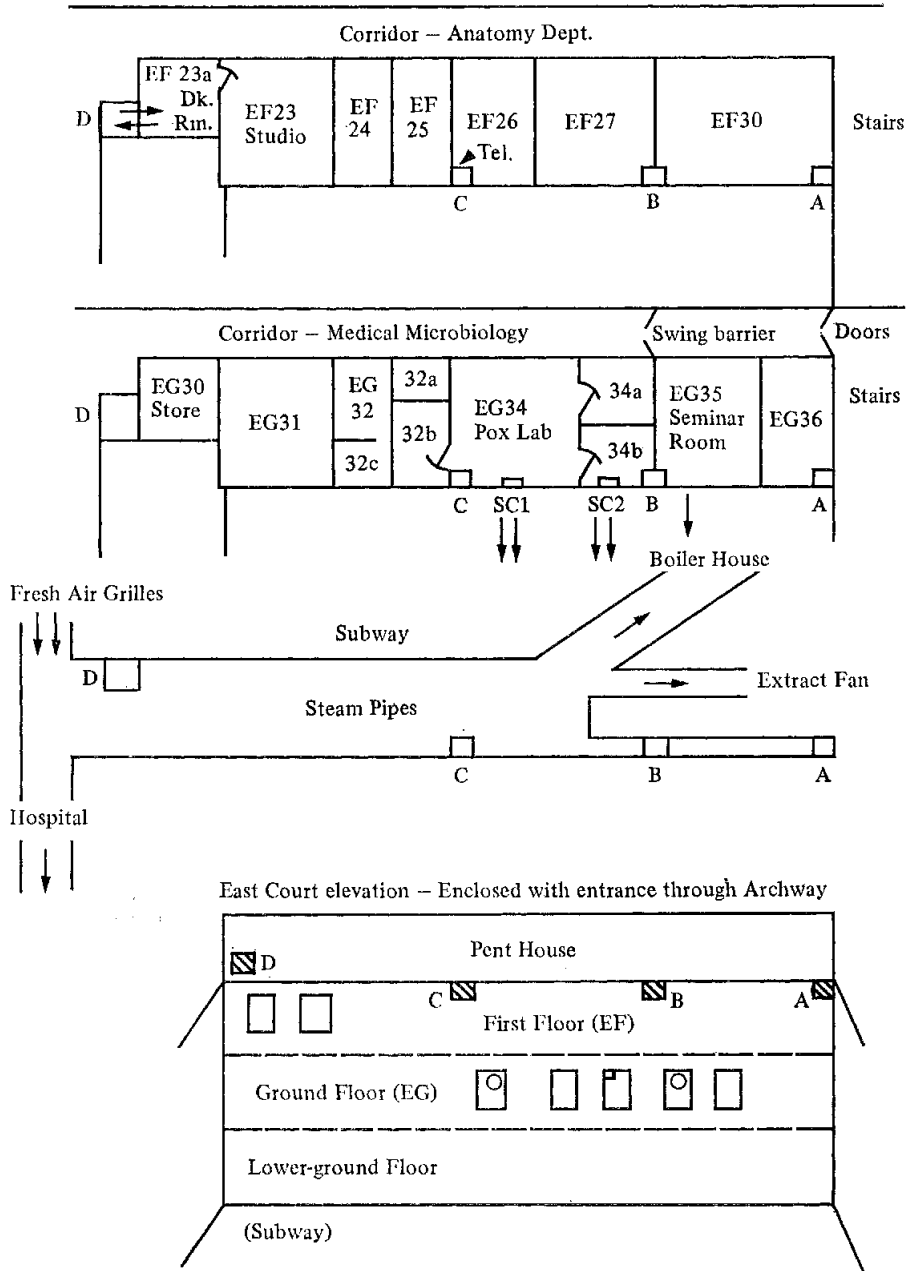
A, B, C, D: the four service ducts running vertically through the building from the subway to discharge grilles about first floor ceiling level.

SC₁, SC₂: the safety cabinets in the Pox lab and the Smallpox lab. The windows shown on the elevation of the buildings facing into the East Court are:—

On the first floor, those of the studio EF23

On the ground floor, from left to right, the two windows of the Pox lab with the discharge from SC₁ shown in the left hand window, the window of the smallpox lab showing the discharge from SC₂ and the two windows of the Seminar Room showing the fan (extract or input) mounted in the left hand window of the pair.

Birmingham University Medical School



Scale 1:375 approx. (Diagrammatic only)

APPENDIX 9

CENTRIFUGES

Report of tests to measure aerosol generation by centrifuges in the Smallpox Reference Laboratory, Birmingham University Medical School

1. Two centrifuges were tested on 23rd October 1978 for aerosol generation *in situ* in rooms 34 and 34(b) of the Smallpox Reference Laboratory. These were:—

- (a) In room 34(b) MSE 25 High Speed Centrifuge.
- (b) In room 34 MSE Super Multex.

2. The request for these tests asked that the centrifuges should be tested in two roles, one, operated normally, and two with a tube breakage. The plastic tubes used in the MSE 25 High Speed Centrifuge could not be broken so another procedure was used. The tubes were centrifuged in the sealed cups with the O ring seals removed. To encourage breakage of the glass screw capped bottles used in the MSE Super Multex Centrifuge the bottles were heavily scored with a glass cutting diamond and a 6 mm diameter steel ball bearing was placed in each of the centrifuge buckets to prevent the bottles sitting snugly on the rubber linings of the buckets.

3. An aqueous suspension of viable spores of *Bacillus subtilis varglobiggi* (BG) concentration 7.5×10^9 per ml was used as the test liquid.

4. Air samples were collected with automatic stepping slit samplers collecting at a rate of 25 litres per minute on to the surface of pre-incubated tryptone agar plates.

- (a) For the tests with the MSE 25 High Speed Centrifuge three samplers were used. One was placed over the lid of the centrifuge, and one at each side of the cabinet. The sampler air intakes were within a few inches of the centrifuge casing.
- (b) For the MSE Super Multex two samplers were used to sample the air a few inches from, and level with, the lid on either side of the casing.

5. The operating conditions for the four tests carried out were:—

Test 1 MSE 25 High Speed Centrifuge. 2×10 ml volumes of BG were placed in open mouthed plastic tubes in sealed buckets with the O ring seals in position. These were then centrifuged at:— temperature 4°C, speed 20,000 rpm, duration of spin 10 minutes.

Test 2 as for Test 1 except that the O ring seals were removed from the buckets before loading.

Test 3 MSE Super Multex Centrifuge. 2×10 ml volumes of BG were placed in screw-capped glass one ounce bottles as normally used in the Smallpox Reference Laboratory. These were then centrifuged at:— speed 3,000 rpm, duration of spin 10 minutes. Inner lid closed.

Test 4 as for Test 3 except that etched bottles were used and a ball-bearing was placed in the bottom of each centrifuge bucket.

6. After loading the centrifuges control air samples were collected for 5 minutes to measure any background contamination with BG before starting the centrifuging cycles. Air sampling was continued for at least 5 minutes after the centrifuges had come to rest and the lids had been opened.

Results

7. The recoveries of BG in the air samples are summarised in Table 1. The very low recoveries recorded in the test runs are indistinguishable from the low level background counts found before starting the centrifuging cycles. The attempt to encourage breaking of the glass bottles used in Test 4 failed as neither of the bottles fractured during the test.

Conclusion

8. In the conditions tested no aerosol generation was detected as a result of centrifuging 1.5×10^{11} BG in either the MSE 25 High Speed Centrifuge or the MSE Super Multex Centrifuge situated in the Smallpox Reference Laboratory, Birmingham University Medical School.

G. J. Harper
 Aerobiology Section
 M.R.E. Porton

Table 1

BG colonies recovered per cubic foot of air sampled during operation of centrifuges containing 1.5×10^{11} BG

Centrifuge	Test	Left side of centrifuge		Over lid of centrifuge		Right side of centrifuge	
		Background	Test	Background	Test	Background	Test
MSE 25 High Speed Room 34(b)	1	0.3	0.5	1.4	0.5	<0.2	<0.2
	2	0.2	0.8	0.3	0.4	0.3	0.1
MSE Super Multex Room 34	3	0.2	0.2	ND	ND	0.7	0.3
	4	0.9	0.7	ND	ND	0.5	0.2

ND Not done.

<0.2 = no BG colonies recovered from 4.4 cubic ft. of air.

APPENDIX 10

THE 1966 OUTBREAK OF SMALLPOX

Since in 1966 and 1978, photographers at the Birmingham Medical School became infected with Smallpox it was necessary to attempt to establish the relationship, if any, between the two incidents.

1. The following correspondence was obtained from Professor Bedson's files

(a) *Safety Precautions in the laboratory*

From: Professor A. W. Downie, Liverpool

To: Dr. H. S. Bedson

13th June 1966

Thank you for your letter of 1st June and the details of the precautions taken in the laboratory to avoid the escape of variola virus. This latter seemed very complete and in consequence I am writing a note to Peter Wildy saying that I approve of the precautions taken.

There is only one thing in the report which one might ask about and this is the precautions taken in the centrifuge room, mentioned under Special Precautions 1a. I know, of course, that the Spinco is pretty well enclosed and sealed to avoid the dispersal of virus from leaking centrifuge tubes, but do you do anything about disinfecting the inside of the centrifuge after spinning virus suspensions? We all know that Spinco centrifuge tubes sometimes leak and I have often been concerned about the contamination of the inside of the Spinco.

I am sorry you were not able to deal with the slides before Cruickshank left for Rhodesia. However, I dare say these will be examined in due course. I shall be interested to know whether you pick out the chickenpox ones correctly from the slides sent to you!

From: Dr. H. S. Bedson

To: Professor A. W. Downie

15th June 1966

Thank you for your letter of 13th June and your general approval of our precautions. Thank you very much for the time you have spared for this matter.

I note what you say with regard to the Spinco. It is, of course, our practice to disinfect the inside of the rotor with formalin as a routine when handling any of the poxviruses. I imagine that there is no chance of dispersal of virus outside the rotor and we have not been in the practice of doing anything to the chamber of the centrifuge. Do you think that it is necessary for us to alter our practice in this respect?

I think it was some time last autumn that you asked for a photograph of me. I had nothing suitable at the time but I have since persuaded myself to be photographed and enclose a print. I hope this is adequate. We have the negative here if some other form of print is required.

From: Professor A. W. Downie

To: Dr. H. S. Bedson

17th June 1966

Thank you for your letter of 15th June together with the photograph. The photograph is very good, although it makes you look a little bit severe. Perhaps reprinting it on a softer paper may improve it.

About the Spinco: although the lid of the Spinco screws on fairly firmly I would have thought that any leakage from tubes in the very high speed spinning rotor might easily have been dispersed to the inside of the centrifuge chamber. Consequently, I believe it might be advisable to disinfect the chamber of the centrifuge from time to time. However, the only way one could check this, I think, would be to spin tubes of dye in the rotor at the usual speeds and see if there is any evidence of dispersal of the dye into the chamber (a) when a tube is purposely allowed to leak a little, and (b) when there seems no obvious leak in the tubes. I think it might be worth while checking on these possibilities. If you do, perhaps you could give us the benefit of your experience!

(b) Investigation of monkeys as source of infection

From: Dr. J. Herbert

To: Dr. H. Bedson

23rd June 1966

My apologies for being so long in sending you the information about McLennan's photographs of my monkeys—but Pardoe is away ill and the information was not available.

It appears that he took photographs on the 28.3.66 and 16.5.66. There are three photographs that are unaccounted for: McLennan thinks that he took me either on the 4th or the 11th of February but I regret that I have been unable to confirm this from my records.

From: Dr. H. S. Bedson

To: Dr. J. Herbert

24th June 1966

Thank you for your letter. There is one further question about these three photographs that are not accounted for. Can you assign them to any particular monkeys and, if so, can you let me have the information about where these monkeys have come from and when they were introduced into your colony?

(c) List of monkeys photographed.

Monkeys photographed by McLennan

<i>Date</i>	<i>Monkey</i>	<i>hrs.</i>
27.7.65	1268	1314
27.9.65 (approx.)	1268	1314
12.10.65	1265	1266
29.3.66	1265	1266, 1314, 1353

(d) *Dr. Bedson's notes on work in poxlab in February 1966*

Work in Lab Feb. 1966

1st-4th Titn of Variola major stocks. Titre $10^{5.3}$ and $<10^{4.3}$
& Electromelia (total 8 pocks) (No pocks)

7th Feb. Infected HeLa PD $\times 30$: Alastrim/Butler
 $\times 40$: Variola major/Hinden

10th Feb. Harvested above—sonicated—particle counts $\rightarrow -70^{\circ}\text{C}$
& Spinco

14th Feb. Rabbitpox in HeLa PD $\times 32$
Harvested $\rightarrow 15/2/66$
Titrated 15/2/66—18/2/66

2. In order to obtain all available information on the 1966 outbreak

(a) *The University of Birmingham was asked for all records to be made available.*

From: Professor R. A. Shooter

To: Professor Owen Wade Dean 26th September 1978

I am writing to ask whether the University has any records of the investigation that was conducted into the source of the 1966 outbreak of variola minor in Birmingham, the primary case of which appears to have been a photographer working in the identical darkroom in the University's Medical School as Mrs. Parker.

I should be grateful for these records to be made available to our investigation or, if none are held by you, for any advice on where we may obtain them.

From: The Lord Hunter of Newington Vice Chancellor

To: Professor R. A. Shooter 28th September 1978

I am replying to your letter of 26th September addressed to the Dean of the Faculty of Medicine & Dentistry, Professor Owen Wade. An impression seems to be abroad that the Department of Virology of the University of Birmingham was the centre of the 1966 epidemic of variola minor. There was certainly no evidence that this was so. Under the circumstances it was not considered necessary for a University investigation or inquiry and none took place. My predecessor, Sir Robert Aitken, confirms this. A report of the epidemic was, however, published in the Lancet (Lancet, 1966, 1, pp. 1311). Reference to the epidemic was also made in the Annual Report 1966 of the Medical Officer of Health of Birmingham, Dr. E. L. M. Millar—the relevant extract is attached.

You have already inspected the files from the Department of Medical Microbiology (Department of Virology in 1966). In one of these there is a copy of the minutes of the Birmingham Regional Hospital Board meeting held on 1st May 1966 at the end of the epidemic. At this meeting, all the local medical officers of health were present and the epidemiology of the outbreak is reviewed. In the same file is a letter from Dr. Godber, Chief Medical Officer, dated 1st August 1966. I understand that Dr.

Godber was kept closely informed throughout the epidemic by Dr. Christie Gordon, the Senior Administrative Medical Officer of the Birmingham Regional Hospital Board. You will be aware that there were a number of outbreaks of variola minor in Britain in 1966. In that file there is also a letter from Dr. Gordon thanking the Department of Virology for the services rendered during the epidemic. I think this referred to the first use on a large scale of an electron microscope for the early diagnosis of smallpox.

On the personal initiative of Professor Wildy, the then Head of the Department of Virology, Professor Downie and Professor Macrae were invited to inspect the laboratory in May 1966. Letters referring to their visit are, I believe, on the file you now have. Professor Macrae, who is now at Nottingham, recently informed the University that he is fully prepared to give you further information about this matter if you so wish.

I know that you have interviewed many people who remember the 1966 epidemic and that Professor Wade has given you a recent letter from Dr. Cruickshank who was present at the laboratory in 1966. Dr. Gordon and Dr. Millar were of course very closely concerned with the epidemic and I am sure that they will be pleased to assist you in your enquiries. In 1966, as you will have seen from the files, Dr. Gordon was arranging for the laboratory to be upgraded to be a smallpox reference laboratory. Professor Wade tells me that Dr. Challenor from the Communicable Diseases Center at Atlanta, Georgia, was an observer of the epidemic and possibly he made a report to the United States Public Health Service.

There may be other sources of information about the epidemic in the files you now have. To the best of my knowledge it is unlikely there will be any relevant information about this matter elsewhere in the University.

Enclosure

Extract from Annual Report 1966 of the Medical Officer of Health of Birmingham Dr. E. L. M. Millar.

Extract from Annual Report 1966 of The Medical Officer of Health of Birmingham—Dr. E. L. M. Millar

Smallpox

Although there were no cases of smallpox in the City during 1966, cases of variola minor occurred in surrounding areas. The first known case, retrospectively diagnosed, was a photographer (not vaccinated), working in Birmingham, but living at Stone, Staffs, who became ill on 18th February whilst staying at his fiancée's house in Cannock. Subsequent cases in the West Midlands appeared at Stone, Walsall, Warley, Stoke-on-Trent and Cheadle.

During May and June further cases appeared in Pontypool but no connection could be established with the West Midlands cases. Subsequently three members of a family residing in Solihull, Warwickshire, developed variola minor and cases were also recognised in Salford, but again no direct connection could be established with cases occurring in the West Midlands and Monmouthshire.

Although Staffordshire and Monmouthshire were free from known infection by mid-July, the appearance of the disease in Solihull and Salford suggested that unrecognised cases may have been occurring in different parts of the country.

The clinical picture was that of an influenza-like illness with the patient complaining of lethargy, headache, backache and sometimes sore throat. There was fever and in some cases sweating was a marked feature with intense pain in the back. This state continued for two to three days, after which a rash appeared, first on the head and face, then on the back, arms and down the legs. It was most profuse on the back, particularly over the shoulder blades and buttocks, and sometimes on the soles of the feet. It was possible by examination of smears by electron microscopy to make a confirmative diagnosis of variola within a matter of an hour. In this respect the Department is entirely grateful to the staff of the University of Birmingham's Department of Virological Studies.

The last patient suffering from variola minor in the West Midlands was discharged from the Isolation Hospital on the 1st August, terminal disinfection of the hospital was completed by the 5th August.

There were no deaths.

Copy of letter from Dr. Cruickshank (referred to in the Vice-Chancellor's letter of 28th September).

From: Dr. I. Cruickshank

*To: Professor Wade
Dean of the Medical School*

10th September 1978

I was surprised to find after your phone call how little detail I could recall of the 1967 affair which at the time I considered to be rather momentous. Most things seem to be recorded in the two Lancet papers dealing with the clinical epidemiological and laboratory aspects of the outbreak.

My first dealings were with the girl in the Moxley Hospital. I did not see the photographer until he had fully recovered and I do not think there were any other cases associated with the Medical School. Dr. Bedson and I were given the job of running the regional Smallpox lab and together with Dr. Flewett dealt with all the cases identified by the MOH and his team. We spent much time in houses and the Catherine de Barnes taking specimens and all the diagnostic work was done specifically in our own lab in Edgebaston. All my further remarks will therefore apply not only to our own experimental work but also to diagnostic specimens.

Stocks of both variola major and variola minor virus were kept in a -70°C fridge in the basement. They were brought in the frozen (and therefore inert) state to our lab where all processing was carried out. Virus went out of the lab only after inactivation (i.e. for electron microscopy or biochemical analysis) or autoclaving and incineration in closed buckets dealt with only by our technician Ashley Dunn. Smoke testing for air flow in the ventilators was done from time to time and personnel at any risk were vaccinated.

Virtually all our work was carried out on variola major virus as three subsequent publications in the Journal of General Virology show. Work on variola minor only began when Dr. Bedson acquired a research student called Cooper whose project was specifically associated with that virus. I do not recall the date of his starting in relation to the outbreak.

During the outbreak our lab was visited by Dr. Millar and Dr. Nicol of the Birmingham Health Department and by Dr. Alistair McCrae of Colindale and I think I recall visits by Professor Alan Downie of Liverpool and Professor Keith Dumbell of St. Mary's though these may possibly not have visited during the epidemic itself.

Following these I do not recall any major recommendations for changes in the system of control already in force. We ourselves naturally reviewed our procedures and found it unnecessary to make other than minor alterations. Concern was expressed about unauthorised persons using the corridor outside the lab and measures were taken to attempt to control and warn personnel of the risks and to offer vaccination etc. It was recognised however that short of either total blockade or a highly elaborate and probably unworkable pass system complete control of passing staff was unlikely to be successful. All students except in rare contraindicated circumstances vaccinated or revaccinated each other during their 3rd year. Primary responses were unusual.

At no time were we restricted in our diagnostic or experimental work which we resumed as soon as the cessation of the outbreak afforded us the time to do so and we continued to work with variola major and minor until I departed for Africa in 1968. I certainly saw no written criticisms or recommendations (as I recall) though I think informal reports were probably made to the Head of Department who acted upon them.

We were acutely aware of the possibility that the virus might have escaped from our lab but our conclusion from what epidemiological evidence we had in relation to work going on at the time contact would have been made by the patient was that such an accident was very unlikely indeed. I know the Birmingham authorities reached the same in conclusion as to the origin of the outbreak.

Further episodes subsequently in Cardiff seemed to add weight to the imperfection theory. Further the absence of further point source cases in the Medical School seemed also to argue against a sizeable escape of the virus.

(b) *Professor Wildy, Head of Virology in 1966, was asked for information.*

From: Professor R. A. Shooter

To: Professor P. Wildy, Cambridge *30th October 1978*

My committee would welcome your help in relation to the 1966 outbreak of smallpox in the Midlands. We know of course that there was no official investigation into the possibility that the smallpox laboratory was the source of the photographer's infection, but we understand that it was discussed as a possibility. When you asked

Professor Downie and Dr. Macrae to visit the laboratory, had you anything in particular in mind, or was it an additional precaution?

From the departmental files we have a number of statements that their report was satisfactory, except for a comment on the high speed centrifuge that was soon resolved. We have not, however, seen the note which is referred to in Downie's letter to Bedson on 13th June 1966 (copy enclosed) and which you apparently sent to the MOH (copy of his reply to you on 16th June 1966 enclosed). If you still have a copy we should be very grateful if you would let us see it.

From the minutes of the Committee for the Control of Pathogenic Organisms we have seen your concern about the use of the corridor through the Department of Virology as a through way, and your view that "it has been impossible to disprove the idea that the last outbreak originated within the Medical School". Do the swing doors at both ends of the corridor date from additional precautions undertaken immediately after the 1966 outbreak?

From: Professor P. Wildy

To: Professor R. A. Shooter

Thank you for your letter of 30th October. With respect to your first point. There was no official enquiry into the means by which the photographer of 1966 became infected but naturally as head of a department in which smallpox virus was being investigated I was concerned that his infection might have originated from our work. Accordingly I decided not to leave the epidemiological tracing to the Medical Officer of Health and his team but to ask independent smallpox experts down as well as the MOH to inspect our safe working. You will have evidence I know about the visit of Dr. Macrae and Professor Downie. At that time we were disinclined to regard the infection as a laboratory escape because (1) there were alternative probable explanations by which the photographer might have become infected naturally. (2) Henry Bedson had evidence that the epidemic strain differed from any in his stocks (this eventually proved insufficiently strong to be conclusive though I understand from heresay that some recent work has tended to support this idea). (3) The likelihood of airborne infection jumping one floor up and several rooms laterally seemed small. (4) No contacts had been established between the photographer and the Virology Department. So in short when in June 1966 we offered ourselves for inspection it was with no specific reason in mind other than to ensure that we were doing all we could to work safely.

With respect to your second point all departmental correspondence was left in Birmingham for my successor when I resigned. However, after the recent tragedy I asked for copies of anything relevant to be sent to me to aid my fickle memory in case your committee should want the information. Among these copies is the letter that I believe you want from Downie to me dated 13th June. I enclose it herewith.

With respect to your third enquiry, the swing doors in the corridor were put in considerably after the 1966 epidemic. I cannot be exactly

sure when they were fitted but I suppose that this could fairly easily be established from the Maintenance Department's files. I had been much concerned about the siting of the Virology Department for a number of years and became more so as the smallpox eradication programme got under way, as the use of general vaccination was discontinued, as the general awareness of infection hazards increased and of course when the 1973 outbreak occurred in London. It was as a result of these changing circumstances that our arguments for closing the corridor to all and sundry became accepted.

When I saw you in Birmingham recently you suggested that I wrote about anything that occurred to me. I was appalled at the unsatisfactory state of the panel in the ducting system demonstrated in the photograph I was shown. Obviously this would make a possible route by which airborne virus might travel to various parts of the building. So here are some thoughts about the ducts.

When the medical school was new, the ducts passed up through the laboratories and discharged on the roof. A few years before my arrival Sir Solly Zuckerman obtained funds and built a fourth floor on the east block. This cut the ducts which were then led out through the vents in the wall which you see today. Because of this, the ventilation was presumably restricted so that whenever there was a steam leak in the sub-basement the shafts became saturated and the inspection panels which were then of plywood became delaminated and rotted.

When I arrived in Birmingham in 1963 the present poxvirus laboratory was in use as a medium room. It was in a bad state; in particular the plywood panels were rotten and steam actually leaked into the room. I saw at once that the only thing to do was to move the medium making and completely renovate that room. This was done early in 1964. Curiously the one item left off the plan of alterations was the need to replace the panels and to seal them. Henry Bedson arrived in the early summer of 1964 and we held up all work on smallpox virus until the panels had been made good. Unfortunately I have no record of when the smallpox work actually began but I remember that work was confined to vaccinia virus until we were satisfied. The plywood panels were replaced with asbestos sheet which I believe was embedded in mastic. Because mastic is apt to crack we had flexible adhesive tape put over the outside of the joints. Until this was done I remember that the small room (then used as an office by Henry Bedson and Ian Cruickshank) had been hot and steamy and since this was cured I conclude that the panels in the small room were satisfactorily sealed as well as those in the larger outer laboratory.

In 1969 or thereabouts there was a very serious steam leak in the sub-basement and this saturated the wall of the seminar room with moisture. It also emerged in the room on the other side of the corridor which has a French window and mini-balcony. I do not believe that this was felt in the poxvirus laboratory at that time.

The University set up the Control of Pathogenic Organisms Committee (1966) which responded to the various national committees as time

passed. This put in hand various improvements in the poxvirus laboratory. I have a note of a meeting 31.7.73 of our departmental executive committee listing a number of jobs outstanding in connection with the improvements at that time. One of these was the sealing of the duct presumably in the small room. Another note dated 6.11.73 recorded that this had been done. So though I don't remember it we must have become concerned about that duct at that time. In 1974 further improvements were carried out and smallpox work was suspended while this was done. The duct in the outer room had to be opened to attend to the services. The plan indicates that the duct was to be made good and resealed. There is no mention at that time of the duct in the inner room and I assume that it was satisfactory then.

I don't know if any of this has value for you—probably by now you have all the information you need anyway.

From: Professor A. W. Downie Liverpool

To: Professor P. Wildy Birmingham 13th June 1966

Since I visited you on 17th May, Henry has sent me a complete summary of the precautions taken in your department to avoid the escape of variola virus. His notes supplement the information we obtained at the time of our visit.

I am perfectly satisfied that the precautions taken are reasonable and adequately safeguard those working in the department and visiting the department, against infection. The one point that I have asked Henry about relates to the disinfection of the Spinco ultra centrifuge in the basement after the spinning of tubes containing live variola virus. This has been a point that has worried us somewhat, as one cannot be sure that the Spinco tubes may not leak during the spinning.

3. Report of National Communicable Disease Center Atlanta.

Representatives from the U.S. Public Health Service's Center for Disease Control observed the 1966 outbreak. Their report was not intended to be definitive or comprehensive, but rather to provide information to the U.S. Government which would be useful in the event of an importation of smallpox into the United States.

To: Director, National Communicable Disease Center

From: Chief, Smallpox Eradication Program

Subject: Variola Minor—England and Wales, 1966 November 1st 1967

INTRODUCTION AND ACKNOWLEDGEMENTS

From April to August 1966, 73 cases of smallpox were reported in the United Kingdom. The first identified were reported to the World Health Organisation on April 29th 1966. Subsequent investigations revealed cases with onsets of illness as early as February 1966. The causative virus was characterized as *variola minor*.

On May 2nd an invitation was extended by Dr. A. T. Roden, Principal Medical Officer (Epidemiology), Ministry of Health, London, for participation of a CDC epidemiologist in the investigations and containment procedures as an observer. Dr. Bernard Challenor, EIS Officer, Smallpox Eradication Program, departed for England on May 3rd 1966.

While Dr. Challenor was in England (May 4th through June 10th), a total of 45 cases were identified, primarily in Staffordshire in the West Midlands, England. Subsequently, an additional 28 occurred in Warwickshire and Lancashire, England, and Monmouthshire, Wales. The UK was declared smallpox free August 18th 1966.

This report deals in detail with the 45 cases occurring in and around Staffordshire. Available information on the remaining cases is included where applicable.

Medical Officers in the West Midlands and in the Ministry of Health in London were most helpful, and hospitable. They provided access to patients for clinical study and arranged visits to local areas for study of transmission patterns and methods of control. We especially appreciate the assistance of Dr. A. T. Roden, Ministry of Health, London; Dr. E. L. M. Miller, Medical Officer of Health, City of Birmingham; Dr. Thomas H. Flewett, Regional Consultant Virologist, East Birmingham Hospital; Dr. Christie Gordon, Director, Birmingham Regional Hospital Board; Dr. Joseph Hamilton, Medical Officer of Health, Stoke-on-Trent; Dr. H. M. Summers, Deputy Medical Officer of Health, Walsall; Dr. R. Fothergill, Consultant on Infectious Diseases, East Birmingham Hospital, and Dr. H. S. Bedson, Virologist, Birmingham University. In addition, Dr. J. Donald Millar, (Chief, Smallpox Eradication Program), who was then a student at the London School of Hygiene and Tropical Medicine, facilitated initial contacts with the Ministry of Health, and provided assistance during the course of the investigations.

I. BACKGROUND

(a) *Description of the Locale—Birmingham and Staffordshire*

The first 45 cases occurred in the city of Birmingham and the nearby county of Staffordshire, both situated in the West Midlands, industrial heart of Britain. This area is one of the most heavily populated in the country. The British Motor Corporation, Landrover, and Jaguar production plants are located here; much of the industrial machinery produced in England is manufactured in the area. The Region consists of a continuous succession of industrial towns which in the course of time have merged into one another eliminating perceptible boundaries. Little countryside is seen; smoke from several hundred factory chimneys generally overlies much of the area. Residents of the area jokingly comment that "In the Midlands the birds wake up coughing, not singing!" In the rest of England, the Midlands is referred to as the "Black Country." Birmingham, with a metropolitan population of 2.2 million persons, is located at the southern tip of Staffordshire and is the largest city and cultural center of the region; it is 100 miles north of London.

The earliest known case of variola minor occurred in Birmingham and was the only case identified from the city. The nearby suburban County Boroughs of Warley (population 170,000) and Walsall (population 130,000) reported 2 and 13 cases, respectively.

Stoke-on-Trent, an industrial city (population 275,000), 50 miles north of Birmingham reported the largest number of cases (twenty) from a single area. There were in the Rural District of Cheadle seven cases, and in the Rural District of Stone, two cases.

Though many immigrants from India, Pakistan, Africa and the British West Indies inhabit Staffordshire and the Birmingham area, all of the first 45 patients were native born English. No cases were identified among overseas travelers.

Areas involved after June 10th.—Following outbreaks in Staffordshire, new foci of infection appeared in June, July and August in Monmouthshire, Wales, and Salford County Borough, Lancashire. Cases were also identified in Solihull County Borough, Warwickshire, near the Catherine de Barnes Isolation Hospital. According to published reports, no epidemiological link could be established between these new cases and those in Staffordshire.

(b) Organization of Health Authorities

The outbreak in the West Midlands involved the City of Birmingham and the County of Staffordshire. To appreciate the steps taken in the control of the outbreak and certain difficulties which were encountered, note should be made of the organization of local health authorities in the areas involved.

The present development of preventive medical services is a complex result of evolution. At various times, divisions of health jurisdiction have been created or superimposed on previous systems. While these steps represent changes made principally to cope with an increasing population; in each, an essential element of local autonomy has been characteristic.

Large cities constitute health jurisdiction with a locally appointed medical officer of Health responsible for public health services. Many English counties, based upon the medieval shires (now with populations of as many as one to five million) have of necessity been divided into more manageable segments. A city with a population of greater than 100,000 persons occurring within a county is designated a "County Borough" and has a municipal administration and its own Medical Officer of Health. Similarly, in the remaining areas of the county, there may be several divisions into "Rural Districts" each of which may constitute a local public health jurisdiction with a locally appointed Medical Officer of Health. In the West Midlands, a large city, Birmingham, and a large county, Staffordshire, were involved in the outbreak. Within Staffordshire, cases occurred within the jurisdictions of several County Boroughs and several Rural Districts. As a result, there were six health jurisdictions and six Medical Officers of Health responsible for investigational and control activities in various affected areas; five of these were within Staffordshire. A list of the local health authorities involved is provided:

1. City of Birmingham
2. Stoke-on-Trent County Borough, Staffordshire
3. Walsall County Borough, Staffordshire
4. Warley County Borough, Staffordshire
5. Cheadle Rural District, Staffordshire
6. Stone Rural District, Staffordshire

It goes without saying that involvement in the same outbreak of multiple semi-autonomous and independent health authorities required a high degree of coordination for effective action.

(c) *Previous Vaccination Practices*

Until 1946, vaccination against smallpox in the United Kingdom was, by law, compulsory. In the years prior to 1946, however, enforcement was quite lax and it is said that 50% or less of the population were vaccinated in many areas. With the passage of National Health Service legislation in 1946, compulsory smallpox vaccination was ended. As a result, a substantial proportion of persons under 20 years of age in Great Britain today have never been vaccinated. In the course of a school vaccination program in Staffordshire during the outbreak elementary grade children were examined for primary vaccination scars. While the data gathered are too crude to justify more than a general impression, very few children appeared even to have been vaccinated.

II. The Epidemic

(a) *The General Considerations*

The first case recognised was in a 16-year old girl from Walsall County Borough who developed an influenza-like illness on April 15th, 1966. Four days later a generalised rash appeared. She was admitted to a contagious disease hospital as a possible chickenpox case; she gave a history of chickenpox several years previously. A consultant visiting the patient 4–5 days later felt that smallpox was a likely diagnosis; laboratory investigation confirmed this.

Rapid investigation of the girl's immediate family and associates revealed 8 persons who had had "chickenpox-like" illnesses during the previous weeks dating back to February 18th. Two of these patients had active exanthems and were immediately diagnosed as smallpox. The remainder were diagnosed on retrospective evidence. All were unvaccinated prior to illness.

During the previous two months, an outbreak of chickenpox was thought to be in progress in the West Midlands. Though the smallpox cases were identified in young adults and teenagers with a history of previous chickenpox, almost all were initially thought to be cases of chickenpox. A few of the patients seen during the period of prodromal symptoms were diagnosed as influenza. When the 16 year old girl was diagnosed as smallpox the outbreak had already progressed into the 4th generation of cases.

The first detected cases clustered in the County Borough of Walsall. The majority of these were teenage members of a youth club associated with a nearby housing project. Subsequent cases in Stoke-on-Trent, Warley and Cheadle were eventually traced to the initial cluster in the Walsall-Birmingham area.

The epidemic curve through June 4th is shown in Figure 2.

Chain of Infection

The earliest case identified occurred in J.A.M., a 23-year-old male photographer employed in the anatomy department at the University of Birmingham Medical School. He fell ill on February 18th with fever, headache, backache, and vomiting, and developed a generalised rash four days later. During the first week of illness he remained at home; when the rash appeared he felt better and returned to work a few days later. He was seen by a physician while the rash was evolving and was thought to have drug eruption. He denied contact with chickenpox, with persons exhibiting a rash similar to his, and with recently arrived immigrants or travelers from foreign countries; he had never been outside the United Kingdom.

During the weeks prior to his illness he had photographed monkeys from India in the course of experiments in the Anatomy Department. Before his illness was recognised in late April all of these monkeys had been sacrificed and were not available for examination. None had appeared ill to their lab handlers.

The Department of Anatomy is situated on the floor immediately above the virology Department. At the time of the outbreak experiments with strains of *variola major* and *minor* were in progress. However, detailed investigations did not disclose any link between the virology department and the photographer. None of the virology personnel knew or had any association with J.A.M., and he denied having visited the department. There was no investigation of possible connections between the ventilating system of the two laboratories.

The remaining cases are best considered according to their epidemiologic association with each other and will be discussed as epidemiologic units. A total line listing providing basic information on each case is provided as Appendix A.

Epidemiological Unit I—The initial six cases

J.A.M., infected five persons. C.F., (case 2), a 16-year-old girl who worked in the same chemist shop as J.A.M.'s fiancée. When J.A.M. fell ill he remained bed-ridden in his fiancée's apartment where she nursed him. Bedridden or no, he drove to the chemist shop daily to meet his fiancée after work. Here he had contact with C.F. She became ill on March 4th, 14 days after onset in J.A.M. J.A.M.'s fiancée, vaccinated in the past, did not become ill.

On the weekend of February 26–27th, J.A.M. visited his parents, (cases 3, 4) in nearby Stone. On both days he shaved with his father's razor, despite a well developed pustular rash on his face. On March 7th, (eight or nine days later), his father developed a facial papule which matured during the next five days to a well developed pustule. On March 13th he developed generalised symptoms of fever, headache, malaise, and backache, and next day a generalised rash. Mrs. J.A.M., (case 4), the mother, became ill on March 13th. Both parents were unvaccinated, remained at home during their illnesses, and gave rise to no further cases.

On the Friday night, February 25th, J.A.M. attended a folk dance party and banquet where, at the table, he sat diagonally opposite A.S. (case 5) a school teacher from Walsall. The two men, who did not know each other, were introduced during the course of the evening. A.S. who remembered seeing "spots" on J.A.M.'s face became ill 14 days later. A.S.'s wife, who danced with the photographer on several occasions during the evening, also noticed the lesions. She had been vaccinated and remained well. There were no cases in other persons who attended the banquet. When A.S. became ill he stopped teaching, feeling embarrassed because of his noticeable lesions. The Easter vacation supervened keeping him home an additional week and when he returned to school his lesions had entirely cleared.

In Stone on Sunday, February 27th, J.A.M. went with his fiancée to a pub called the White Cock Inn, 5 miles outside Stoke-on-Trent. In the pub that afternoon was a 72-year-old man, G.H.C., (case 39), from Stoke-on-Trent standing at the bar with his brother-in-law and two friends when the photographer arrived. The bartender serving drinks remembered seeing a young man enter with a lady friend and noticed that the man's face was covered with

“spots.” He remarked to customers at the bar: “that’s the worst case of acne I’ve ever seen.” There was no known direct contact between G.H.C. and the photographer; however, G.H.C. became ill on March 11th or 12th with an illness compatible with *variola minor*. When questioned G.H.C. was truculent, refused to be examined or give a blood sample for seriological tests, and subsequent information regarding his illness was obtained from relatives. Though he claimed vaccination several times in the past, there was no direct evidence of this. He proved to be the only connection between the initial Birmingham case, J.A.M., and the subsequent series of cases in Stoke-on-Trent, Warley and Cheadle.

Following the first 6 patients, the outbreak gave rise to two main streams of transmission; one series of cases in Walsall derived from C.F., (case 2), the girl in the chemist shop; and the other series in Stoke-on-Trent derived from the old man in the pub, (case 39).

Epidemiologic Unit 2—Walsall

C.F., (case 2), the girl in the chemist shop, was a member of a Walsall teenage club affiliated with the recreation center of a nearby housing development. Following her illness cases occurred in Walsall involving club members and their families. M.A., (case 6), the 17-year-old boyfriend of C.F. became ill on March 27th. The prolonged serial interval (23 days) between their onset dates suggests either a missed case or a late transmission event despite constant close contact.

M.A. infected his brothers and sister who came down as follows: P.A., (case 11), April 16th; M.A., (case 12), April 16th; and B.A., (case 16), April 20th. Their parents had been vaccinated and did not develop illness. Youth club members stricken included: J.F., (case 9), April 8th; P.P., (case 15), April 15th; and P.L., (case 21), April 28th. P.P., (case 15), was the 16-year-old girl whose diagnosis uncovered the outbreak. She infected her mother Mrs. A.P., (case 23), and her brother, J.P., (case 24), who became ill on May 5th and 8th respectively. Her father was vaccinated and did not become ill.

While P.P. was hospitalised at Moxley Hospital, Walsall, April 25–29th, awaiting diagnosis a 5-year-old boy with measles, J.J.W., was placed in a cubicle next to hers. There was no known contact between the two, but J.J.W., (case 33), became ill on May 12th. This was the only instance of hospital transmission.

During Easter weekend, (April 9–11th), J.F., (case 9), a 14-year-old girl, while experiencing prodromal symptoms, slept on three successive nights with her 4-year-old cousin M.L. M.L., (case 20), became ill approximately two weeks later on April 24th.

Epidemiological Unit 3—Stoke-on-Trent, Cheadle, and Warley

The Stoke-on-Trent cluster was much larger than the Walsall cluster. A teenage bus outing, April 8th, was an important transmitting mechanism. By this means the disease spread beyond a predominantly family chain to several unrelated individuals and also to Warley.

G.H.C., the old man in the White Cock Inn, became ill on March 11th or 12th; he infected his grandchildren A.C.¹, (case 7), and A.C.¹¹, (case 8), (Figure 4)

who lived in the same household; both became ill on March 28th. The vaccination status of the parents is not known; both children were unvaccinated. The disease spread from the children to their cousins K.B., (case 13), and B.B., (case 19), and throughout the entire "B" household (cases 25, 29, 30, 32). B.B. also infected a playmate (case 22) who passed the disease on to his brother (case 36).

4. An account of the 1966 outbreaks of *variola minor* was given in "On the State of Public Health" "The Annual Report of the Chief Medical Officer of the Ministry of Health for the year 1966."

TABLE II.24

	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966
Cases	4	6	1	1	2	66	—	—	—	62
Deaths	2	1	—	—	—	26	—	—	—	—
Importations ...	1	1	—	1	2	6	—	—	—	—

During 1966 there were 4 outbreaks of *variola minor* in England and Wales—2 in the West Midlands, 1 in Monmouthshire and 1 in Salford C.B. 62 cases were notified and a further 9 cases were diagnosed retrospectively on serological grounds. No connection could be established between these outbreaks but in each outbreak spread of infection appeared to be mainly by close personal contact. It can only be assumed that there were undiagnosed intermediaries. The earliest known case occurred in Birmingham with onset on February 18th and the last known case occurred in Salford with onset on July 13th. For international purposes England and Wales was declared free from smallpox on August 18th.

Outbreaks

(a) The West Midlands Outbreaks

There were 2 separate outbreaks in the West Midlands, the first comprising 47 cases (Table II.25) and the second a family of 3 (Table II.28). No connection could be established between these two outbreaks.

The first case to be recognised was a 17-year-old girl (case No. 4:1 in Table II.25) who resided in Walsall and was admitted to Moxley Isolation Hospital on April 25th suspected to be suffering from chickenpox. Because of atypical features specimens were sent for virological examination. Variola was confirmed on April 29th and the patient was transferred forthwith to the Regional Smallpox Hospital.

She worked as an assistant in a chemist's shop in Walsall and enquiries revealed that another assistant, a 16-year-old girl, was taken ill with an influenza-like illness on March 4th followed by a rash on March 9th. Blood taken from this girl on May 26th had a neutralising antibody titre of 1/625 to vaccinia/variola virus (case No. 2:1, Table II.25).

It was ascertained retrospectively that a photographer working in Birmingham University became unwell on February 18th and developed a rash on February 23rd (case No. 1:1, Table II.25). He visited the girls in the chemist's shop during

the time he had the rash. Blood taken on April 30th had a neutralising antibody titre of 1/625 to vaccinia/variola virus. This is the earliest known case and, although careful enquiries were made into his movements during the relevant period, it has not been possible to determine how he acquired infection. He had not been out of the country and detailed enquiries failed to establish that there had been contact with any known source of infection.

TABLE II.25
Smallpox (*variola minor*)—West Midlands

Case No.	Location	Sex	Age	Infection	Onset of Illness	Time of Vaccination	Retrospective Diagnosis	Date of admission to smallpox hospital	Diagnosis confirmed by virus isolation	Date of Discharge
1 : 1	Birmingham C.B.	M	23	Contact of 1 : 1	18.2	Unvaccinated	Yes	—	—	—
2 : 1	Walsall C.B.	F	16	Father of 1 : 1	4.3	Unvaccinated	Yes	—	—	—
2 : 2	Stone R.D. Staffs.	M	57	Father of 1 : 1	7.3	Unsuccessfully vaccinated in past	Yes	—	—	—
2 : 3	Stone R.D. Staffs.	F	62	Mother of 1 : 1	13.3	Unvaccinated	Yes	—	—	—
2 : 4	Walsall C.B.	M	25	Contact of 1 : 1	11.3	Unvaccinated	Yes	—	—	—
2 : 5	Stoke-on-Trent, C.B.	M	70+	Contact of 1 : 1 Grandfather of 3 : 3 : 4	20.3	Not vaccinated within past 20 years	Yes	—	—	—
3 : 1	Walsall C.B.	F	14	Father of 3 : 5	2.4	Unvaccinated	Yes	—	—	—
3 : 2	Walsall C.B.	M	17	Sister of 2 : 1	2.3	Unvaccinated	Yes	—	—	—
3 : 3	Stoke-on-Trent C.B.	M	14	Friend of 2 : 1	2.4	Unvaccinated	Yes	—	—	—
3 : 4	Stoke-on-Trent C.B.	F	6	Grandson of 2 : 5 Grand-daughter of 2 : 5	3.4	Unvaccinated	Yes	—	—	—
3 : 5	Stoke-on-Trent C.B.	M	40+	Son of 2 : 5	? 31.3	Not vaccinated within past 20 years	Yes	—	—	—
4 : 1	Walsall C.B.	F	17	Contact of 3 : 1	16.4	Unvaccinated	—	29.4	Yes	18.5
4 : 2	Walsall C.B.	M	16	Brother of 3 : 2	16.4	Unvaccinated	Yes	30.4	Yes	20.5
4 : 3	Walsall C.B.	M	23	Brother of 3 : 2	16.4	Unvaccinated	—	—	—	—
4 : 4	Stoke-on-Trent C.B.	M	16	Contact of 3 : 3	18.4	Unvaccinated	Yes	—	—	—
4 : 5	Stoke-on-Trent C.B.	M	6	Contact of 3 : 3	16.4	Unvaccinated	Yes	—	—	—
4 : 6	Walsall C.B.	F	21	Contact of 3 : 2	20.4	Unvaccinated	Yes	1.5	Yes	25.5
4 : 7	Walsall C.B.	F	4	Contact of 3 : 1	24.4	Unvaccinated	—	3.5	Yes	18.5
4 : 8	Walsall C.B.	F	14	Contact of 3 : 1	28.4	Unvaccinated	—	—	—	—
4 : 9	Cheadle R.D.	M	25	Contact of 3 : 3	19.4	Unvaccinated	—	7.5	Yes	28.5
4 : 10	Stoke-on-Trent C.B.	M	11	Contact of 3 : 3	23.4	Unvaccinated	—	3.5	Yes	22.5
4 : 11	Stoke-on-Trent C.B.	F	15	Contact of 3 : 3	23.4	Unvaccinated	—	—	—	—

TABLE II.25 (continued)

Case No.	Location	Sex	Age	Infection	Onset of Illness	Time of Vaccination	Retrospective Diagnosis	Date of admission to smallpox hospital	Diagnosis confirmed by virus isolation	Date of Discharge
4 : 12	Warley C.B.	M	17	Contact of 3 : 3	20.4	Unvaccinated	—	3.5	Yes	20.5
4 : 13	Stoke-on-Trent C.B.	M	13	Contact of 3 : 3	19.4	Unvaccinated	Yes	—	—	—
4 : 14	Stoke-on-Trent C.B.	M	13	Contact of 3 : 3	End April	Infancy	Yes	9.5	—	25.5
5 : 1	Walsall C.B.	F	46	Mother of 4 : 1	6.5	30.4.66	—	13.5	Yes	25.5
5 : 2	Walsall C.B.	M	13	Brother of 4 : 1	7.5	30.4.66	—	16.5	Yes	13.6
5 : 3	Walsall C.B.	M	6	Contact of 4 : 1	12.5	Unvaccinated	—	7.5	Yes	8.6
5 : 4	Stoke-on-Trent C.B.	M	12	Contact of 4 : 5	2.5	Unvaccinated	—	16.5	Yes	8.6
5 : 5	Stoke-on-Trent C.B.	F	5	Contact of 4 : 5	13.5	7.5.66	—	18.5	Yes	8.6
5 : 6	Stoke-on-Trent C.B.	F	5	Contact of 4 : 5	15.5	7.5.66	—	21.5	Yes	8.6
5 : 7	Stoke-on-Trent C.B.	F	6	Contact of 4 : 5	18.5	7.5.66	—	21.5	Yes	8.6
5 : 8	Stoke-on-Trent C.B.	F	41	Mother of 4 : 4	11.5	8.5.66	—	12.5	Yes	11.6
5 : 9	Stoke-on-Trent C.B.	F	11	Sister of 4 : 4	8.5	Unvaccinated	—	12.5	Yes	31.5
5 : 10	Stoke-on-Trent C.B.	M	36	Father of 4 : 10	6.5	Infancy	—	13.5	Yes	22.5
5 : 11	Stoke-on-Trent C.B.	M	58	Grandfather 4 : 10	12.5	Infancy	—	13.5	Yes	4.6
5 : 12	Stoke-on-Trent C.B.	F	58	Grandmother 4 : 10	13.5	Infancy	—	16.5	Yes	4.6
5 : 13	Stoke-on-Trent C.B.	F	43	Aunt of 4 : 10	12.5	Infancy	—	15.5	Yes	31.5
5 : 14	Warley C.B.	F	49	Mother of 4 : 12	9.5	Infancy	—	13.5	Yes	23.5
5 : 15	Stoke-on-Trent C.B.	F	12	Sister of 4 : 13	12.5	3.5.66	—	18.5	Yes	4.6
5 : 16	Cheadle R.D.	F	43	Mother of 4 : 9	12.5	Unvaccinated	—	26.5	Yes	4.6
6 : 1	Stoke-on-Trent C.B.	M	4	Brother of 5 : 4	16.5	Unvaccinated 6.5.66	—	18.5	Yes	4.6
6 : 2	Cheadle R.D.	M	10	Brother of 4 : 9	22.5	3.5.66	—	26.5	Yes	—
6 : 3	Cheadle R.D.	F	19	Sister of 4 : 9	24.5	Unvaccinated	—	26.5	Yes	—
6 : 4	Cheadle R.D.	M	50	Father of 4 : 9	26.5	Unvaccinated	—	29.5	Yes	—
6 : 5	Cheadle R.D.	F	15	Sister of 4 : 9	31.5	27.5.66	—	31.5	Yes	—
6 : 6	Cheadle R.D.	F	17	Sister of 4 : 9	31.5	26.5.66	—	1.6	Yes	9.6

Control of the Outbreak

One of the difficulties encountered in planning satisfactory control measures, was that the disease was not recognised until the fourth generation (see Table II.25). By this time it was not easy to identify all the cases in retrospect and, of course, still less easy to identify all possible contacts. Every effort was made to trace and place under surveillance all known contacts.

The policy with regard to vaccination of contacts varied in different parts of the region. In most districts contacts, when identified, were offered immediate vaccination but in one district this was not done initially on the grounds that:

- (a) contacts were first recognised at a late stage in the incubation period and it was considered that vaccination might confuse the diagnosis of any subsequent illness.
- (b) The illness itself was extremely mild and it was felt that the risks of complications from vaccination were disproportionate.

It so happened that one of the unvaccinated contacts developed a mild attack of variola which was not recognised while she was under surveillance, and only came to light when other unvaccinated members in her household developed variola. The source of infection pointed to this person and it was then learned that she had developed a sparse rash which she had regarded as "heat lumps" and had not mentioned this to the officer maintaining surveillance. Variola virus was subsequently recovered from the lesions.

Vaccination Status

The Vaccination status of the 50 persons involved in the two outbreaks is given in Table II.25 and II.28. It will be seen that 32 patients had never been vaccinated before the onset of their illnesses. Seven had been vaccinated in infancy only (none of whom had been vaccinated within the previous 10 years) and 11 had been vaccinated after contact with infection (7 within a week of onset of illness). Not one of the 50 could be regarded as protected by vaccination.

(b) Outbreak in Monmouthshire

This outbreak involved principally a primary school in Pontypool—7 out of a total of 8 cases attended this school.

The first case to be recognised was a baby of 4½ months who fell ill on June 2nd and developed a rash on June 6th. He was admitted to the Infectious Diseases Hospital on June 9th with a provisional diagnosis of chickenpox, but, because of atypical features, particularly the distribution of the lesions, scrapings were sent for virology. On June 14th variola was confirmed by virus isolation and the child was immediately transferred to the Regional Smallpox Hospital. The difficulty of diagnosis is emphasised by the fact that two siblings from whom infection was presumably received were retrospectively diagnosed as smallpox and two others who had vesicular rashes at the same time as chickenpox,

Spread of Infection

In most cases spread of infection was through close personal contact such as between members of a family, schoolchildren or youth club members. In a few instances, however, the only possible source of infection appeared to be a single chance encounter with an infected person:

1. Infection was thought to have been introduced into Stoke-on-Trent in this way through the chance meeting at an inn on Sunday, March 6th between an elderly man from Stoke (case No. 2:5 Table II.25) and the photographer who was accompanied by his father. The photographer still had a rash at this time which was the day prior to the onset of his father's illness. The man from Stoke became ill about March 20th and subsequently developed a rash. Blood taken on May 25th gave a neutralising antibody titre of 1/625.
2. A chance encounter between a school teacher from Walsall and the photographer at a dinner-dance on February 25th was considered to have been the source of the school teacher's infection. They were unknown to each other but the school teacher recalled that the photographer, who at that time had a spotty face, sat diagonally opposite him at dinner. The school teacher (case No. 2:4 Table II.25), became ill on March 11th and developed a rash on March 14th. Blood taken on April 29th gave a neutralising antibody titre of 1/625.
3. There was a fateful 'bus outing to Blackpool on April 8th (Good Friday) during the course of which several people were thought to have acquired infection. The following travelled on the same floor of the bus: in Table II, case No. 3:3, case No. 4:4, case No. 4:11 and case No. 4:13. Case No. 3:3 became ill on April 5th and developed a rash on April 8th—the day of the outing. It seems likely that he was responsible for infecting the other three patients. An interesting chance encounter might have occurred at a cafe on the M6 where the party stopped for refreshments. A youth from Warley, case No. 4:12 Table II.25, hitch-hiking to the Lake District was probably in the cafe at the same time. There is no evidence that he spoke to any member of the party but the date of onset (April 20th) suggests that he was infected at about this time. Careful enquiry into his history did not establish any other contact with a known or likely source of infection.

Clinical Features

An account of the first outbreak described the clinical features (Gordon *et al*, 1966). Subsequent to the appearance of this article three further patients have been regarded retrospectively, on serological findings, as having suffered from *variola minor* bringing the total to 47.

The second outbreak comprised a family of three (see Table II.28). Careful enquiry failed to reveal a connection with any of the persons involved in the main outbreak.

Details of the cases are summarised in Table II.26. Five of the eight cases had previously been successfully vaccinated, four within five years of onset of illness. This is unusual in *variola minor* and conflicts with previous experience (Marsden, 1936).

(c) *Outbreak in Salford*

This outbreak came to light on July 16th when a 52-year-old woman who had never been vaccinated was admitted to the Infectious Diseases Hospital suspected to be suffering from chickenpox. Following admission her condition was considered on clinical grounds to be strongly suggestive of variola and the patient was transferred forthwith to the Regional Smallpox Hospital. Diagnosis was subsequently confirmed by virus isolation.

It will be seen (Table II.27) that the outbreak involved two families and spread of infection was probably through the children who played together. The vaccination status of the patients was more in line with the West Midlands experience—11 had never been vaccinated, 1 was vaccinated in infancy and 1 in 1961. This latter patient had an influenzal-like illness without a rash and diagnosis was made retrospectively on serological findings.

Although the original source of infection could not be ascertained in any of these outbreaks it was considered unlikely that four separate importations had occurred and that the most probable explanation was that there were missed cases in the community. For this reason the Chief Medical Officer sent a letter to all doctors on August 1st inviting their co-operation in bringing to the attention of district medical officers of health any case which could possibly be smallpox. It was particularly important to bear in mind that confirmed cases of *variola minor* had frequently presented as atypical cases of chickenpox. This led to close scrutiny and investigation of many cases of chickenpox but no further case of *variola minor* was brought to light.

The Royal College of General Practitioners had produced a tape recorded talk illustrated with colour slides following the last smallpox incident. This was made available at once in the affected and many other areas. It was supplemented by a new recording specifically on *variola minor*.

The Public Health Laboratory Service provided excellent virological services without which diagnosis would have been most difficult. The College and the laboratories have together greatly strengthened our measures for smallpox control but even with this help neither the origin of the outbreak nor the method of spread between areas was ascertained—as happened in the last outbreak of *variola minor* at Rochdale.

Electron microscopy proved a valuable aid in the rapid diagnosis of smallpox in the West Midlands outbreaks. It was particularly helpful to the clinician in that it was possible to distinguish clearly variola and varicella (Cruickshank, Bedson and Watson, 1966).

Vaccination against Smallpox

In Table II.29 are shown the numbers of vaccinations and revaccinations against smallpox declared by local health authorities to have been performed at different ages under arrangements made in accordance with Section 26 of the National Health Service Act 1946, during the years 1957–1966.

The figures for 1966 show that the trends evident in the previous year—increases in (a) primary vaccinations of children aged 1 to 4 years, and (b) revaccinations of schoolchildren—have continued. The latter, however, may have been partly due to the exigencies of travel abroad during the *variola minor*

TABLE II.26
Smallpox (*variola minor*)—*Monmouthshire*

Case No.	Location	Sex	Age	Infection	Onset of Illness	Time of Vaccination	Retrospective Diagnosis	Date of admission to smallpox hospital	Diagnosis confirmed by virus isolation	Date of Discharge
1 : 1	Pontypool	M	6		11.5	1962	—	—	Yes	—
2 : 1	Pontypool	M	8	Brother of 1 : 1	25.2	1962	—	15.6	Yes	22.6
2 : 2	Pontypool	F	10	Sister of 1 : 1	26.3	Unvaccinated	—	13.6	Yes	22.6
2 : 3	Pontypool	M	4½ mths.	Brother of 1 : 1	2.6	Unvaccinated	—	14.6	Yes	9.7
3 : 1	Pontypool	F	9	School contact of 1 : 1, 2 : 1, 2 : 2	9.6	1962	—	17.6	Yes	9.7
3 : 2	Pontypool	F	5	School contact of 1 : 1, 2 : 1, 2 : 2	6.6	1961	—	18.6	Yes	9.7
3 : 3	Pontypool	M	8	School contact of 1 : 1, 2 : 1, 2 : 2	6.6	Unvaccinated	—	18.6	Yes	9.7
3 : 4	Pontypool	M	9	School contact of 1 : 1, 2 : 1, 2 : 2	8.6	1957	—	18.6	Yes	9.7

TABLE II.29

Year	Primary vaccinations					Re-vaccinations				
	Under 1 Year	1-4 years inclusive	5-14 years inclusive	15 years and over	Total	Under 1 Year	1-4 years inclusive	5-14 years inclusive	15 years and over	Total
1957	303,406	51,906	29,766	39,189	424,267	826	4,679	18,052	90,286	113,843
1958	327,063	48,241	18,929	27,008	421,241	512	3,143	13,569	75,570	92,794
1959	337,310	47,831	14,248	23,433	422,822	679	3,540	10,228	61,471	75,918
1960	312,331	56,521	15,322	24,462	408,636	428	3,379	10,965	66,648	81,420
1961	319,532	81,852	21,188	30,322	452,894	431	3,912	12,927	72,585	89,855
1962	409,195	422,218	976,129	1,423,373	3,230,915	998	70,223	613,699	2,373,354	3,058,274
1963	76,139	79,105	18,480	30,142	203,866	275	4,841	16,938	77,975	100,029
1964	67,043	246,445	10,816	20,413	344,717	160	5,487	15,946	68,551	90,144
1965	50,381	328,441	15,102*	—	393,924	83	4,873	27,589*	—	32,545
1966	43,705	396,206	40,539*	—	480,450	112	6,260	64,083*	—	70,455

*5-15 years inclusive

outbreaks; this explanation is supported by the marked increase in *primary* vaccinations in the same age group (5-15 years). The total number of children vaccinated in the first two years of life is 38% of this age-group as compared with 33% in 1965.

Complications of Vaccination

(a) *Benign generalised vaccinia*

Nine cases of this condition were reported by local health authorities to have occurred in children after primary vaccinations performed during 1966 under Section 26 of the National Health Service Act. 8 of the children were in the second year of life and 1 was 4 years old.

Reports were also received of a further 8 cases, 1 in a baby of 4 months vaccinated in Greece, and 7 in adults all but 1 of whom had received *primary* vaccination.

All the above cases were mild and recovered fully within a few days.

(b) *Eczema vaccinatum*

4 cases were associated with vaccinations performed under local health authority arrangements. 3 of these were in children in the 2nd year of life; 1 child was a known case of atopic eczema and the others had a history of the condition. The 2 most severe cases received methisazone and antivaccinial gamma-globulin respectively. All made satisfactory recoveries.

The fourth case was in a boy of 2½. He had a history of infantile eczema but had been clear for 4 months. The child recovered fairly quickly, although areas of permanent depigmentation were left.

Information was also received about a man of 22 with a past history of eczema; there had been no observed lesion for at least two years. Primary vaccination was performed and a few days later numerous fresh lesions appeared, particularly on the face and neck. There was little systemic upset, however, and he made a good recovery.

5 cases, two of which were fatal, were reported in which eczema vaccinatum occurred in persons not themselves recently vaccinated. In one case, the source of vaccinia infection was unknown; the other four cases show the risk entailed in introducing vaccinia virus into a household where there is anyone suffering from, or with a history of, eczema.

TABLE II.27
Smallpox (*variola minor*)—Salford C.B.

Case No.	Location	Sex	Age	Infection	Onset of Illness	Time of Vaccination	Retrospective Diagnosis	Date of admission to smallpox hospital	Diagnosis confirmed by virus isolation	Date of Discharge
1:1	Salford C.B.	F	52	Grandson of 1:1	Mid May 29.5	Unvaccinated	Yes	—	—	—
2:1	Salford C.B.	M	2½	Grand-daughter of 1:1	29.5	Unvaccinated	Yes	—	—	—
2:2	Salford C.B.	F	3½	Grand-daughter of 1:1	29.5	Unvaccinated	—	—	Yes	—
2:3	Salford C.B.	F	5	Grand-daughter of 1:1	29.5	Unvaccinated	Yes	21.7	—	13.8
3:1	Salford C.B.	M	54	Paternal Grandfather of 2:1	19.6	Unvaccinated	—	—	Yes	—
3:2	Salford C.B.	M	2½	Son of 3:1	Mid June 17.6	1961 Infancy	Yes	—	—	—
3:3	Salford C.B.	F	24	Wife of 3:2	17.6	Unvaccinated	Yes	18.7	—	—
3:4	Salford C.B.	F	5	Contact of 2:3	5.7	Unvaccinated	—	16.7	Yes	—
4:1	Salford C.B.	F	52	Wife of 3:1	9.7	Unvaccinated	—	18.7	Yes	—
4:2	Salford C.B.	F	28	Mother of 3:4	9.7	Unvaccinated	—	18.7	Yes	—
4:3	Salford C.B.	M	7	Son of 4:2	9.7	Unvaccinated	—	18.7	Yes	—
4:4	Salford C.B.	M	4	Son of 4:2	9.7	Unvaccinated	—	18.7	Yes	—
4:5	Salford C.B.	M	2	Son of 4:2	9.7	Unvaccinated	—	18.7	Yes	—

TABLE II.28
Smallpox (variola minor)—Solihull C.B.

Case No.	Location	Sex	Age	Infection	Onset of Illness	Time of Vaccination	Retrospective Diagnosis	Date of admission to smallpox hospital	Diagnosis confirmed by virus isolation	Date of Discharge
1 : 1	Solihull C.B.	M	18		10.6	Unvaccinated	---	10.7	---	20.7
2 : 1	Solihull C.B.	F	48	Mother of 1 : 1	24.6	Unvaccinated	---	10.7	Yes	1.8
2 : 2	Solihull C.B.	M	15	Brother of 1 : 1	30.6	Unvaccinated	---	10.7	Yes	28.7

The details are as follows:

1. A boy of 2, who was suffering from atopic eczema, developed eczema vaccinatum a fortnight after his cousin, who was staying in the same house at the time, had received primary vaccination. Despite the administration of antivaccinial gamma-globulin, very widespread lesions developed, and he died on the eighth day of illness.
2. The sister of (1), aged 3, who was also eczematous, developed the same complication. She was severely affected but eventually made a satisfactory recovery, after receiving antivaccinial gamma-globulin.
3. The infant twin sisters of a girl aged 2 with a history of atopic eczema were vaccinated. Nearly 3 weeks after this the unvaccinated child developed slight pyrexia and patchy skin lesions. Antivaccinial gamma-globulin was given and she rapidly made a complete recovery.
4. A girl of 3 with a history of atopic eczema developed eczema vaccinatum 2 weeks after her younger sister had been vaccinated. She became very ill, with high fever and an extensive pustular eruption; antivaccinial gamma-globulin was administered. The eruption was slow to clear and her convalescence protracted.
5. A man of 47 with widespread seborrhoeic dermatitis developed severe eczema vaccinatum. Vaccinia virus were isolated on egg culture of material from some of the lesions. Bronchopneumonia supervened and the patient died 10 days after the onset of symptoms. It is not known how he contracted the vaccinial infection, but at that time more smallpox vaccinations than usual were being performed in the area.

(c) *Post-vaccinal Encephalomyelitis*

Four cases were associated with routine vaccinations performed under local health authority arrangements. These involved 2 girls aged 16 months, a boy of 13, and a boy aged 3. This last patient, the only one of the 4 not to recover completely, became ill 10 days after primary vaccination with high fever and coma. He regained consciousness after 2 days, but it is feared that there may have been considerable brain damage with resultant mental handicap.

4 other cases of this condition, 1 of which was fatal, were reported.

- i. A woman aged 53 received primary vaccination before going on holiday abroad. 2 weeks later she had slight pyrexia and complained of pain in the limbs. Muscle weakness and sensory disturbances were noted, and she was admitted to hospital 5 days after the onset of the illness. By the following day the patient's condition had deteriorated a great deal; drowsiness was marked and there was difficulty in speaking, swallowing and breathing. She was put in a respirator but died within a few minutes.
- ii. A woman aged 56 received primary vaccination before going on a cruise to North Africa. 17 days later, while in the Canary Islands, she suddenly developed paraplegia, with retention of urine. On her return to this country a month afterwards bladder function was normal but there was bilateral muscle weakness from the hips downwards, so that she required help to stand. This patient was admitted to Stoke Mandeville Hospital for specialised management.

- iii. A woman of 40 had a primary vaccination before going on holiday abroad. Nine days later she became dizzy and semi-comatose and was admitted to hospital. There was headache and nausea, with slight neck rigidity, and the cerebro-spinal fluid showed a slight increase in protein. Recovery was rapid and complete.
- iv. A soldier of 18 received primary vaccination and 2 weeks later headache, malaise and nuchal rigidity were noted. Protein in C.S.F. was considerably raised. He made a rapid and complete recovery.

One other case should be mentioned in this context. A boy aged 12 was certified as having died from status epilepticus. His first fit had occurred in 1954 shortly after primary vaccination. Further convulsions followed diphtheria inoculation and an attack of tonsillitis; later they became more frequent. In retrospect, post-vaccinal encephalitis was considered to have been the cause of the epileptic condition.

APPENDIX 11

HUMAN BLOOD TESTS

Samples of blood were donated by 90 members of the Anatomy and Medical Microbiology Departments. Haemagglutination-inhibition titres were measured and reported by Dr. M. S. Pereira, PHLS, Colindale.

No. of persons tested	No. of persons with antibody titre of				
	10 or less	20	40	80	160
90	54	19	6	7	4

APPENDIX 12

TESTS ON MONKEY BLOOD

During the early part of the investigation the poxvirus concerned had not been identified and the primate colony was a potential source of infection.

Blood was taken from animals in the primate house to determine their haemagglutination titres. The tests were carried out by Dr. M. S. Pereira, (PHLS Colindale), who submitted the following report:

Results of haemagglutination-inhibition tests on monkey and marmoset sera for antibody to vaccinia virus.

1. 99 blood samples from monkeys, received 18.9.78
All negative at 1/10
2. 84 blood samples from monkeys, received 22.9.78
All negative at 1/10
except *Monkey No. 566 which has a titre of 1/40*
3. 17 blood samples from marmosets, received 22.9.78
All negative at 1/10
4. Monkey 566
1st blood received 22.9.78
2nd blood received 6.10.78

Retested by haemagglutination-inhibition with 4AD vaccinia virus before and after treatment with M/90 Potassium Periodate.

- 1st blood 1/20
- 2nd blood 1/20

These results suggest antibody rather than non-specific inhibitor.

Professor Dumbell has the first serum and perhaps may be able to test it against monkey pox. Dr. Makane thought it could represent antibody to this virus.

APPENDIX 13

COX REPORT CODE OF PRACTICE

The Cox Report* included a suggested interim Code of Practice for Safety in Laboratories handling smallpox virus which had been agreed by Virologists from the Universities of Birmingham, Liverpool and Reading, the London School of Hygiene and Tropical Medicine and St. Mary's Hospital Medical School, London.

Interim Code of Practice

A. *Protection by vaccination:*

1. All new members of the staff of the laboratory to be vaccinated as a condition of their employment, and at intervals not greater than two years thereafter.
2. Regular vaccination and revaccination also to be done on the cleaners, maintenance staff, service engineers, window cleaners, relevant groups of students and any others needing frequent access to the department.
3. Regular vaccination and revaccination to be offered, with reasons, to members of departments in the same building.
4. Regular vaccination and revaccination to be offered to families of staff.
5. One person to be responsible for arranging vaccinations and keeping records.
6. All vaccinations and revaccinations to be inspected subsequently and repeated if no "major" reaction is observed.

B. *Reporting of illness:*

1. All members of the department to be provided with a card stating that the holder works in a department of microbiology where pathogenic viruses, including smallpox, are handled, and that special consideration should be given to any febrile illness or rash. This card is intended to be given to the general medical practitioner. Those actually working with smallpox virus should also be provided with a card to carry themselves, stating the nature of their work.
2. The laboratory to keep a record, wherever possible, of the doctors with whom members of the staff are registered. Those working in the department should ensure that the director is informed if they develop any febrile illness or rash.

C. *Access to the laboratory:*

1. Work with smallpox virus to be confined to designated rooms. These rooms to be clearly labelled with a warning notice.
2. Access to the smallpox area to be available only to those known to have been vaccinated within the previous 2 years, or holding a valid International Certificate of vaccination.

*Cmnd 5626 HMSO London June 1974.

D. *Handling of virus:*

1. Technique must be of the highest quality at all times. This is probably the most important single factor in the safe handling of smallpox.
2. A suitable safety cabinet is to be used for procedures such as preparing clinical specimens for inoculation, making dilutions, inoculation and harvesting of eggs, where aerosols are likely to be generated.
3. All discarded materials to be sterilized within the room or removed in a closed container for immediate autoclaving.
4. Separate protective gowns (rear-fastening) to be worn while handling smallpox virus. These to be autoclaved or steamed before being sent to the laundry.
5. Washing facilities to be provided with elbow or foot control.
6. Care to be taken not to contaminate apparatus. Important examples are:
 - (a) Electron microscopes. Grids with suspect smallpox material should be sterilized before being loaded into the machine.
 - (b) Centrifuges. Models should be chosen, preferably with a sealed rotor or sealed buckets, or with at least a windshield and cover. It is desirable to keep bench centrifuges in a safety hood and to insert an absolute filter in the line to the vacuum pump in high speed centrifuges.
7. Records made in the working area to be disinfected before removal.

E. *Inoculation of animals:*

Inoculation of animals presents particular hazards and should not normally be undertaken, except in institutes with specially designed facilities.

APPENDIX 14

COX REPORT RECOMMENDATIONS

Recommendations concerning the future control for work with Category A pathogens were made in the Cox Report.*

RECOMMENDATIONS

Laboratory Work

Permanent Committee of Experts

1. We RECOMMEND the establishment of a permanent committee of experts, including laboratory experts in smallpox, which would:
 - i. designate a list of pathogens including smallpox virus, laboratory work with which constitutes a major threat to public health;
 - ii. maintain for public inspection a register of establishments and departments within them where any work with designated pathogens is being undertaken;
 - iii. formulate and regularly review a code of practice necessary for the safe conduct of all procedures in the appropriate laboratories of such registered premises; and
 - iv. have the requisite powers to ensure that no potentially hazardous work is undertaken in those laboratories unless the code is followed.

Code of Practice

2. While we do not consider it appropriate for us to draft the complete details of such a code nor to list the detailed facilities required for its effective implementation we RECOMMEND the inclusion of the following:
 - i. all open manipulations of smallpox virus, whether for research or for diagnostic purposes, should be carried out in suitable safety cabinets;
 - ii. such work should be carried out in laboratory rooms solely used for this purpose. These should be locked when not in use and disinfected at intervals and, in any event, before reverting to other use;
 - iii. smallpox virus should be stored within the designated laboratory room or if in a refrigerator elsewhere this should be kept locked;
 - iv. wherever possible work with smallpox not involving open manipulation of the virus, e.g. centrifuging or incubating infected eggs or tissue cultures should also be confined to the designated laboratory room. If this is not possible the work must be done in such a fashion as to prevent the escape of virus from its container which should only be opened in the safety cabinet. If incubator rooms are used they must be locked when left unattended;

*Cmnd 5626 HMSO London June 1974.

- v. access to the designated laboratory room should be restricted to specifically identified persons whose immunity status is known and whose names are listed on the door of that laboratory or who carry written authorisation from the head of the department or his appointed representative. Casual authorised visitors should be required to sign a visitors' book;
- vi. laboratory rooms designated for manipulative work with smallpox virus should not be connected to the general ventilation extract ducts unless a suitable filter is interposed. Separate ventilation with filtration of the extracted air is preferable;
- vii. experimental animal rooms used for smallpox infected animals capable of shedding virus must be separated from other animal rooms by a suitable air lock where protective clothing is put on. Air extracted from the animal room and air lock should be filtered or otherwise disinfected;
- viii. effective vaccination against smallpox should be made a condition of service of all staff, including clerical, cleaning and maintenance, of all smallpox diagnostic and research units and this requirement should be extended to all the staff of all departments of microbiology, virology, etc. within which there is a unit carrying on smallpox work;
- ix. revaccination with a check for proper take should be carried out annually on all those who have regular daily access to the designated smallpox laboratory room while those who have occasional access for the purpose of cleaning or maintenance and the like when no actual smallpox work is being done should be revaccinated with a check for take every two years;
- x. complete up-to-date records of the vaccination status of all the persons employed in the whole administrative unit or department, whether or not they have access to the designated smallpox laboratory room should be maintained in a form which enables them to be made available for inspection by third parties without offending medical confidence;
- xi. vaccination and revaccination every two years with checks for take should be offered to the families of staff engaged directly upon regular or occasional smallpox work;
- xii. all persons working with dangerous pathogens should be instructed as to the early symptoms of the disease produced by such pathogens;
- xiii. appropriately worded cards indicating that the holder is working with smallpox virus or is employed in a laboratory or department where smallpox work is being carried on, should be carried by all staff with instructions that the card is to be shown to any medical practitioner who is called or consulted in the event of illness. The card should bear the address and telephone number of the person or persons at the laboratory to be consulted by the doctor. Such cards could usefully include details of the early symptoms of smallpox;

- xiv. gowns fastening at the back and without unnecessary openings elsewhere should be worn at all times by persons engaged in manipulative smallpox work. Clean gowns should be donned before entry to the designated laboratory room and, unless disposable, they should be removed and autoclaved as a matter of routine after every occasion of use;
 elbow taps or preferably foot operated water taps should be provided at all sinks and wash basins within the designated laboratory room;
- xvi. printed accident report forms should be provided for all laboratories, and all staff should be made aware of the procedure to be followed in the event of a laboratory accident;
- xvii. the designated smallpox laboratory room should not open onto a communal corridor. An ante-room or at least a glass vestibule should intervene and a viewing window should allow observation of the inner room;
- xviii. the provision of special shoes to be worn only within the laboratory, or a disinfection soaked mat at the entrance should be considered;
- xix. the provisions of a laboratory inter-com to be used in an emergency should be considered;

The London School of Hygiene and Tropical Medicine

3. In addition to those general recommendations in relation to smallpox work set out in 2 above we RECOMMEND that the London School of Hygiene should:

- i. appoint an appropriately trained safety officer as a full time appointment responsible to the Dean for safety throughout the school premises, including those laboratories occupied by other bodies, and charged inter-alia with the duty to:
 - a. investigate laboratory procedures and detect hazards;
 - b. implement committee decisions on safety and progress other safety work;
 - c. be responsible for the training of technicians and other staff in safety matters;
 - d. approve the entry of cleaning and maintenance staff to hazardous laboratories;
 - e. supervise the central sterilising unit and animal house;
 - f. advise upon the safety implications of all new research projects;
 - g. keep the school up to date upon new safety knowledge;
 - h. receive all accident reports and if necessary refer the matter to an appropriately qualified doctor; and
 - j. agree with departmental heads the departmental immunisation programmes including the maintenance of records.
- ii. ensure that the Public Health Laboratory Service (Mycological Reference Laboratory) and its staff are subject to all the safety requirements of the school.

Other Laboratories

4. We RECOMMEND that pending implementation of recommendation 1 other establishments where laboratory work involving dangerous pathogens, including smallpox, is carried on should continue to follow the Interim Code and should review their safety organisation in the light of recommendations 2 and 3.

Finance

5. Substantial sums of money will be required if the above recommendations are to be implemented, and we RECOMMEND that urgent consideration be given to the provision of appropriate grants for this purpose.

APPENDIX 15

GODBER RECOMMENDATIONS

The Godber Committee* was set up to consider whether there are organisms capable of causing communicable diseases that require measures to be taken in laboratories or elsewhere additional to those now recommended, in order to prevent infection in man or in animals and to make recommendations as to the measures required.

In consultation with coopted members a sub-group drew up:—

Code of Practice for Use in Laboratories Holding Category A Pathogens

Introduction

1. This code of practice is for use in laboratories holding category A pathogens and should be regarded, for the time being as supplementary to the basic safety procedures commended in the PHLs monograph "The Prevention of Laboratory Acquired Infection," and in due course to the code of practice we propose should be drawn up for the handling of category B pathogens.

2. As Category A pathogens are not a homogeneous group, but display widely differing properties it is not expected that the whole code would be applied in all circumstances (see paragraph 48 of our report).

3. The Dangerous Pathogens Advisory would be able to exercise discretion in advising Departments:

either if it were satisfied that the ends which the Code sought to achieve were fully met by other means

or if it decided that the hazards presented by a certain type of work on a specific pathogen in a particular laboratory required either reinforcement or relaxation of the measures laid down in the code.

4. Thus, the Dangerous Pathogens Advisory Group would advise on the precise precautions necessary to be taken in each laboratory individually. As this involves a consideration of the particular pathogen(s) held and of the type of work proposed it follows that any authority to proceed would be given for specified work on specified pathogens. Any extension of the pathogens held or the scope of the work performed would need a separate application to the appropriate Department.

5. The practice appropriate to a particular laboratory depends upon the nature of the work being carried out, and this is determined to some extent by the purpose that is being served. In terms of objectives, laboratory work with pathogens can be divided into the following categories. One laboratory may be carrying out work of several different types at the same time.

*Cmnd 6054 HMSO 1975.

Service diagnostic laboratories
Reference diagnostic laboratories
Culture reference collections
Research
Teaching
Work associated with manufacturing procedures

6. Service diagnostic laboratories receive large numbers of specimens containing unidentified micro-organisms. For example, NHS laboratories in England received over 10 million requests for work in general microbiology in 1972. Pathogens in category A are encountered rarely in this country, although the possibility exists that such a pathogen may be present in a specimen sent to a service diagnostic laboratory. All laboratories handling pathogens should observe a suitable code of practice. However, it is not practicable for service diagnostic laboratories to handle all the large numbers of specimens received as though they contained category A pathogens. Obviously extreme care must be exercised in dealing with a specimen if there is any reason to believe that it may contain one of the pathogens in category A. Such belief might be based on clinical symptoms, or may arise in the course of laboratory examination. In such cases, it will be appropriate to observe certain of the precautions detailed herein, for example, those relating to protective clothing and the handling and packaging of specimens.

Material suspected of containing a pathogen in category A should be removed at the earliest opportunity from a service diagnostic laboratory to a properly equipped reference diagnostic laboratory. Appropriate precautions should be taken when the material is moved, and it may be necessary to carry out disinfection procedures at the service laboratory.

7. Reference diagnostic laboratories receive specimens suspected of containing category A pathogens (particularly smallpox) so that the identification can be confirmed or disproved. They should be constructed and equipped in such a way that this work can be carried out without hazard to the staff and to the general public: their structure, equipment and methods of working should be subject to approval by the appropriate Department.

8. Culture reference collections which hold pathogens in category A carry out a minimal amount of manipulation in order to maintain the cultures. The appropriate parts of the code of practice given herein should be observed when this is done, and the cultures should be held under proper security.

9. Research, teaching and work associated with manufacture procedures include a variety of activities. When pathogens in category A are used, this Code of Practice should be applied, subject to any modifications advised by the Dangerous Pathogens Advisory Group. Teaching practices, in particular, should be reviewed critically to ensure that category A pathogens are only used when there is no suitable alternative.

NOTE: Throughout this code the term "laboratory" is used to mean any room or rooms in which category A pathogens are handled, and as appropriate, linking corridors.

A. THE TOXIC LABORATORY—SITING AND STRUCTURE

1. Whereas the toxic laboratory need not be physically separated from other laboratories it should not be sited next to a known fire hazard (e.g. the solvent store) or be in danger of flooding (e.g. under a room where water is, or may be, flowing unattended).

2. The laboratory should be isolated from the corridor (or another room) by an air lock. Air locks and rooms must be ventilated by a plenum and exhaust (filtered) air system. The air pressure within the laboratory must be maintained at least 0.3" water gauge below that in the corridor and must be displayed on a manometer which can be read without entering the laboratory.

3. The laboratory must be sealable so as to permit fumigation.

4. If work is carried out on category A pathogens which can be transmitted by animal or insect vectors, the laboratory must be proof against entry or exit of such animals or insects.

5. Liquid effluent should not be flushed directly from the laboratory to the public sewer.

B. LABORATORY FACILITIES

1. Work on Category A pathogens must not be carried out in normal safety (exhaust protective) cabinets in an otherwise standard laboratory.

2. Each toxic laboratory must have direct access to an autoclave with double doors in which all discarded materials should be sterilized prior to cleaning or disposal. There should be no possibility of removing the load on the "clean" side without the autoclave cycle having been completed.

3. Each member of staff working in the laboratory should have adequate air space.

4. Pathogens must be stored in suitable containers (depending on the mode of storage, frozen or freeze-dried) in a locked cabinet reserved for category A pathogens. A key should be available on demand only to nominated individual(s).

C. PROTECTIVE CLOTHING

1. *Laboratory Gowns* should wrap over the chest and fit tightly at the wrists. Ordinary white laboratory coats are unsuitable. Staff should have a clean gown for each uninterrupted period spent in the laboratory.

2. *Gowns* must be autoclaved before they are removed from the toxic laboratory.

3. *Gloves*: Surgical gloves must be worn in the toxic laboratory.

4. *Face-shields*, caps respirators and plastic or otherwise impervious clothing must be available and used in appropriate circumstances, e.g. when there are hazards from splashes or aerosols.

D. SAFETY OFFICER

1. A Safety Officer must be appointed.
2. The Safety Officer should have appropriate qualifications and laboratory experience in working with Category A pathogens.
3. The Safety Officer will act as adviser to the Director of the establishment in all matters which may affect the safety of the staff and the containment of the organisms.
4. He will take control, render first aid in, and investigate, all accidents in toxic laboratories and take what other action he considers necessary.
5. Where his responsibilities are not sufficient to warrant his full-time employment as safety officer then, provided that he is readily accessible to the laboratory during normal hours, he may hold another appointment.
6. He will be responsible for the safe storage of pathogens and the maintenance of the inventory.
7. He will be responsible for organising the admission to the laboratory of cleaners and maintenance men and for the disinfection of any apparatus, etc. which is to be removed.
8. He will be responsible for advising staff on all aspects of the application of this Code of Practice.
9. He will liaise with the Medical Officer for Environmental Health and the family doctors of staff with health cards (see Section K below).
10. He will organise the initial training in the safe handling of pathogens of staff required to begin work in a toxic laboratory.

E. TRAINING IN HANDLING PATHOGENS

1. The Safety Officer should be responsible for the initial training of all junior, or inexperienced, staff joining the laboratory.
2. Training will cover, e.g. the correct use of safety-hoods; pipettes; syringes/needles; hot/cold rooms; centrifuges; blenders; freeze-drying; shaking machines; ultra-sonic disintegrators; glassware and the disposal of contaminated protective clothing and laboratory materials.
3. Since it is imperative that laboratory discipline should not be relaxed, junior staff, while being encouraged to be safety conscious, should not train others in safe handling.
4. A senior laboratory staff member should continuously supervise the work of the more junior.
5. Staff should only work with Category A pathogens if they have some previous experience in microbiology and have had a course of training supervised by the Safety Officer and are at least 18 years of age.

F. SUPERVISION

1. Work in the toxic laboratory should, at all times, be supervised by a senior, trained and experienced member of the staff in person.
2. Laboratory staff should never work alone.
3. The supervisor will be personally responsible to the Safety Officer for the safety of the work actually in progress at any time, although he may not be responsible for the overall project.
4. Suitable restrictions should be imposed on contact between handlers of pathogens and patients and/or livestock.

G. LABORATORY DISCIPLINE

1. Each toxic laboratory should be identified clearly with a large sign.
2. When not in use the laboratory must be locked. The key(s) should be kept in a central position, under the supervision of the Safety Officer, and released only to authorised personnel.
3. In normal hours the supervisor will be responsible to the Safety Officer for ensuring that no unauthorised individual enters it.
4. The Safety Officer will hold a list of all those authorised to enter the toxic laboratory.
5. No unlisted personnel (e.g. visitor, observer, cleaner or maintenance/ repair man) will enter the laboratory unless he has received a signed statement from the Safety Officer that it is safe for him to do so.
6. The Safety Officer will be responsible for confirming that a laboratory and its apparatus have been disinfected.
7. On entering, laboratory personnel must go through the air lock to a "clean" side changing area (locker room) separated from the "dirty" side by a shower. Normal clothing, rings, watches etc. are removed into a locker. Clean sterile protective clothing (see Section D) is put on. Where appropriate, protective overgarments, including respirator and hood should be worn. Rubber boots should be put on just prior to entering the toxic area. The "clean" and "dirty" areas should be clearly distinguished physically.
8. On the way out boots and gloves should be washed in a suitable disinfectant (e.g. 5% chlorox). Overgarments should be placed in a bin on the "dirty" side of the showers and all remaining clothing also removed to a bin. Gloves should be the last to go. The individual then showers, transfers to the "clean" side and dresses.
9. This procedure must be adhered to whenever, and for whatever purpose, the room is vacated.

10. Eating, drinking or smoking will not be permitted in any toxic laboratory or animal room at any time.

11. All accidents, or spillages, in the toxic laboratory must be reported immediately to the Safety Officer. Every such incident must be regarded as a full medical or animal disease hazard.

12. The day-to-day cleanliness of a toxic laboratory is the responsibility of those working in it. Only when the Safety Officer has confirmed that it has been successfully disinfected can other cleaning/maintenance work be carried out.

13. At the end of a working day benches and working surfaces should be disinfected.

14. Periodically, and certainly at the end of any particular experimental procedure, the rooms and everything in them must be fumigated with gaseous formaldehyde.

H. HANDLING INCOMING SPECIMENS

1. Clerical staff should not be permitted to open incoming specimens, or packages purporting to contain pathogens.

2. Packets should be opened by someone trained to take appropriate action if the contents are found to be damaged or leaking.

3. It is undesirable for laboratories to transfer category A pathogens by any form of public carrier but, if it is unavoidable then the specimen should be sealed in a leak-proof container and the intended recipient warned of its despatch. (See Section I below).

4. Particular care is necessary when material is to be transferred from the toxic to other laboratories. Pathogens may remain viable after being prepared for electron microscopy. The Safety Officer must be consulted before all transfers.

I. PACKAGING

1. An externally-identified liquid sample should be sealed in a tin can filled with sufficient absorbent material wholly to mop up a spill. The can may if necessary be cooled in solid carbon dioxide or liquid nitrogen.

2. Solid samples should be so wrapped that, in the event of the container being ruptured, it will be apparent whether or not material could have escaped.

3. A specimen for diagnostic purposes should be treated as described by Collins *et al.* (The Prevention of Laboratory Acquired Infection, pp 11-14).

J. SECURITY

1. It is imperative that the laboratory and animal rooms should be secure against the entry of intruders or vandals.

2. Security patrols, etc. should not enter toxic laboratories, or animal rooms. If it appears that an adjacent fire or water hazard threatens the room then the Safety Officer should be informed immediately.

3. A key to the laboratory should be held centrally (see Section G above) for emergency access but should only be released on the instructions of the Safety Officer (e.g. if he knows that the room has been disinfected then he can do this by telephone).

4. The Safety Officer should have a list of pathogens (categories A and B) held in all toxic laboratories in his charge and know where they are deposited (see Section D above).

5. Any pathogens removed should be signed for, and none should be added without the Safety Officer's knowledge.

K. HEALTH OF STAFF

1. The conventional health declaration form may not be adequate to eliminate those who ought not to work with category A pathogens and it may be necessary to supplement this with a medical examination and, if necessary, to insist on this, and on vaccination where appropriate, as a condition of employment.

2. Each employee in a toxic laboratory should carry a card which tells his family doctor that, if he is ill, he may have contracted a serious infectious disease requiring his isolation, and requesting the doctor to contact the Safety Officer.

3. The name of the doctor, to whose list an employee is attached, should be recorded by the Safety Officer.

4. It is desirable that, on appointment of an employee to work in the toxic laboratories, his GP should be informed of the nature of this work.

5. The card should be carried by everyone who could have contact at work with the toxic laboratory/animal room.

6. Each such employee should be vaccinated against the organisms with which the laboratory is working so far as this is possible.

7. The immune status of vaccinees should be maintained at an optimum level, and where possible and desirable measured periodically.

8. Records of the health and vaccination status of staff in toxic laboratories must be maintained at a central point and be accessible in an emergency.

9. Vaccination should also be offered to the immediate families of the staff.

10. Staff members should be responsible for reporting absences, due to ill-health, to the Safety Officer. He will enquire, where appropriate, of the patients' own doctor.

11. Where a member of staff fails to attend, without notifying the Safety Officer, his supervisor should immediately institute enquiries.

L. ANIMAL ROOM

NOTE: All relevant regulations in this Code of Practice apply to any room in which animals are under treatment with a category A pathogen. There are, in addition, hazards arising from the natural diseases of animals which may be transmissible to man. These include rabies, leptospirosis, ornithosis, Monkey B etc. Diseases can be contracted following bites, scratches, droplet infection or the bites of insect vectors. There are particular hazards associated with the generation of aerosols in animal rooms.

In addition to the staff utilizing the animals others may be engaged to clean and feed them and the code applies also to them.

1. Dust: accumulations of dust in the ventilation system must be cleared.
2. Drains: (see Section A above).
3. Dead animals: after post-mortem examination carcasses must be incinerated on site or autoclaved before they leave the site. Where incineration would create a radio-biological hazard, carcasses must be suitably sealed.
4. Bedding, dung, etc.: these materials must also be rendered innocuous.
5. Cages: all cages must be autoclaved before being cleaned and returned to store.
6. Escapes: animal rooms should have double doors. In no circumstances should there be a direct exit to the outside. However, animals can be "misaid" and when this happens the Safety Officer must be informed.
7. Vermin: suspected, or obvious, infestation with insects, or wild rodents, must be reported at once to the Safety Officer.
8. Monkeys: the principal hazard in monkey handling not common to the handling of other animals is the risk of infection with Monkey B virus, which can produce a fatal paralytic encephalitis in man. In monkeys, the disease consists of herpetic lesions of lips and mouth, and, whilst it can be transmitted to primates from other parts of the globe, is generally confined to eastern species. The following basic rules for handling must be observed:—
 - i. Monkeys from different intake batches must not be accommodated in the same room.
 - ii. Cages and droppings must be handled as if the animals were known to be infected.
 - iii. Whenever monkeys are handled two or more persons must be present, one of whom must be an experienced handler.
 - iv. Nets or cages traps must be provided for the capture of escaped monkeys, and windows fitted with bars. Doors must be kept shut during handling. All other openings in walls, floors or ceilings must be suitably secured.

- v. Unless experimental conditions absolutely contra-indicate it monkeys must always be anaesthetised before handling. Care must be taken to ensure the animals really are "out" before removal from the cage.
 - vi. Whenever monkeys are anaesthetised the opportunity should be taken to examine the lips, tongue and gums for herpetic lesions. This should be done with the aid of blunt forceps. Any monkey suspected of being infected must be destroyed IMMEDIATELY.
 - vii. Protective clothing will consist of gown, gloves, gum-boots, face shield, surgical mask and cap. A change of undergarments and a shower are required afterwards.
 - viii. Care should be taken to ensure that adequate quantities of freshly made up disinfectant solution are available in dunk troughs and hand basins.
 - ix. Skin punctures and abrasions resulting from handling monkeys or potentially monkey-contaminated material must be treated IMMEDIATELY with disinfectant and reported to the Safety Officer forthwith.
 - x. Injured personnel must be kept under daily observation for a minimum of 3 weeks, and any indisposition, particularly fever or muscular weakness, must be reported IMMEDIATELY at onset.
9. Responsibility: general animal house staff should not service toxic rooms. This staff should be specially trained and the Safety Officer should be responsible for them.

APPENDIX 16

DPAG RECOMMENDATIONS

In October 1976 the DHSS issued a handbook approved by the Dangerous Pathogens Advisory Group entitled:—

“Control of laboratory use in the United Kingdom of pathogens very dangerous to humans”. The section concerned with safety procedures is recorded here.

Safety Precautions for Laboratories Handling or Holding Category A Pathogens

Note: The term laboratory is used throughout to mean any room or rooms and as appropriate, linking corridors, in which category A pathogens are handled or stored.

Introduction

1. The precautions described here are those which may be required of a laboratory handling or holding category A pathogens in addition to the basic safety precautions which are needed when dealing with other pathogens (see, for example, “The Prevention of Laboratory Acquired Infection”—Collins C. H; Hartley E. G; and Pilsworth R, PHLs Monograph No. 6 London HMSO 1974). A code of practice for the prevention of infection in clinical laboratories is being prepared by a Department of Health and Social Security Working Party under the chairmanship of Sir James Howie (1976).

2. As category A pathogens are not a homogeneous group, but display widely differing properties it is not expected that the whole range of precautions will be applied in all circumstances.

3. The Dangerous Pathogens Advisory Group may exercise discretion in advising Departments:—

either if it is satisfied that the ends which the Precautions sought to achieve are fully met by other means

or if it decides that the hazards presented by a certain type of work on a specific pathogen in a particular laboratory require either reinforcement or relaxation of the measures laid down in the Safety Precautions.

4. Thus, the Dangerous Pathogens Advisory Group will advise on the precise precautions necessary to be taken in each laboratory individually. As this involves a consideration of the particular pathogen(s) held and of the type of work proposed, it follows that any authority to proceed will be given for specified work on specified pathogens. Any extension of the pathogens held or the scope of the work performed will need a separate application to the appropriate Department.

5. The practice appropriate to a particular laboratory depends upon the nature of the work being carried out, and this is determined to some extent by

the purpose that is being served. In terms of objectives, laboratory work with pathogens can be divided into the following categories. One laboratory may be carrying out work of several different types at the same time.

- Service diagnostic laboratories
- Reference diagnostic laboratories
- Culture reference collections
- Research
- Teaching
- Work associated with manufacturing procedures

6. Service diagnostic laboratories receive large numbers of specimens containing unidentified micro-organisms. For example, NHS laboratories in England received over 10 million requests for work in general microbiology in 1972. Pathogens in category A are encountered rarely in this country, although the possibility exists that such a pathogen may be present in a specimen sent to a service diagnostic laboratory. All laboratories handling pathogens should observe a suitable code of practice. However, it is not practicable for service diagnostic laboratories to handle all the large numbers of specimens received as though they contained category A pathogens. Obviously, extreme care must be exercised in dealing with a specimen if there is any reason to believe that it may contain one of the pathogens in category A. Such belief might be based on clinical symptoms, or may arise in the course of laboratory examination. In such cases, it will be appropriate to observe certain of the precautions detailed herein, for example, those relating to protective clothing, and the handling and packaging of specimens.

Material suspected of containing a pathogen in category A should be removed at the earliest opportunity from a service diagnostic laboratory to a properly equipped reference diagnostic laboratory. Appropriate precautions should be taken when the material is moved, and it may be necessary to carry out disinfection procedures at the service laboratory.

7. Reference diagnostic laboratories receive specimens suspected of containing category A pathogens (particularly smallpox) so that the identification can be confirmed or disproved. They should be constructed and equipped in such a way that this work can be carried out without hazard to the staff and to the general public: their structure, equipment and methods of working should be subject to approval by the appropriate Department.

8. Culture reference collections which hold pathogens in category A carry out a minimal amount of manipulation in order to maintain the cultures. The appropriate parts of the Safety Precautions given herein should be observed when this is done, and the cultures should be held under proper security.

9. Research, teaching and work associated with manufacturing procedures include a variety of activities. When pathogens in category A are used, these Safety Precautions should be applied, subject to any modifications advised by the Dangerous Pathogens Advisory Group. Teaching practices, in particular, should be reviewed critically to ensure that category A pathogens are only used when there is no suitable alternative.

A. THE LABORATORY—SITING AND STRUCTURE

1. Whereas the laboratory need not be physically separated from other laboratories it should not be sited next to a known fire hazard (e.g. the solvent store) or be in danger of flooding.

2. The laboratory should be isolated by an air lock and provided with a suitably placed shower (see G7). Air locks and rooms must be ventilated by an exhaust air system. The air pressure in the laboratory should be monitored and displayed both within and immediately outside the laboratory. The laboratory should be maintained at a differential negative pressure of 0.3 inches (7.6 mm) water pressure.

3. The exhaust air must be filtered before discharge through two HEPA filters. The system must include a device to prevent back flow through the filters.

4. The laboratory must be sealable so as to permit fumigation.

5. If work is carried out on category A pathogens which can be transmitted by animal or insect vectors, the laboratory must be proof against entry or exit of such animals or insects.

6. Effluent should be held in a standing tank, sterilised, and its sterility confirmed before discharge to the public sewer. Since sterilisation and tests may take some time, it will be necessary to have more than one standing tank if work is to be carried out continuously. If heat sterilisation is to be used, temperature recording facilities should be provided to monitor the process. The standing tank(s) and recording equipment form parts of the facilities of the laboratory, so the Safety Officer is responsible for ensuring their proper functioning.

B. LABORATORY FACILITIES

1. Work on category A pathogens must not be carried out in normal safety (exhaust protective) cabinets in an otherwise standard laboratory.

2. All material must be sterilised prior to removal from the laboratory. Therefore, each laboratory should have direct access to an autoclave which should have double doors. There should be no possibility of removing the load without the autoclave cycle having been completed.

3. Each member of staff working in the laboratory should have adequate air space.

4. Pathogens must be stored in suitable containers (depending on the mode of storage, frozen or freeze-dried) in a cabinet reserved for category A pathogens and kept under lock and key. A key should be available on demand only to nominated individual(s).

C. PROTECTIVE CLOTHING

1. Laboratory gowns should wrap over the chest and fit tightly at the wrists. Ordinary white laboratory coats are unsuitable. Staff should have a clean gown for each uninterrupted period spent in the laboratory.

2. Gowns must be autoclaved before they are removed from the laboratory.

3. Surgical gloves should be worn in the laboratory.

4. Special protective clothing is needed in particular circumstances, for example, when there are hazards from splashes or aerosols. Depending on the nature of the work, it may be necessary to use face-shields, caps, plastic or other protective clothing, respirators (a sterilisable full-face type with a high-efficiency filter complying with British Standard Specification 2091, 1969). As an alternative to a respirator, particularly for those with beards, it may be preferable to use a ventilated helmet: some types require a supply of compressed air.

D. SAFETY OFFICER

Note: Throughout this document the term Safety Officer refers to a person having responsibility, delegated by the Head of the Laboratory, for infectious hazards.

1. A Safety Officer able to advise on infectious hazards, and a deputy, must be appointed or designated. The establishment may have a Safety Officer with general responsibilities, and he may or may not be qualified to take on responsibility for infectious hazards. If not, an additional individual must be designated.

2. A Safety Officer should have appropriate qualifications and laboratory experience in working with category A pathogens.

3. The safety officer will act as adviser to the Head of the Department in all matters which may affect the safety of the staff and the containment of the organisms, and should be able to stop practices, considered unsafe pending guidance when necessary from the Laboratory Head.

4. He will take control, implement first aid in, and investigate, all accidents in laboratories and take what other action he considers necessary.

5. Where his responsibilities are not sufficient to warrant his full-time employment as Safety Officer then, provided that he is readily accessible to the laboratory during normal hours, he may hold another appointment.

6. He will be responsible for the safe storage of pathogens and the maintenance of the inventory.

7. He will be responsible for organising the admission to the laboratory of cleaners and maintenance men and for the disinfection of any apparatus, etc. which is to be removed.

8. He will be responsible for advising staff on all aspects of the application of these Safety Precautions.

9. He will liaise through the Head of the Laboratory with the Medical Officer for Environmental Health and the family doctors of staff with health cards (see Section K below).

E. TRAINING IN HANDLING PATHOGENS

1. The safety officer will organise the initial training in the safe handling of pathogens of staff required to begin work in a category A laboratory.

2. Training will cover, eg. the correct use of safety hoods; pipettes; syringes/needles; hot/cold rooms; centrifuges; blenders; freeze-drying; shaking machines; ultra-sonic disintegrators; glassware and the disposal of contaminated clothing and laboratory materials.

3. Staff should only work with category A pathogens if they have some previous experience in microbiology and have had a course of training supervised by the Safety Officer.

F. SUPERVISION

1. Laboratory staff should not work alone.

2. Work in the category A laboratory should, at all times, be supervised by a senior, trained and experienced member of the staff in person.

3. The supervisor will be personally responsible to the Safety Officer for the safety of the work actually in progress at any time, although he may not be responsible for the overall project.

4. When necessary suitable restrictions should be imposed on contact between handlers of category A pathogens and patients and/or livestock.

G. LABORATORY DISCIPLINE

1. Each category A laboratory must be identified clearly with a large sign.

2. When unoccupied, the laboratory must be locked. The key(s) must be kept under the supervision of the Safety Officer, and released only to authorised persons. A key, however, should be kept at a secure central point, available at all times, in case of emergency.

3. In normal hours the supervisor will be responsible to the safety officer for ensuring that no unauthorised person enters the laboratory.

4. Only the Safety Officer or his deputy can authorise staff to enter the laboratory, and he will hold a list of names of those so authorised.

5. No unlisted personnel (e.g. visitor, observer, cleaner or maintenance/repair man) will enter the laboratory unless he has received a signed statement from the Safety Officer that it is safe for him to do so.

6. The Safety Officer will be responsible for confirming when a laboratory and its apparatus have been disinfected.

7. The category A laboratory is entered through a "clean" side changing area (locker room) separated from the "dirty" side by a shower and airlock. All clothing, rings, watches, etc. should be removed into a locker. Clean protective clothing (see Section C) should be put on. Where appropriate, protective overgarments including respirator and hood should be worn. Rubber boots should be put on just prior to entering the toxic area. The "clean" and "dirty" areas should be clearly distinguished physically.

8. On the way out boots and gloves should be washed in a suitable disinfectant (hypochlorate, available chlorine 5,000 ppm, e.g. 5% chlorox). Overgarments should be placed in a bin on the "dirty" side of the showers and all remaining clothing also removed to a bin. Gloves should be the last to go. The individual should then shower, transfer to the "clean" side and dress.

9. This procedure should be adhered to whenever, and for whatever purpose, the room is vacated.

10. Eating, drinking or smoking will not be permitted in any laboratory or animal room at any time.

11. All accidents or spillages of potentially dangerous material in the laboratory must be reported immediately to the Safety Officer. Every such incident must be regarded as a full medical or animal disease hazard.

12. The day-to-day cleanliness of a toxic laboratory is the responsibility of those working in it. Only when the Safety Officer has confirmed that it has been successfully disinfected can other cleaning/maintenance work be carried out.

13. At the end of a working day benches and working surfaces should be disinfected.

14. Periodically, and certainly at the end of any particular experimental procedure, the rooms and everything in them must be fumigated with gaseous formaldehyde.

H. AND I. HANDLING OF SPECIMENS

1. Clerical staff should not be permitted to open incoming specimens, or packages purporting to contain pathogens.

2. All packages thought to contain category A pathogens must be opened by trained staff, in the laboratory.

3. An externally-identified liquid sample should be sealed in a tin can filled with sufficient absorbent material wholly to mop up a spill. The can may, if necessary, be cooled in solid carbon dioxide or liquid nitrogen.

4. Solid samples should be so wrapped that, in the event of the container rupturing, it will be apparent whether or not the material could have escaped.

5. A specimen for diagnostic purposes should be treated as described by Collins *et al.* (The Prevention of Laboratory Acquired Infection, pages 11-14.)

6. Particular care must be taken when biological material, which cannot be autoclaved, is to be removed from the category A laboratory. The Safety Officer must be consulted before unsterilised material is removed. Precautions must be taken to sterilise the outer surfaces of containers and to sterilise the material itself, as far as possible.

J. SECURITY

1. It is imperative that the laboratory and animal rooms must be secure against intruders or vandals.

2. Security patrols, etc. should not enter laboratories, or animal rooms. If it appears that an adjacent fire or water hazard threatens the room then the Safety Officer should be informed immediately.

3. A key to the laboratory should be held centrally (see Section H and I above) for emergency access but should only be released on the instruction of the Safety Officer or his deputy (e.g. if he knows that the room has been disinfected then he can do this by telephone).

4. The Safety Officer must maintain a list of Category A pathogens, showing exactly where they are held (incubator, deep freeze, etc.).

K. HEALTH OF STAFF

1. The conventional health declaration form may not be adequate to eliminate those who ought not to work with category A pathogens and it may be necessary to supplement this with a medical examination and, if necessary, to insist on this, and on vaccination where appropriate, as a condition of employment.

2. Each employee in a category A laboratory should carry a card which states that if he is ill, he may have contracted a serious infectious disease requiring his isolation, and requesting the doctor to inform the Safety Officer.

3. The card should also be carried by everyone who has contact at work with the laboratory/animal room.

4. The name of the doctor, to whose list an employee's name is attached, should be recorded by the Safety Officer.

5. It is desirable that on appointment of an employee to work in the laboratory, his GP should be informed of the nature of this work.

6. Each such employee should be immunised against the organisms with which the laboratory is working so far as this is possible.

7. The immune status of staff should be maintained at an optimum level, and where possible and desirable, measured periodically.

8. Records of the health and immunisation status of staff in toxic laboratories must be maintained at a central point and be accessible in an emergency.

9. Where appropriate immunisation should also be offered to the immediate families of the staff.

10. Staff members should be responsible for reporting absences, due to ill-health to the Safety Officer. He will enquire, as appropriate, of the patient's own doctor.

11. Where a member of staff fails to attend, without notifying the Safety Officer his supervisor should immediately institute enquiries.

12. Appropriate measures must be readily available for emergency treatment of staff who either show early signs of laboratory infection or who have been involved in an accident likely to lead thereto.

L. ANIMAL ROOM

Note: All relevant regulations in these Safety Precautions apply to any room in which animals are under treatment with a category A pathogen. There are, in addition, hazards arising from the natural diseases of animals which may be transmissible to man. Diseases can be contracted following bites, scratches, droplet infection or the bites of insect vectors. There are particular hazards associated with the generation of aerosols in animal rooms.

In addition to the staff utilizing the animals others may be engaged to clean and feed them and the Safety Precautions also apply to them.

1. Dust: accumulations of dust in the ventilation system must be cleared.

2. Drains: (see Section A above).

3. Dead Animals: should if possible be autoclaved before they leave the site. Where incineration would create a radiobiological or infective hazard, carcasses must be suitably sealed.

4. Bedding, dung etc.: these materials must also be rendered innocuous.

5. Cages: all cages must be autoclaved before being cleaned and returned to store.

6. Escapes: in no circumstances should there be a direct exit to the outside. The Safety Officer must be informed if an animal cannot be accounted for.

7. Vermin: suspected or obvious, infestation with insects or wild rodents, must be reported at once to the Safety Officer.

8. Monkeys: the principal hazard in monkey handling not common to the handling of other animals is the risk of infection with monkey viruses which can produce a serious disease in man. The established basic rules for handling must be observed.

9. Responsibility: Servicing of category A rooms in the animal house must not be carried out by general animal house staff. Suitably trained personnel approved by the Safety Officer should carry out these duties under the day-to-day supervision of the person in charge of the animal house.

CONTROL PROCEDURE FOR CATEGORY A PATHOGENS

General Principles

1.1 The control system described is for planned projects and is not designed to cover emergency situations, such as may arise when a category A pathogen is found or suspected in a specimen sent to a diagnostic laboratory not equipped to deal with it. In such cases the competent medical authority should act in accordance with existing guidance and with regulations relating to infectious and notifiable diseases; but the safety precautions assist contingency planning.

1.2 As a pre-requisite to control, all laboratories holding and/or handling category A pathogens should continually and critically review holdings so that the number of types and quantity of each is kept to an absolute minimum.

1.3 All laboratories holding category A pathogens at the time of receipt of this memorandum are requested to seek clearance. Laboratories which have already been visited by a representative of DPAG may not need to be visited again.

1.4 A laboratory holding category A pathogens but wishing to acquire additional types should not do so until given clearance. Further clearance should be obtained for any significant change in a work programme or in facilities available.

1.5 A laboratory which does not hold category A pathogens should not acquire any until clearance is obtained.

1.6 A laboratory should not transfer any category A pathogens to another laboratory in the United Kingdom unless the recipient confirms that clearance has been obtained to use them for specific work.

1.7 On completion of the project for which clearance to hold a particular category A pathogen was given, all the pathogens should be destroyed and the DPAG notified.

1.8 When a category A pathogen is to be transported over public roads or by rail the arrangements for transport (except in emergency—see paragraph 1.1) are subject to clearance. It may be convenient for this clearance to be sought by a supplying laboratory at the same time as clearance to acquire the pathogen is sought by the receiving one. Requests for clearance for transport only may normally be made direct to the DPAG.

APPENDIX 17

COMPLIANCE OF BIRMINGHAM UNIVERSITY WITH DPAG RECOMMENDATIONS

A detailed comparison of the list of safety precautions laid down by DPAG and the precautions actually in force in the Birmingham smallpox laboratory is presented below:

A. THE LABORATORY—SITING AND STRUCTURE

1. Whereas the laboratory need not be physically separated from other laboratories it should not be sited next to a known fire hazard (e.g. the solvent store) or be in danger of flooding.

The Birmingham smallpox laboratory complied with this requirement.

2. The laboratory should be isolated by an air lock and provided with a suitably placed shower (see G7). Air locks and rooms must be ventilated by an exhaust air system. The air pressure in the laboratory should be monitored and displayed both within and immediately outside the laboratory. The laboratory should be maintained at a differential negative pressure of 0.3 inches (7.6 mm) water pressure.

The Birmingham laboratory did not have an airlock or a shower. A negative air pressure was created in the smallpox room when the fan of the safety cabinet in that room was operating and the door of the smallpox laboratory was closed. We were told that the airflow through the safety cabinet was checked regularly. However, there was no constant monitoring and display of the air pressure within and immediately outside the laboratory. Staff were in the habit of passing in and out of the smallpox room during their work with smallpox virus so that the door was frequently being opened.

3. The exhaust air must be filtered before discharge through two HEPA filters. The system must include a device to prevent back flow through the filters.

There was no system in the laboratory for air filtration other than the filters fitted to the cabinet.

4. The laboratory must be sealable so as to permit fumigation.

The laboratory was not easily sealable but fumigation was possible.

5. If work is carried out on category A pathogens which can be transmitted by animal or insect vectors, the laboratory must be proof against entry or exit of such animals or insects.
6. Effluent should be held in a standing tank, sterilised, and its sterility confirmed before discharge to the public sewer. Since sterilisation and tests

may take some time, it will be necessary to have more than one standing tank if work is to be carried out continuously. If heat sterilisation is to be used, temperature recording facilities should be provided to monitor the process. The standing tank(s) and recording equipment form parts of the facilities of the laboratory, so the Safety Officer is responsible for ensuring their proper functioning.

The laboratory did not have standing tanks for holding or disinfecting its effluent.

B. Laboratory Facilities

1. Work on category A pathogens must not be carried out in normal safety (exhaust protective) cabinets in an otherwise standard laboratory.

Work with smallpox virus was carried out in a special room with special precautions. The room was ventilated through filters in the safety cabinet. However, work with smallpox virus was not always carried out inside the safety cabinet and was occasionally conducted in the animal pox room.

2. All material must be sterilised prior to removal from the laboratory. Therefore, each laboratory should have direct access to an autoclave which should have double doors. There should be no possibility of removing the load without the autoclave cycle having been completed.

The laboratory did not have direct access to an autoclave with double doors. Instead, a small portable autoclave was in use inside the smallpox room for the sterilisation of gowns, eggs used and equipment. This autoclave was found on test to be functioning efficiently. Some used glassware was not autoclaved before leaving the laboratory but immersed in chlorox and stored in the laboratory overnight before being removed, along with the material that had been sterilised in the portable autoclave, for autoclaving in another part of the building. Infected material was also being regularly carried to the animal pox room without being disinfected.

3. Each member of staff working in the laboratory should have adequate air space.

This condition was satisfactorily met.

4. Pathogens must be stored in suitable containers (depending on the mode of storage, frozen or freeze-dried) in a cabinet reserved for category A pathogens and kept under lock and key. A key should be available on demand only to nominated individual(s).

Smallpox virus in this laboratory was stored in lockable incubators and a freezer in suitable containers. However, the freezer was not used exclusively for the storage of smallpox virus and other organisms e.g. Herpes virus being worked on elsewhere in the Medical Microbiology Department were also stored in it. Our enquiries revealed that smallpox viruses were being returned to storage in this freezer (and the incubators) without the outsides of the containers being disinfected and by staff wearing gloves and gowns that could possibly be contaminated. This presented a risk to anyone subsequently retrieving stocks of virus from the freezer.

C. Protective Clothing

1. Laboratory gowns should wrap over the chest and fit tightly at the wrists. Ordinary white laboratory coats are UNSUITABLE. Staff should have a clean gown for each uninterrupted period spent in the laboratory.
2. Gowns must be autoclaved before they are removed from the laboratory.

Special rear fastening gowns were being worn in the smallpox laboratory and complied with this condition. The gowns were autoclaved in the portable autoclave in the smallpox room before being bagged and removed from the laboratory to be re-autoclaved. However, clean gowns were not provided for each uninterrupted period spent in the laboratory and we were told that staff used the same gown for a week before it was autoclaved and a fresh gown provided. It was also the practice for staff to go into the animal pox room wearing their gowns.

3. Surgical gloves should be worn in the laboratory.

It is apparent from the report by WHO inspectors when they visited the laboratory in May 1978 that gloves were not always being worn while virus work was in progress. The WHO inspectors recommended the wearing of gloves and their recommendation was challenged by Professor Bedson who said that he was happy to adopt it but "one could argue about the extent to which they affect the safety of work". If gloves are not worn while work with smallpox virus is being carried out, it is possible for splashes or virus on the hands to contaminate the person carrying out the work.

4. Special protective clothing is needed in particular circumstances, for example, when there are hazards from splashes or aerosols. Depending on the nature of the work, it may be necessary to use face-shields, caps, plastic or other protective clothing, respirators (a sterilisable full-face type with a high-efficiency filter complying with British Standard Specification 2091, 1969). As an alternative to a respirator, particularly for those with beards, it may be preferable to use a ventilated helmet: some types require a supply of compressed air.

Not applicable.

D. Safety Officer

1. A Safety Officer able to advise on infectious hazards, and a deputy, must be appointed or designated. The establishment may have a Safety Officer with general responsibilities, and he may or may not be qualified to take on responsibility for infectious hazards. If not, an additional individual must be designated.
2. A Safety Officer should have appropriate qualifications and laboratory experience in working with category A pathogens.

Professor Bedson made himself responsible for the safety in the pox virus laboratory suite. He had the qualifications and the expertise to take on responsibility for infection hazards. There was no deputy.

3. The safety officer will act as adviser to the Head of the Department in all matters which may affect the safety of the staff and the containment of the organisms, and should be able to stop practices, considered unsafe pending guidance when necessary from the Laboratory Head.
4. He will take control, implement first aid in, and investigate, all accidents in laboratories and take what other action he considers necessary.
5. Where his responsibilities are not sufficient to warrant his full-time employment as Safety Officer then, provided that he is readily accessible to the laboratory during normal hours, he may hold another appointment.

It is arguable whether it was right that Professor Bedson as Head of the Department should have also been his own safety officer. He was the most knowledgeable in the Department about infectious hazards and therefore eminently qualified for this duty, but, as safety officer-cum-Head of Department there was no obvious way an independent check could be carried out on whether he was performing his safety officer duties properly. Because of his administrative and teaching responsibilities he spent very little time in the laboratory where it is now known that unsafe practices were taking place.

6. He will be responsible for the safe storage of pathogens and the maintenance of the inventory.

We have already indicated that we did not consider the storage of the smallpox virus to be "safe" because of the risk of infection through failure to disinfect the outsides of the containers before storage and because other viruses were being stored in the same freezer. As Head of Department, Professor Bedson must have given his permission for the freezer to be used for the storage of these other viruses. We are satisfied that a proper inventory of the smallpox viruses was maintained.

7. He will be responsible for organising the admission to the laboratory of cleaners and maintenance men and for the disinfection of any apparatus, etc, which is to be removed.

Two cleaners cleaned the animal pox laboratory once a fortnight. They held keys to the laboratory and were allowed to work unsupervised, finishing their work before the staff arrived. They were responsible workers but we doubt if it was right that one of their keys to the Department should have been also the key to the smallpox room. Cleaning of the smallpox room was undertaken by the laboratory staff. As far as the removal of apparatus was concerned, a perspex gel electrophoresis apparatus which was occasionally used in the animal pox room for work with "dead" smallpox virus, was also used elsewhere in the Department. We were told that this apparatus was not considered to be infected because it was not used with live virus, nevertheless it was disinfected by wiping down with formalin before it left the pox virus suite.

8. He will be responsible for advising staff on all aspects of the application of these Safety Precautions.

A comprehensive Departmental Information Book containing general guidance on safety in the Medical Microbiology Department was available to all

staff. In addition, a separate typewritten set of safety instructions for work involving smallpox virus was issued to the staff in the pox virus laboratory. The staff working in the smallpox laboratory recalled at some stage seeing the DPAG Memorandum but were not fully conversant with its contents. The Department appeared to rely for safety too heavily on its vaccination policy.

9. He will liaise through the Head of the Laboratory with the Medical Officer for Environmental Health and the family doctors of staff with health cards (see Section K below).

This condition was rigorously and meticulously followed in respect of liaison with family doctors, but there was no liaison with the Medical Officer of Environmental Health.

E. Training in Handling Pathogens

1. The safety officer will organise the initial training in the safe handling of pathogens of staff required to begin work in a category A laboratory.
2. Training will cover, e.g. the correct use of safety hoods; pipettes; syringes/needles; hot/cold rooms; centrifuges; blenders; freeze-drying; shaking machines; ultra-sonic disintegrators; glassware and the disposal of contaminated protective clothing and laboratory materials.
3. Staff should only work with category A pathogens if they have some previous experience in microbiology AND have had a course of training supervised by the Safety Officer.

One member of the staff who undertook smallpox work was a technician who had been employed in the pox virus laboratory for about eleven years. She had been instructed in smallpox work by Professor Bedson but the next most experienced member a former PhD student who joined the laboratory in 1974 was not formally trained by him. The third member of the staff, a trainee technician, joined the laboratory immediately after leaving school and had been working there for about a year. She was being trained by the other technician. We learned that only 9 months after she had joined the laboratory she was allowed to handle smallpox virus and allowed access to the smallpox room.

F. Supervision

1. Laboratory staff should not work alone.
2. Work in the category A laboratory should, at all times, be supervised by a senior, trained and experienced member of the staff in person.
3. The supervisor will be personally responsible to the Safety Officer for the safety of the work actually in progress at any time, although he may not be responsible for the overall project.
4. When necessary suitable restrictions should be imposed on contact between handlers of category A pathogens and patients and/or livestock.

There was only enough room in the smallpox laboratory for one person to work and it was the usual practice for staff to work alone. The whole room was clearly visible through the glass louvres in the door. Since he became acting head of the Department at the end of 1975, Professor Bedson spent very little time in the pox virus laboratory because he was occupied with his administrative work and teaching. The PhD student told us that from the time she began smallpox work in 1975 she was on no occasion supervised at work with live virus by Professor Bedson. Thus it appears that work in the smallpox laboratory has been taking place inadequately supervised possibly since 1975. In Professor Bedson's absences from the Department no proper deputising arrangements were made.

G. Laboratory Discipline

1. Each category A laboratory must be identified clearly with a large sign.

This was done.

2. When unoccupied, the laboratory must be locked. The key(s) must be kept under the supervision of the Safety Officer, and released only to authorised persons. A key, however, should be kept at a secure central point, available at all times, in case of emergency.

We were told that the keys to the pox virus laboratory were available only to the staff working in the laboratory, the cleaners, and a lecturer in the Department who held a key for emergency use. However, we were also told that on one occasion the laboratory had been found unlocked and unoccupied.

3. In normal hours the supervisor will be responsible to the safety officer for ensuring that no unauthorised person enters the laboratory.
4. Only the Safety Officer or his deputy can authorise staff to enter the laboratory, and he will hold a list of names of those so authorised.
5. No unlisted personnel (e.g. visitor, observer, cleaner or maintenance/repair man) will enter the laboratory unless he has received a signed statement from the Safety Officer that it is safe for him to do so.

Access to the smallpox room was strictly controlled and limited to nominated individuals whose names were recorded in a notice on the laboratory door. These included individuals not named in the laboratory's application to DPAG. Visitors who wished to enter the smallpox room had their vaccination status checked and were required to record their names in a visitors' book that hung from the door. Maintenance engineers were also vaccinated and required to record their names in the visitors' book, but as far as we are aware, no signed statements were issued by Professor Bedson as Safety Officer to say that it was safe for them to enter the laboratory.

6. The Safety Officer will be responsible for confirming when a laboratory and its apparatus have been disinfected.

The laboratory benches were wiped down with formalin at the end of each day's work. As far as we are aware no regular disinfection with gaseous formaldehyde of the laboratory took place.

7. The category A Laboratory is entered through a "clean" side changing area (locker room) separated from the "dirty" side by a shower and airlock. All clothing, rings, watches, etc. should be removed into a locker. Clean protective clothing (see Section C) should be put on. Where appropriate, protective overgarments including respirator and hood should be worn. Rubber boots should be put on just prior to entering the toxic area. The "clean" and "dirty" areas should be clearly distinguished physically.
8. On the way out boots and gloves should be washed in a suitable disinfectant (hypochlorite, available chlorine 5000 ppm, e.g. 5% chlorox). Overgarments should be placed in a bin on the "dirty" side of the showers and all remaining clothing also removed to a bin. Gloves should be the last to go. The individual should then shower, transfer to the "clean" side and dress.
9. This procedure should be adhered to whenever, and for whatever purpose, the room is vacated.

The laboratory did not have these facilities. We learned that it was the practice for staff occasionally to go from the smallpox laboratory to the animal pox laboratory still wearing the undisinfected gown and gloves used while working with smallpox virus, in order to retrieve or deposit smallpox virus in the incubators or freezer or to use the low-speed centrifuge. This demonstrates a clear breach of laboratory discipline since the staff were not only transgressing on the DPAG Safety Code but also their own Departmental safety instructions.

10. Eating, drinking or smoking will not be permitted in any laboratory or animal room at any time.

As far as we know this was adhered to.

11. All accidents or spillages of potentially dangerous material in the laboratory must be reported IMMEDIATELY to the Safety Officer. EVERY SUCH INCIDENT MUST BE REGARDED AS A FULL MEDICAL OR ANIMAL DISEASE HAZARD.

We learned that in 1977 one of the smallpox laboratory staff dropped a tray containing dishes of vaccinia virus on the laboratory floor. The incident was reported to Professor Bedson. The Department's two other Safety Officers had no knowledge of the incident and we were unable to trace any records of it in the Department's accident books. Laboratory accidents and incidents that do not result in immediate injuries to staff should be recorded because their effects may only become apparent after a period of time and furthermore, because a regular examination of such a record provides useful information on the efficiency of safety procedures and of the staff themselves.

12. The day-to-day cleanliness of a toxic laboratory is the responsibility of those working in it. Only when the Safety Officer has confirmed that it has been successfully disinfected can other cleaning/maintenance work be carried out.
13. At the end of a working day benches and working surfaces should be disinfected.

14. Periodically, and certainly at the end of any particular experimental procedure, the rooms and everything in them must be fumigated with gaseous formaldehyde.

The laboratory benches were wiped down with formalin at the end of each day's work. However, regular fumigation of the smallpox laboratory did not take place, not even annually.

H and I. Handling of Specimens

1. Clerical staff should not be permitted to open incoming specimens, or packages purporting to contain pathogens.
2. All packages thought to contain category A pathogens must be opened by trained staff, in the laboratory.
3. An externally-identified liquid sample should be sealed in a time can filled with sufficient absorbent material wholly to mop up a spill. The can may, if necessary, be cooled in solid carbon dioxide or liquid nitrogen.
4. Solid samples should be so wrapped that, in the event of the container rupturing, it will be apparent whether or not the material could have escaped.
5. A specimen for diagnostic purposes should be treated as described by Collins *et al.* (The Prevention of Laboratory Acquired Infection, pages 11-14).

Not applicable.

6. Particular care must be taken when biological material, which cannot be autoclaved, is to be removed from the category A laboratory. The safety officer must be consulted before unsterilised material is removed. Precautions must be taken to sterilise the outer surfaces of containers and to sterilise the material itself, as far as possible.

As we have already indicated in this report, infected material was being transferred almost daily from the smallpox room to the animal pox laboratory without the outer surfaces of containers being sterilised. We do not know whether the practice took place with Professor Bedson's approval, as Safety Officer he was not consulted each time it was undertaken.

J. Security

1. It is imperative that the laboratory and animal rooms must be secure against intruders or vandals.
2. Security patrols, etc. should not enter laboratories or animal rooms. If it appears that an adjacent fire or water hazard threatens the room then the Safety Officer should be informed immediately.
3. A key to the laboratory should be held centrally (see Section H and I above) for emergency access but should only be released on the instruction of the Safety Officer or his deputy (e.g., if he knows that the room has been disinfected then he can do this by telephone).

4. The safety officer must maintain a list of Category A pathogens, showing exactly where they are held (incubator, deep freeze, etc.).

We are satisfied that the laboratory was secure from intruders after working hours. Security patrols kept watch over the Department and since they entered the Medical Microbiology corridor, they were required to be vaccinated against smallpox. Professor Bedson's home telephone number and that of one of the other Departmental Safety Officers was given on the entrance door to the pox virus suite so that either one could be contacted in the event of an emergency.

K. Health of Staff

1. The conventional health declaration form may not be adequate to eliminate those who ought not to work with category A pathogens and it may be necessary to supplement this with a medical examination and, if necessary to insist on this, and on vaccination where appropriate, as a condition of employment.
2. Each employee in a category A laboratory should carry a card which states that if he is ill, he MAY have contracted a serious infectious disease requiring his isolation, and requesting the doctor to inform the safety officer.
3. The card should also be carried by everyone who has contact at work with the laboratory/animal room.
4. The name of the doctor, to whose list an employee's name is attached, should be recorded by the Safety Officer.
5. It is desirable that on appointment of an employee to work in the laboratory his GP should be informed of the nature of this work.
6. Each such employee should be immunised against the organisms with which the laboratory is working so far as this is possible.
7. The immune status of staff should be maintained at an optimum level, and where possible and desirable measured periodically.
8. Records of the health and immunisation status of staff in toxic laboratories must be maintained at a central point and be accessible in an emergency.
9. Where appropriate immunisation should also be offered to the immediate families of the staff.
10. Staff members should be responsible for reporting absences, due to ill-health, to the safety officer. He will enquire, as appropriate, of the patient's own doctor.
11. Where a member of staff fails to attend, without notifying the Safety Officer, his supervisor should immediately institute enquiries.

12. Appropriate measures must be readily available for emergency treatment of staff who either show early signs of laboratory infection or who have been involved in an accident likely to lead thereto.

Our enquiries showed that these conditions were being met. All staff working in the pox virus laboratory were vaccinated annually, other staff in the Department, and staff from other Departments who worked on the Medical Microbiology corridor who also had access to the pox virus laboratory were vaccinated every two years. These staff also received a card for their General Practitioner to be filed with their NHS records. In addition they carried a card to be shown to their doctor in case of illness—it notified him that they worked in close proximity to a laboratory handling dangerous organisms. Staff were also required to notify their Department immediately of any absence through illness. This, and the keeping of the necessary records, was meticulously followed.

APPENDIX 18

APPROVAL OF THE BIRMINGHAM LABORATORY TO DIAGNOSE AND HOLD CATEGORY A PATHOGENS

The Birmingham Laboratory was inspected in February 1966 and approved by DPAG in August 1976.

1. Report by DPAG Inspector

BIRMINGHAM UNIVERSITY—Virus Laboratory and Regional Smallpox Laboratory Visited—4th February 1976

The Virus Laboratory of the University of Birmingham contains the Regional Smallpox Laboratory. The Regional Smallpox Laboratory examines scrapings from lesions suspected of being smallpox by culture on eggs, gel diffusions test and electron microscopy, and it should be emphasized that smallpox diagnosis is the only diagnostic work carried out in this Laboratory. At present, smallpox is the only Category A pathogen handled but so-called whitepox viruses are handled on the same basis as if they were smallpox. In addition to the diagnostic work, smallpox virus is handled for reference purposes and for research aimed at extending the basis of identification of unknown viruses related to smallpox. It is not used for teaching in the Medical School (vaccinia is used for that). Dr. H. S. Bedson, principal virologist, and Dr. G. R. B. Skinner and Dr. R. H. George, assistant virologists, are the only persons handling smallpox specimens. Dr. Bedson is extremely experienced in smallpox techniques and taught Drs. Skinner and George. Dr. Flewett, Regional Virologist at the East Birmingham Laboratory, also an extremely experienced virologist, is in reserve and could function at the Smallpox Laboratory if required. The research and reference work is, at present, restricted to Dr. Bedson although in the past he has been assisted by others—University staff and postgraduate research assistants—whose training he has supervised and approved. There is one technician, Mrs. J. Durham, O.N.C., but otherwise unqualified, who provides technical support and she has been doing smallpox work since 1967.

The Smallpox Laboratory deals with about 12 to 20 specimens yearly which must be cleared for smallpox. In addition animal pox isolates are received, mostly from Africa, for comparison with smallpox. Twenty have been received in the last three years.

The smallpox complex consists of a large laboratory (34 in accompanying text), at one end of which is Dr. Bedson's office with a door leading to the main corridor, and at the other end there are two rooms, constructed by partitioning the main laboratory, one of which (34a) is used as an incubating room for eggs and the other (34b) is the smallpox room proper. This room is approximately 8' × 8' × 10', has one window and contains an MSE 25 centrifuge, a portable autoclave and a PHLS type (visual indicator) exhaust protective cabinet opening through the top of the window. The cabinet sits on a bench. There is also a wash hand basin. The door to 34b has a louvred window. The egg room (34a)

has an air intake grill high up on the wall dividing it from 34b but this communicates with the exterior and not with 34b. Anemometer readings have been carried out and the exhaust protective cabinet functions satisfactorily. When the fan is on in 34b it causes a negative pressure with respect to 34. It is always left on for 15 minutes after work in the cabinet is over. The smallpox room is locked except at times of entry and exit. The vaccinia and other pox virus work is carried out in 34. There is a taccymat outside the door at 34b.

Room 34 opens on to the main laboratory corridor. There is no airlock between 34 and 34b or any facility for having a shower or changing clothes before emerging from 34b. The external doors of the smallpox complex are locked when not in use and carry appropriate warning notices.

The remainder of the laboratory consists of ten or so large sized working rooms on this floor, a Director's office, a general office, two rooms for the Chief Technician, a seminar room and a common room. On the lower floor are wash up, autoclave and media room, the electron microscope suite, animal rooms and an animal isolation room.

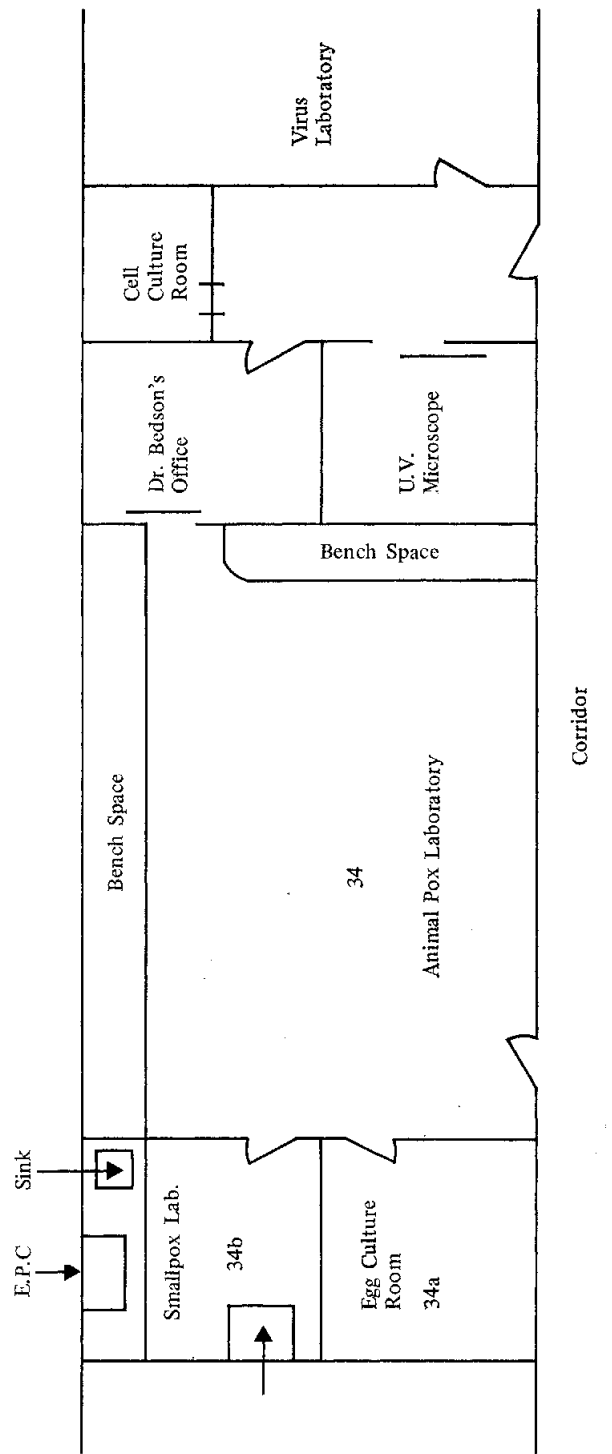
Smallpox specimens (on grids) from 34b for the electron microscope are sterilised in glutaraldehyde before leaving 34b. No infectious material leaves 34b without being autoclaved except gowns. These are bagged in 34b and the bag put in another bag in room 34 before being autoclaved.

The question is whether in view of the lack of airlock, shower and changing facilities, smallpox work should be allowed to continue in the Smallpox Laboratory. I think smallpox work could be allowed to continue in view of the following.

1. Dr. Bedson, who would normally undertake the work, is a virologist of considerable repute, both here and abroad, for smallpox diagnostic work and work on pox viruses; he is very experienced and seems a very conscientious worker. Drs. Skinner and George, who were taught by Dr. Bedson, are also knowledgeable and experienced. All three fully understand the danger of the virus escaping.
2. The vaccination programme (see accompanying text) is most thorough and is personally supervised by Dr. Bedson. Students coming to the Virus Laboratory for instruction are vaccinated on the first day of attendance by Dr. Bedson, this forms part of their instruction and no one appears to be missed.
3. The smallpox diagnostic work is *never* delegated but carried out by one of the three doctors.
4. The drill for not allowing escape of the virus is thorough and more than makes up for the lack of shower and changing facilities.
5. The laboratory serves a large and important area in which are a very large number of immigrants with a continual flow to and from tropical and sub-tropical parts of the world.

Dr. Bedson has been invited by the Region to consider examining blood and other infectious material from any P.U.O. which could be Lassa Fever, admitted

Annexe to the Report by the DPAG Inspector



to the East Birmingham Hospital. The material would *not* be examined for Lassa virus, but only cleared for bacterial infection after which the material would be forwarded to the Lassa Fever Laboratory proper, or if this was not possible, destroyed. The material would be brought from the East Birmingham Hospital to the Virus Laboratory in special (Porton) containers. No attempt would be made to propagate Lassa virus.

I think the Laboratory could safely be allowed to carry out this work also.

General Comment

Apparently smallpox work was formerly carried out on the open bench in room 34. A safety cabinet was installed in 34 in 1973 and a year later room 34b, which had previously been used as an office, was re-equipped and converted to its present state.

I was impressed by the tidyness, atmosphere of quiet, and absence of bustle in this laboratory. There appeared to be commendable attention to detail and serious appreciation of the risks involved.

Dr. R. J. Henderson

2. Recommendation of DPAG.

DANGEROUS PATHOGENS ADVISORY GROUP

To: The Department of Health
and Social Security,
Alexander Fleming House,
Elephant and Castle, LONDON SE1.

3rd August, 1976

LABORATORY REPORT

NAME AND ADDRESS OF
LABORATORY:
AND DATE OF VISIT

University of Birmingham, Virus
Laboratory and Regional Smallpox
Laboratory, The Medical School,
Birmingham B15 2TJ.
Visited 4th February 1976.

NAME OF LABORATORY HEAD:
Names of staff handling
Category A pathogens

Dr. H. S. Bedson.
Dr. H. S. Bedson, Dr. G. R. B. Skinner,
Dr. R. H. George, Mrs. J. Durham.

CATEGORY "A" PATHOGENS HELD:

Smallpox virus.

DETAILS OF WORK BEING DONE
WITH EACH OF THE ABOVE AND
ESTIMATED DURATION:

Diagnosis of smallpox. Examines 12-20
specimens/annum. Receives animal pox
isolates from Africa and compares them
with smallpox virus. Research on White-
pox and other members of orthopox
group. Duration, indefinite.

ADDITIONAL CATEGORY "A" None.

PATHOGENS NOW REQUIRED:

PURPOSE AND ESTIMATED DURATION
OF WORK:

Other work contemplated with
Category "A" pathogens: The laboratory has been invited by the
Region to examine specimens which could
be from Lassa fever patients for bacterial
infection and malaria.

RECOMMENDATIONS: 1. The laboratory is considered suitable
to work with the Category "A"
pathogens held.

OTHER REMARKS:

The Group considers that the skill and experience of the staff are of a high
order and that the precautions in force are thorough.

Taking these factors into account, together with the facilities available, they
take the view that the present Category "A" work could continue. They also
consider that the laboratory is suitable to examine possible Lassa fever speci-
mens for bacterial and malarial infection.

Fresh clearance should be sought in the event of significant changes in staff,
facilities or work programme.

(Signed) W. A. Walters
Secretary.

3. *Letter of approval of DHSS*

From: Dr. S. L. Waiter, DHSS

To: Professor H. S. Bedson

10th September 1976

*Dr. Buttolph, who was concerned with the earlier arrangements, has now
left us and I am therefore writing to you on behalf of the Department.*

*The Department has considered the report submitted by the Dangerous
Pathogens Advisory Group following Dr. Henderson's visit to your laboratory.*

*The Group considers the laboratory suitable to work with the Category
"A" pathogen held, namely smallpox virus and in addition for the examination
of specimens from possible Lassa fever patients for bacterial and malarial
infection.*

*The Department of Health has accepted the Group's recommendations and
you may like to inform your appropriate University committee accordingly.
A copy of this letter is enclosed.*

*It is requested that fresh clearance should be sought if there is significant
change in staff, facilities or work programme.*

APPENDIX 19

CATEGORY "A" LABORATORIES

1. The following is a list of laboratories approved by the Dangerous Pathogens Advisory Group to hold specific Category "A" pathogens as at 12th December 1978.

<i>Laboratory</i>	<i>Category "A" Pathogen</i>
Department of Microbiology University of Reading	Rabies virus
Central Public Health Laboratory Colindale	Rabies virus
Central Veterinary Laboratory Weybridge, Surrey	Rabies virus
Evans Biologicals Ltd. Liverpool	Rabies virus
Animal Virus Research Institute Pirbright	Rabies virus
Lister Institute Elstree	Rabies virus
Microbiological Research Establishment Porton, Wilts.	Rabies virus Lassa fever virus Marburg virus Simian herpes B virus Crimean haemorrhagic fever virus (Congo) Venezuelan equine encephalitis virus Ebola virus
London School of Hygiene and Tropical Medicine Winches Farm, St. Albans	Crimean haemorrhagic fever virus (Congo) Venezuelan equine encephalitis virus
Department of Virology St. Mary's Hospital Medical School London	Smallpox virus
Wellcome Research Laboratories Ltd. Beckenham, Kent	Rabies virus

All these laboratories, bar two, have also been inspected by the Ministry of Agriculture, Fisheries and Food.

2. The following is a list of laboratories designated by the DHSS for the laboratory diagnosis of smallpox and able to undertake examinations to exclude possible treatable infections in patients with Pyrexia of unknown origin where the possibility of Lassa fever is considered. Specimens are forwarded for Lassa fever virus isolation to M.R.E. Porton.

Designated Laboratories

Central Public Health Laboratory
Colindale

Public Health Laboratory
Institute of Pathology
General Hospital
Newcastle upon Tyne

Public Health Laboratory
Myrtle Road
Bristol

Public Health Laboratory
York Road
Leeds

Public Health Laboratory
Cardiff

APPENDIX 20

WHO SMALLPOX LABORATORY SAFETY RECOMMENDATIONS

At a workshop meeting on Safety Measures in Smallpox Laboratories in August 1977 the following code of practice was drawn up.

1.0 Introduction

With the interruption of smallpox transmission expected to occur in the near future, the only known source of variola virus and potential for smallpox epidemics will be in laboratories maintaining the virus. Following the recommendation of the 30th World Health Assembly (1977) that variola virus be retained only by World Health Organization (WHO) Collaborating Centres under conditions ensuring maximum safety, WHO convened a group of experts (Annex 1) to consider safety standards for the maintenance and use of variola virus in laboratories. The group recognized the need to retain a minimum number of such laboratories for archival, diagnostic and research purposes.

1.1 Objectives

The objectives of the meeting were to define physical containment standards for maintaining the virus, establish requirements to ensure the safety of personnel and propose administrative control measures. The group formulated recommendations addressed to these objectives and, with WHO, strongly urges that national safety measures for containing variola virus in laboratories embody these recommendations.

1.2 Laboratories with variola virus

Since 1975 WHO queried 181 countries and territories in the world regarding maintenance of stocks of variola virus in laboratories within these countries and territories. One hundred and seventy six of these countries and territories have responded as of 31st July 1977 and it is expected that the remaining countries (Cape Verde, China, Comoros, Democratic Kampuchea and Seychelles)* will respond shortly. Of 823 laboratories contacted, 74 reported that they retained variola virus. Fifty-seven of these transferred or destroyed their strains of variola leaving 17 known laboratories currently maintaining this virus (Annex 2).

2.0 Agents subject to safety recommendations

2.1 Variola and whitepox viruses

Among the orthopoxviruses only variola virus is recognized as a highly dangerous pathogen but because whitepox virus is currently indistinguishable from variola it too must be subject to these safety measures.

*The Comoros and Seychelles report that variola virus is not retained in laboratories (26 September 1977)

2.2 *Other orthopoxviruses*

Monkeypox and vaccinia viruses pose no major public health danger. Although suitable precautions, including vaccination, should be taken by personnel working with these and other orthopoxviruses, they need not be subject to the same safety measures as variola and whitepox viruses.

3.0 **Numbers and functions of laboratories**

Risk is directly related to the number of laboratories maintaining variola virus stocks. It was recommended that only the WHO Collaborating Centres for Poxvirus Research and the WHO Collaborating Centre for Smallpox Vaccine (hereinafter called WHO Centres) be repositories of variola virus and this number should be subject to periodic review. Further recommendations were:

3.1 *Archival*

Only WHO Collaborating Centres should maintain variola virus for archival purposes and there should be assurance that a representative group of strains will be retained for the future.

3.2 *Diagnostic*

The laboratories at the Viral Exanthems Branch, CDC, Atlanta, and the Laboratory of Smallpox Prophylaxis, Research Institute of Virus Preparations, Moscow, should continue as the principal WHO Centres for diagnosis of suspect human smallpox cases.

3.3 *Research*

3.3.1 The use of variola for research purposes should be restricted to only the two institutions cited above and in three other WHO Centres (Rijks Instituut voor de Volksgezondheid, Bilthoven, Netherlands; Virology Department, the Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London; Poxvirus Laboratory, Department of Enteroviruses, National Institute of Health, Tokyo).

However, should national authorities deem smallpox research necessary in their institutions, the WHO should be notified and be assured that the physical containment system of the laboratory and the personnel safety measures meet the standard safety requirements. However, it is urged that national authorities and their institutions follow the procedures presented in section 3.3.2.

3.3.2 It is strongly recommended that all other institutions maintaining variola virus destroy these stocks or transfer them to one of the above-mentioned WHO Centres; they should be informed that the WHO Centres would accept visiting investigators who wish to work with variola if the research protocol involves the differentiation of variola and whitepox viruses, differentiation of antibodies to variola virus from antibodies to other poxviruses, and comparison of variola viruses and monkey pox viruses. Other research projects for which there is no possible substitute for variola virus should not be excluded.

4.0 Recommended safety procedures pertaining to physical construction and administration of laboratories with variola virus

4.1 Physical containment

A place authorized to hold, or work with, variola virus stocks (hereinafter called the laboratory) must be constructed and operated in such manner to prevent dissemination of variola virus. Experiments involving smallpox virus shall be confined to work areas in a laboratory of the type designed to contain microorganisms that are extremely hazardous to man or may cause serious epidemic disease. The laboratory is either a separate building or it is a controlled area, within a building, which is isolated from all other areas of the building. Access to the laboratory is under strict control, excluding entry of unauthorized persons. Requirements for laboratories holding and working with variola are:

4.1.1 Imperviously sealed walls, floors and ceilings in which all penetrations (such as for air ducts, electrical conduits, and utility pipes) are sealed to assure the physical isolation of the work area and to facilitate housekeeping and space decontamination.

4.1.2 Air locks through which supplies and material can be brought into the laboratory without breach of containment.

4.1.3 Contiguous clothing change and shower rooms through which personnel enter into and exit from the laboratory.

4.1.4 Double-door autoclaves to sterilize and safely remove wastes and other materials from the laboratory.

4.1.5 A biowaste treatment system to decontaminate liquid effluents if laboratory drains are installed.

4.1.6 A separate ventilation system which maintains negative air pressures and directional air flow within the laboratory.

4.1.7 Passage of supply air through a prefilter and high efficiency particulate air (HEPA) filter before entering the laboratory. Exhaust air should be decontaminated by passage through two HEPA filters before discharge to the atmosphere.

4.1.8 All primary doors leading into the laboratory are always locked except when in use, making entry of unauthorized persons impossible. The laboratory director controls the keys.

4.1.9 Rooms for animals infected with variola virus and diagnostic cultures kept locked.

4.1.10 A biohazard warning sign on all exterior doors of the laboratory and a list of authorized personnel posted on the entries.

4.1.11 Laboratory windows not accessible from the outside of the building.

4.1.12 Biological safety cabinets to prevent release of virus into the air of the room.

- 4.1.13 Windows from which all parts of the laboratory can be seen.
- 4.1.14 Special biocontainment procedures for personnel and environmental protection used for animals.
- 4.1.15 Appropriate design and operational measures employed to prevent and eliminate introduction of insects, rodents and other pests.

4.2 *Storage*

For security and biocontainment reasons, storage of variola and whitepox viruses, as well as their handling, must be subject to the physical containment requirements described in section 4.1. Secure storage is considered part of standard laboratory procedure and should be described in the laboratory operations manual. Containers of variola virus must be locked when not in use.

4.3 *Administrative control*

4.3.1 *Responsibility, authority and compliance*

An effective safety system defines clear lines of responsibility and authority. It is appreciated that different countries have different methods for ensuring safety. The day-to-day safety in the laboratory is the responsibility of the laboratory director, who is responsible to national health authorities. National authorities should delegate a local safety committee to ensure compliance with established standards. The local safety committee should be independent of the management structure of the laboratory itself. The local committee should submit yearly reports to national authorities. WHO should be informed of the safety measures in each country and will be available to consult on such matters. WHO will devise a safety report form which the laboratories will be requested to submit yearly.

4.3.2 *The authorization* to receive, maintain and use variola virus shall be issued by national authorities and only to WHO Centres. This authorization should be obtained in writing and WHO should be kept informed of all such authorizations issued.

4.3.3 *Personnel*

Only personnel authorized by the director shall enter the laboratory and these persons shall be indicated on a list posted on entries to the laboratory. This list shall be updated as necessary. All such persons must have been satisfactorily trained, briefed and immunized as judged by the director. Persons can be added to the list only on authorization of the director.

4.3.3.1 Prerequisites for authorization to enter the laboratory:

- i. Vaccination within the previous 3 years with potent WHO approved vaccine and proper technique and measurement of detectable antibodies at least every 3 years. This information must be recorded.
- ii. All such persons must have been given a written copy of the safety instructions and must have signed a statement that they have been read and understood.

4.3.3.2 All untoward incidents and accidents, even minor ones, must be reported to the director immediately and recorded.

4.3.3.3 All entries into the laboratory should be documented in a permanent record.

4.3.3.4 Any absence must be reported to the director who should verify cause of absence.

4.3.3.5 Workers in the laboratory must inform their personal physician that they work with variola virus in case of illness. The physician should be provided with the telephone number of the director.

4.3.4 *Special situations*

Action in case of major accidents and other emergencies will be detailed in the laboratory operations manual.

5.0 Packaging and shipping

Diagnostic specimens and cultures should be packaged and shipped in accordance with national regulations and those of the International Air Transportation Association (IATA) and International Postal Union (IPU). Shipments should be sent by airfreight to prevent loss. The shipment and arrival details should be cabled to the receiving laboratory before arrival.

ANNEX 1

PARTICIPANTS

Temporary Advisers:

1. Professor K. R. Dumbell Dept. of Virology, The Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London (Discussion coordinator).
2. Dr. T. Kitamura Division of Poxviruses, National Institute of Health, Tokyo.
3. Dr. N. N. Maltseva Research Institute of Virus Preparations, Moscow.
4. Dr. J. H. Nakano Viral Exanthems Branch, Center for Disease Control, Atlanta (Secretary).
5. Dr. J. H. Richardson Office of Biosafety, Center for Disease Control, Atlanta.

WHO staff:

1. Dr. I. Arita Chief, Smallpox Eradication Unit (SME).
2. Dr. J. G. Breman Medical Officer, (SME), (Secretary).
3. Dr. A. Gromyko Medical Officer, (SME).
4. Dr. E. Shafa Medical Officer, (SME).

DOCUMENTS

1. Working Paper 1 Registration and safety measures of laboratories retaining variola virus.
(Dr. J. H. Richardson and Dr. J. H. Nakano).
2. Working Paper 2 Safety regulations for laboratory work using variola virus in the present facilities of the smallpox laboratory (Division of Poxviruses, National Institute of Health, Tokyo, Japan).
3. Working Paper 3 Control of laboratory use of pathogens very dangerous to humans (Dangerous Pathogens Advisory Group, Department of Health and Social Security, Ministry of Agriculture, Fisheries and Food, United Kingdom).
4. Working Paper 4 Progress Report on Register of Laboratories retaining Variola Virus, WHO, 28th July 1977.
5. Working Paper 5 Resolution of the Thirtieth World Health Assembly. Smallpox Eradication (WHA 30.52), 19th May 1977.
6. Working Paper 6 Resolution of the Executive Board of the WHO. Smallpox Eradication (EB 59.R28), 25th January 1977.

7. Working Paper 7 Nineteenth Report of the Committee on International Surveillance of Communicable Diseases: Control of Variola Virus in Laboratories (WHO/IQ/76.155 Rev. 1, page 56), 22–26th November 1976.
8. Working Paper 8 “Collection, packaging and despatch of specimens, Reference 2” in Protocol for Investigation and Reporting of Smallpox-like Disease in African Regions where human monkeypox has occurred (SME, WHO, 1976).
9. Working Paper 9 “Specimen Collection Kits”, SME, WHO, 8th February 1977.
10. Working Paper 10 Facilitation and Safety in the International Transfer of Research Materials (CDS/SMM/76.1 Rev. 1).

ANNEX 2
LABORATORIES RETAINING VARIOLA VIRUS¹ (28 July 1977)

Number	Region/Country	Laboratory	Reason for retaining		
			Archival	Diagnosis	Current research Unknown
1	AFRO/South Africa	National Institute for Virology, Sandringham	x		
2	AMRO/Brazil	Instituto Adolfo Lutz, Serv. de Virol., Sao Paulo	x		
3	AMRO/Peru	Virus Instituto Salud Publica, Lima	x		
4*	AMRO/USA	Viral Exanthems Branch, CDC, Atlanta		x	
5	AMRO/USA	American Type Culture Collection, New York	x		
6	AMRO/USA	Walter Reed Army Institute of Research, Washington	x		
7*	EURO/France	Laboratoire National de la Santé Publique, Paris		x	
8	EURO/FR Germany	Landesimpfstalt Dusseldorf, Dusseldorf	x		
9	EURO/FR Germany	Bayerische Landesimpfstalt, Munchen			x
10	EURO/FR Germany	Institut für Schiffs und Tropenkrankheiten, Virus abteilg., Hamburg			x
11*	EURO/Netherlands	Rijks Instituut voor de Volksgezondheid, Bilthoven		x	
12*	EURO/USSR	Laboratory of Smallpox Prophylaxis, Research Institute of Virus Preparations, Moscow		x	
13*	EURO/United Kingdom	Virology Department, St. Mary's Hospital Medical School, London		x	
14	EURO/United Kingdom	University of Birmingham, Dept. of Bacteriology, Medical School, Birmingham			x
15	EURO/United Kingdom	University of Liverpool, Dept. of Medical Microbiology, Liverpool	x		
16	EURO/United Kingdom	Microbiological Research Establishment, Virus Section, Porton Down, Salisbury	x		
17*	WPRO/Japan	Poxvirus Laboratory, Dept. of Enteroviruses, National Institute of Health, Tokyo		x	

*WHO Collaborating Centre.

¹Countries not yet responding to query: Cape Verde, China, Comoros, Democratic Kampuchea, Seychelles, (The Comoros and Seychelles report that variola virus is not retained in laboratories, 26th September 1977.)

APPENDIX 21

WHO CORRESPONDENCE

WHO decided against the designation of the Birmingham laboratory as a WHO Collaborating Centre. This was communicated to Professor Bedson in September 1977 and in 1978 inspections of Professor Bedson's laboratory by WHO took place.

The following are the relevant documents:

From: J. G. Breman Smallpox Eradication Unit WHO Geneva

To: Professor H. S. Bedson

16th September 1977

Our proposal to have your laboratory designated as a WHO Collaborating Centre for Poxvirus Research has been refused at a high level in WHO. It was felt that, at this stage of the worldwide eradication programme, the creation of another official Centre would give the impression that WHO itself is increasing the danger of laboratory accidents and is encouraging more laboratories to work with variola. We have repeatedly emphasized that your work, more than ever, is extremely important and should be supported and that your laboratory is suitably equipped to contain variola and whitepox viruses. There was no disagreement on these points.

Nevertheless, we are still able to support your poxvirus research with a grant of \$7,500 for 1977. I understand that the UK Department of Health and Social Security was considering approval of smallpox research only in UK laboratories designated as WHO Collaborating Centres. Please give us your appraisal of this situation.

From: Professor H. S. Bedson

To: Dr. J. G. Breman

4th October 1977

Thank you for your letter of 16th September. I apologise for not having replied sooner but it was a bit of a bombshell and I have been trying to see what reaction there would be at the UK and DHSS end.

Naturally, I am very anxious that we should continue our work with smallpox for the present developments look extremely promising. Some of the results will come out quite quickly but we shall need to look at a much larger range of smallpox viruses if we are to exploit the new approach to the full.

We have always taken the view that Keith Dumbell's laboratory would ultimately become the UK Smallpox Laboratory and that our work would come to an end after perhaps 2 or 3 years. The setback at WHO means that we may now have to work on a shortened timescale but we might still get a worthwhile stay of execution. As you suggest in your letter, the principal difficulty is the WHO Executive Board resolution which talks of Collaborating Centres, but I believe the DHSS could accept that they were acting in the spirit of that resolution if they were told

by you and Dr. Arita that you wanted us to have time to complete our work and that you would be continuing your support of the work. The sort of formula that I have tentatively suggested is:—

“that work with variola virus should continue at Birmingham for a limited period while certain projects, which are being pursued with the collaboration and support of the WHO (Smallpox Eradication Unit) are brought to a conclusion”.

If pressed for a date, I would have thought that we should aim to complete our studies with smallpox/whitepox viruses by the end of 1978. It might be possible to do a few things after that time by acting in concert with Keith Dumbell at St. Mary's but this would be a rather unwieldy arrangement and would seriously hold us up if we had to adopt it any sooner.

With regard to the financial support of the work, I believe that Dr. Arita is happy that we should have the grant of \$7,000 that you mention. We can certainly use it and it will provide tangible evidence of your support for the UK authorities. Fortunately, we have just learnt that we have been successful in our grant application to the MRC, so Linda Harper's salary as Research Assistant is provided for the next 2 years. Obviously, our first priority is the smallpox/whitepox viruses and we should try to get them wrapped up as soon as possible. We would then move on to the monkeypox viruses and to the cowpox-elephantpox-ratcarnivore-Turkmania group where we also appear to have some useful prospects. Work with these viruses can, of course, run on into 1979 without difficulty.

I think the vital thing in all this is that you and Dr. Arita communicate directly with the UK International Representative at WHO and convince him that you want us to continue and that we have your active support. These triangular negotiations are always complicated but we shall be very grateful for your help.

From: Dr. J. G. Breman

To: Professor H. S. Bedson

18th October 1977

Thank you very much for your letter of 4th October 1977 with the reasonable time plan for completing work with variola virus.

Firstly, please be assured that we feel your work with variola virus is important. You should already have received the grant documents for receipt of \$7,500 for 1977.

Secondly, your suggested plan to finish work with variola/whitepox viruses by the end of 1978 would certainly satisfy us and our recently established advisory group, the “International Commission for the Certification of Global Smallpox Eradication.”

Indeed, Dr. John L. Kilgour, Senior Principal Medical Officer, Head of the International Health Division at the Department of Health and Social Security, will be a member of the Global Commission and we discussed your particular situation with him last week during the “Consultation on Certification of World-wide Smallpox Eradication”.

We shall be in continuing dialogue with Dr. Kilgour and DHSS officials and will again specify our intention to support your activities during the near future.

(copy to Dr. J. L. Kilgour).

From: Dr. J. G. Breman

To: Professor H. S. Bedson

28th February 1978

It was a pleasure talking with you on 23rd February. I am very happy that you will be able to receive Dr. R. Netter, Director, Laboratoire National de la Santé Publique, Paris; Dr. J. H. Richardson, Director, Office of Biosafety, Center for Disease Control, Atlanta; and Dr. A. H. Wahba, Regional Adviser for Health Laboratory Services, WHO European Regional Office, on the morning of 4th May in Birmingham. The team will arrive in the morning as you have requested and their visit should be completed by the time you have to leave for Liverpool. Let me reiterate that this visit is very informal. Nevertheless, it is important that each laboratory be visited to assure that the Directors understand the wishes of WHO and our advisory group (Global Commission) regarding safety in laboratories retaining variola virus. The discussions will include a review of our policies and hopefully the team will be able to discuss and evaluate the measures which have been taken to assure maximum security of variola and whitepox viruses in your laboratory.

We will be keeping you informed as to when the viruses sent by Dr. Marennikova will be forwarded to you. Thank you for giving us the details which will expedite your receipt of these strains.

We would be very interested in receiving your annual report as we are currently preparing the research allocations for 1978.

(Copy to Dr. R. Netter, Paris. Dr. J. H. Richardson, Atlanta. Dr. A. H. Wahba, RA-HLS, EURO).

From: Professor H. S. Bedson

To: Dr. I. Arita, Chief Smallpox Eradication Unit WHO Geneva

31st March 1978

I enclose the promised Research Report for 1977-78. I think it is a little premature to circulate this in its entirety to the whole group but I will put my mind to producing an edited version in due course.

As you will see, we are now putting most of our effort into the polyacrylamide gel electrophoresis studies in order to get as much of the smallpox|whitepox comparisons completed before we have to give up work with these viruses. Progress has been a little slowed while we filled in some of the necessary controls, but we are now in a position to get ahead both more quickly and, I hope, intelligently. These studies, of course, concern mainly late proteins but I hope to have another look at early proteins to see if there are additional distinguishing features before we finish with smallpox|whitepox viruses.

I think two additional points need to be made when you are considering the matter of further support for our research. The first is that last year we were concerned about the need to carry Linda Harper on to continue the polyacrylamide studies. In the event, the MRC gave us a Project Grant which will pay her salary to the end of 1979, so we don't have to find this out of WHO money.

The second point concerns the possible consequences of the visit of your inspecting group which we are expecting in May. I hope that it is clearly understood that, while we are satisfied that what we are doing is sensible and secure and has been approved by our national bodies (DHSS|DPAG), our facilities in no way match

those set out for the definitive smallpox labs. in your workshop report SME/77.2. It would be expensive and very costly in time if we were to try and establish such a laboratory and quite unjustified in view of our projected halt to the smallpox/whitepox work at the end of the year. I hope the visiting group will accept that this is a reasonable approach and that we should concentrate on finishing off these lines of research in the short time that remains.

Enclosure: *Progress Report on Smallpox|Whitepox—Monkeypox Studies 1977-78*

From: Dr. I. Arita

To: Professor H. S. Bedson

14th April 1978

Your confidential report dated 31st March was read with great interest.

Your findings are fascinating, although no conclusions can be drawn at this moment. The study certainly should continue.

There are also important studies continuing in Jim Nakano's laboratory in terms of protein analysis. I recently heard that Dr. Marennikova has now found some lead which may clarify many mysterious points of whitepox virus.

Perhaps late this year or early next year, it will be worth having the fourth poxvirus meeting. What do you think?

With regard to your laboratory safety, simply the expected benefit of your study far exceeds the minimal risk which is currently present in your laboratory and I believe your rationales will be well understood by the visiting team. (Copy to Dr. Breman).

From: Dr. J. G. Breman

To: Professor H. S. Bedson

27th April 1978

Your activity report of 31st March 1978 is extremely valuable. We would be most interested in sharing this with the monkeypox study group in any way you see fit. We would, therefore, appreciate an edited version when convenient to you.

It is a bit unclear whether you would like further funding from WHO in 1978.

Rest assured that the inspection team coming to your laboratory will be fully briefed on the circumstances concerning your special situation.

Enclosure: *Document on handling of Pox viruses prepared by Professor Bedson for WHO visit on 4th May 1978.*

From: Dr. I. Arita

To: Professor H. S. Bedson

15th May 1978

The WHO team reported the results of their visit to your Laboratory as quoted below:

"Dr. Netter, Dr. Wahba and I (Dr. Richardson), have considerable reservations about Dr. Bedson's facility. While surveillance and immunization practices are very good, the physical facilities clearly do not meet the WHO recommendations.

“Professor Bedson (Birmingham);

“Laboratory facility and practices do not meet with recommendations. Recommendations were made: Prohibiting all mouthpipetting in lab; using back-fastening gowns which will remain in laboratory; the use of chemical (hypochlorite solution) as permanent barrier in sinks and gloves to be worn for all activities in BSC involving infectious materials. The use of tabletop hot water “sterilizers” was questioned”.

For the time being, it appears that some safety measures can be immediately applied and improved upon which I believe you are now doing. Whilst your study is important, I would like to receive your assessment of the risks involved.

At the present time, it would be difficult to invest additional funds for remodelling of the laboratory but I feel that further modification in technical procedures and management in the laboratory will certainly lead to strengthening of the safety measures.

Enclosure: WHO Laboratory Facilities Checklist for Birmingham.

From: Professor H. S. Bedson

To: Dr. I. Arita

2nd June 1978

Thank you for your letter of 15th May about the comments of the WHO team on our laboratory.

Their reservations about our physical facilities were, of course, expected. I have already told you of the respects in which they do not match the recommendations of WHO (SME 77.2) for laboratories which are to be the ultimate repositories of smallpox viruses.

On the other hand, I feel that some of the detailed criticisms make our operations sound less well-controlled than they are. The principal reason for this is that they do not distinguish between practices affecting work with smallpox viruses themselves and those affecting work with “ordinary” poxviruses. The confusion is natural since the “open” work with smallpox is restricted to a small laboratory which is reached through the outer “ordinary” poxvirus laboratory and because smallpox viruses in closed containers are stored and incubated in locked refrigerators and incubators in the outer laboratory. Access is, of course, rigidly controlled to both these laboratories.

With regard to the detailed criticisms themselves, mouthpipetting has not been used with smallpox for about 10 years. That observed by the WHO team occurred in connection with an “ordinary” poxvirus and was a temporary aberration which we will ensure does not recur.

The use of back-fastening gowns which remain in the laboratory is also standard practice in the smallpox laboratory. The front-fastening coats used in the “ordinary” poxvirus laboratory can readily be distinguished from the smallpox gowns—a factor which our local Safety Committee thought important—and have, of course, to be worn when work with “ordinary” poxviruses extends to other areas in the Department, e.g., animal house, EM suite, autoclave suite.

They are not worn outside the Department or in clean areas (e.g. offices, tea-room, seminar room) and they are left in the laboratory at the end of any work session.

We have been happy to adopt the use of chemical (hypochlorite solution) as a permanent barrier in sinks and gloves to be worn in BSC for all activities involving infective materials, even though one could argue about the extent to which they affect the safety of the work.

The use of hot water "sterilizers" is something which I would defend for disinfection of poxvirus-contaminated instruments. If cross-contamination from this source were a possibility, we should have known about it by now and there are, of course, data to show the rapid inactivation of poxviruses at much lower temperatures (e.g. 60°C). We also use these "sterilizers" as boiling water baths in biochemical operations.

Finally, you ask for my assessment of the risks involved. Although all work with pathogens involves some risk and no one concerned can afford to be complacent, I see no reason to depart from my previous statement that the risks must be minimal. In support of this, I would cite 1) the long history of laboratory work with smallpox viruses, 2) the progressive decline in the scale and diversity of our operations, particularly since 1973, 3) the marked increase in the level of physical containment which has been introduced, again in the period since 1973, and 4) the maintained high level of our surveillance and immunization practices.

I hope these answers cover all the points on which you required comment but please don't hesitate to come back to me if you feel that something further is needed.

From: Dr. Arita

To: Professor H. S. Bedson

1st August 1978

Dr. Richardson wrote to me as follows:

"I agree with Dr. Bedson's assessment that the risks are probably minimal and feel that there is a reasonably effective surveillance system in effect. It is also apparent that actions to upgrade the containment capability of his laboratory have been minimal."

"I am still concerned over the following:

- 1. Absence of a shower for routine or emergency use.*
- 2. The lack of secondary containment in the outer laboratory where the smallpox stock viruses are stored.*
- 3. The performance capability and certification and maintenance of the biological safety cabinet in the isolation cubicle."*

"The laboratory falls short of the WHO Standard and should be upgraded to meet the Standard or discontinue work with variola at the earliest possible date."

I believe you are making every effort to modify the safety procedures wherever possible.

Do you plan to continue studies on monkeypox next year after your study on variola virus until the end of this year?

From: Professor H. S. Bedson

To: Dr. I. Arita

24th August 1978

Thank you for your letter of 1st August about Dr. Richardson's further comments on our laboratory. This arrived while I was on holiday but I will be giving further thought to anything that we can do to improve our safety procedures now that I am back at work. As you know, there is no question of our being able to upgrade our facilities to meet the full WHO standards and we are therefore proceeding with our plans to complete our studies with variola/whitepox by the end of this year.

We certainly plan to continue work on poxviruses at least until the end of 1979 and probably further. There is quite a lot of work to do looking at the virus isolates of monkeypox virus by our newer techniques and we also have to complete our studies of the cowpox-like viruses which include elephantpox and the virus isolates connected with the rat carnivore poxvirus. We also need to continue studies on camelpox virus. Should comparisons with smallpox/whitepox viruses be required, I am hopeful that we should still be able to arrange this in collaboration with Professor Dumbell at St Mary's but this will obviously involve increased time and expense on travel.

I have no doubt that we shall have the opportunity to discuss these plans in greater detail when we meet in Geneva in November.

From: Dr. I. Arita

To: Professor H. S. Bedson

30th August 1978

Thank you for your two letters of 24th August.

Your findings on white variant from monkeypox have greatly relieved my concern. Let us see how the other laboratories comment on this at the November meeting.

I note that your letters had been written when the case in Birmingham had not come to your notice. I hope this will be variola virus' last revenge—just as it is being exterminated. I am sure you must be feeling very tired these days but take heart and think what constructive steps can now be taken.

**ENCLOSURES CONTAINED IN PROFESSOR BEDSON'S LETTER OF
31st MARCH 1978**

**THE HANDLING OF SMALLPOX, WHITEPOX AND RELATED
ANIMAL POXVIRUSES IN THE DEPARTMENT OF MEDICAL MICRO-
BIOLOGY, UNIVERSITY OF BIRMINGHAM**

Smallpox viruses and whitepox viruses are handled for the purposes of diagnosis and reference and for research directed at extending the basis of identification of these and other unknown viruses related to smallpox virus. Work with smallpox and whitepox viruses is restricted to EG 34(b). The outer laboratory (EG 34) is used for work on related poxviruses and for servicing the inner smallpox laboratory.

The safety of this work depends upon:—

1. Vaccination and regular revaccination of all concerned.
2. Restriction of access to protected individuals.
3. A check on illness occurring in Departmental staff.
4. Containment of the virus while it is being handled.

Information about the first three of these is contained in the Departmental Information Book and only repeated here in outline. The fourth requires careful forethought and planning in experimental work, the highest standards of technique and strict attention to detail, particularly in the matter of disposal of infected items. This applies to **all** those working in EG. 34, whether or not they are also involved in the work with smallpox virus in EG. 34(b).

1. *Vaccination*

Vaccination and the results of inspection for “take” are recorded by Professor Bedson. Those working in EG. 34 and EG. 34(b) are revaccinated each year, all others in the Department, including special cleaners, are revaccinated at 2-year intervals. The University Maintenance Staff, Security Staff, Medical School porters and service engineers of outside contractors are likewise revaccinated at 2-year intervals. Vaccination is offered to those working in departments elsewhere in the Medical School and to the families of the staff of the Department of Medical Microbiology.

2. *Restriction of access*

Only those successfully vaccinated in the last 2 years are admitted to EG. 34. The vaccination status of visitors must be checked with Professor Bedson, the Departmental Safety Officer or another medical member of staff **before** they are allowed into the laboratory. The names and addresses of casual visitors are recorded in the Visitors' Book. Entrance to EG. 34(b) is restricted to those listed on its door or to those who have express permission from Professor Bedson or, in his absence, the Departmental Safety Officer. EG. 34(b) is kept locked except at times of entry and exit (single Yale lock—restricted key). The door to EG. 34 (two Yale locks with restricted keys) and both refrigerators in this room are locked when the room is not in use.

3. *Check on illness*

At the time of starting work in the Department, all members of staff receive a card for their general practitioner which is intended to be filed with their NHS records. In addition, they carry a card to be shown to their doctor in case of illness and are told of their duty to notify the Department immediately of any absence through illness. A record of the doctors with whom members of the Department are registered is kept in the Departmental Office.

4. *Containment*

Routine practice for working with pathogenic microorganisms applies to **all** working within EG. 34, i.e., no mouth pipetting, no eating, drinking or smoking, no licking of labels, immediate attention to spillage and breakage, disinfection of working surfaces after use, wearing of protective clothing properly fastened, washing of hands after practical operations, adequate labelling of experimental material—particularly in incubators and refrigerators, strict adherence to the laboratory drills for discard of infective material.

I. WORK WITH SMALLPOX VIRUS

- (a) All open work with smallpox virus is restricted to the safety cabinet within EG. 34(b), i.e., operations such as making dilutions, inoculating and harvesting eggs and tissue cultures, loading and unloading centrifuge vessels, preparing diagnostic specimens. The operation of the safety cabinet, whenever smallpox virus is being handled, keeps this room at negative pressure with respect to EG. 34. After any period of use, the extract fan is left on for a further 15 minutes. The flow of air is checked routinely by observation of the indicator in the outflow trunking and intermittently by direct anemometer readings. Changes of filters will only be made after they have been disinfected by liberation of formaldehyde within the cabinet. (NB. The micro-bunsen burner within the cabinet is for use only in connection with the preparation of EM grids from diagnostic specimens, since its use at other times might produce distortions in air flow.)
- (b) Those working with smallpox virus within EG. 34(b) wear rear-fastening white gowns quite separate from those worn for work in EG. 34. These are supplemented by disposable plastic "overgowns" and disposable gloves as appropriate. After use disposable items are placed within a Garbena bag and autoclaved within EG. 34(b). This bag is then removed to the paper waste bag in EG. 34 for subsequent incineration. Used white gowns in EG. 34(b) are disinfected by autoclaving within EG. 34(b), removed to EG. 34 and re-autoclaved with the laboratory coats from EG. 34 before being sent to the laundry. No special footwear is worn in EG. 34(b) but those leaving the room must step with both feet on the Tacmat at the entrance in EG. 34.
- (c) Live smallpox virus is removed from EG. 34(b) in sealed specimen containers for storage in the refrigerators in EG. 34 or in inoculated eggs and tissue cultures for incubation in the special locked incubators in EG. 34. The outer door of EG. 34 is kept locked with the sneck on whenever eggs and tissue cultures are being transferred either into or out of EG. 34(b). Live smallpox virus is not stored outside EG. 34 or removed from this room, unless in transit to another approved smallpox laboratory.
- (d) All other smallpox-infected or potentially contaminated material is disinfected within EG. 34(b) before removal to EG. 34 either by boiling in the instrument bath, autoclaving in the portable Baird and Tatlock electric autoclave, or by treatment with chlorox, formaldehyde or stericol.
- (e) Special short 10 ml and 1 ml pipettes are reserved for smallpox work in EG. 34(b). After use they are immersed in a pipette jar containing 10% chlorox. Pasteur and 0.2 ml pipettes are discarded into 1% stericol. Rubber policemen and syringes and needles are disinfected by boiling.
- (f) Pipette canisters, tissue culture trays, egg racks and other similar items of equipment are wiped over with 10% formalin before removal to EG. 34.
- (g) Tissue culture glassware is disinfected by autoclaving or by immersion in chlorox. Medium from infected tissue cultures is aspirated into a reservoir containing neat formalin (sufficient for a final dilution of 1/20) by suction from a water pump via a trap vessel containing 10% formaldehyde. When

full the contents of the reservoir are emptied into a bucket and held for at least 24 hr before removal to EG. 34 and disposal via the sink.

- (h) Eggs are collected in an autoclavable plastic bag, placed inside a stout black paper bag and autoclaved within EG. 34(b). On removal to EG. 34 they are placed with the eggs from this room and given a second cycle of autoclaving before their ultimate disposal.
- (i) Centrifuge operations with smallpox virus are made in the MSE 25 ultra-centrifuge within EG. 34(b). The MSE 25 log book is kept in EG. 34(b) and must not be removed. Centrifuge buckets are disinfected after use by immersion in 10% formaldehyde. Certain low-speed centrifuge operations may be made in EG. 34 using the MSE sealed buckets, the loading and unloading of which is performed within the safety cabinet in EG. 34(b).
- (j) The sink in EG. 34(b) is reserved for hand-washing (foot-operated tap). Used paper towels are collected along with other disposable items in a Garbena bag for autoclaving in EG. 34(b) before removal to EG. 34 and eventual incineration.
- (k) Notes made within EG. 34(b) are not to be removed from the room. Where necessary results can be dictated by phone to the outer laboratory.
- (l) Cleaning within EG. 34(b) is the responsibility of those working in this laboratory. The items of cleaning equipment are kept within the room and disinfected before removal should they need replacement.
- (m) Winchestersters of 10% formaldehyde and 10% formol-saline and a bucket of 10% chlorox (renewed at the start of each working day) are always available in EG. 34(b) for emergency use in case of accidents (*vide infra*).

II WORK WITH RELATED POXVIRUS IN EG. 34

Although less pathogenic than smallpox viruses, many of the related poxviruses handled in EG. 34 are nevertheless capable of causing disease in man. Their handling therefore needs careful attention to the conditions for safe-working. Particularly is this so for disinfection/disposal procedures since material already disinfected in EG. 34(b) is collected with similar items discarded from work in EG. 34 and the original smallpox material in this way receives a second disinfection before ultimate disposal.

- (a) Work with poxviruses other than smallpox and whitepox is carried out on the open wall benches or within the safety cabinet in EG. 34 as appropriate. The safety cabinet should be used for all operations involving ultrasonic disintegration. The centre bench in EG. 34 must not be used for virus work, it is reserved for clean operations such as writing up records, etc.
- (b) Those working in EG. 34 must wear white coats. When not in use these are left on the pegs in EG. 34(c). Outdoor clothing, etc., may be placed on the pegs in the office or kept in lockers outside EG. 34. White coats are changed regularly each Monday, discarded coats being placed in a black disposal bag and autoclaved along with any gowns that have been collected after disinfection in room EG. 34(b).

- (c) Waste-paper basket contents from EG. 34 are collected daily into a large brown paper bag. Disinfected paper waste from EG. 34(b) is also collected in this bag. Each Friday this is closed, put in a black plastic lining bag, which is tied at the neck, and taken to the East Courtyard outside the animal house, whence it is collected and incinerated by the University Services Department.
- (d) *Disposal procedures*
- i. *Infected pipettes*: 10 ml and 1 ml—tall canisters—10% chloros. 0.2 ml and Pasteur pipettes—separate short canisters—1% stericol. (NB. Special care is necessary to see that immersion is total and that the containers are emptied and recharged with disinfectant first thing each day before freshly-infected pipettes are added.)
 - ii. *Infected glassware*: small bottles in “front” autoclave bucket. Burrells and 500 ml bottles are autoclaved direct. Petri dishes are immersed in the 10% chloros bucket.
 - iii. *Infected disposable material*: in “rear” autoclave bucket (these items include paper, plastic syringes, plastic Petri dishes, wee bottles, discarded plastic caps).
 - iv. *Infected tissue culture media and protein-containing fluids*: small amounts are aspirated into a reservoir containing neat formalin (sufficient for final dilution 1.20) and held overnight. Suction is applied to the reservoir through a second “trap-vessel” containing 10% formaldehyde. Large amounts are collected directly into a bucket containing formaldehyde and held overnight before disposal via the sink (NB. Protein-containing fluids must never be put into chloros for disinfection.)
 - v. *Eggs*: collect in autoclavable plastic bag and place this within a black stout paper bag in an autoclave bucket and remove to autoclave. Final discard is to the refuse container outside the East Courtyard.
 - vi. *Clean tissue culture glassware*: pipettes are dealt with as if infected: 200 ml medical flats to water + Quix bucket and McCartneys to chloros bucket in wash-up trolley. Burrells and 500 ml flats are filled with dilute chloros and placed in the wash-up trolley.

III. ACCIDENT DRILL

Coping with accidental spillage or breakage requires the active co-operation of *all* using EG. 34 and its connecting rooms. The area of the accident should be covered with paper towels soaked in disinfectant and time given (30 minutes) for aerosols to settle. During this time, traffic in and out of the room concerned must cease and the door should be kept locked with the sneck on where appropriate. At the end of this time the area of spillage can be dealt with as described in the Information Book. Professor Bedson and the Departmental Safety Officer, or his deputy, must be informed as soon as possible. They will consider whether it is necessary to close the East Ground corridor to traffic or to inform the Medical Officer for Environmental Health. They will also decide what further action is to be taken in respect of matters such as total disinfection of the premises, showering, changes of clothing, and the need for surveillance of

individuals for subsequent illness. Adequate supplies of formaldehyde disinfectants, chlorox and stericol must be maintained and available for emergency use at any time. Those working regularly within EG. 34(b) keep a spare set of clothing and shoes available within the Department should a complete change be necessary.

All untoward incidents and accidents, even minor ones, must be reported to Professor Bedson (or, in his absence, the Departmental Safety Officer,) who will record these by entries in the laboratory day-book in EG. 34 and, where appropriate, a duplicate record will be placed in the Department's Accident Book held by the laboratory superintendent.

CONFIDENTIAL

PROGRESS REPORT ON SMALLPOX/WHITEPOX/MONKEYPOX STUDIES, 1977-78

Department of Medical Microbiology Birmingham University, England
(Professor H. S. Bedson and Linda Harper)

1. *Enzyme Studies*

(a) *Thymidine Kinase*

During the year additional poxvirus isolates have been tested for their sensitivity to feedback inhibition by thymidine triphosphate. The results (Table 1) are consistent with those previously obtained. Three strains of smallpox all gave the high inhibition expected and the three other viruses gave only the low inhibition expected of non-smallpox orthopoxviruses.

Further studies have been made of the neutralisation of this enzyme employing antisera raised in rabbits against different orthopoxviruses. Sera with activity against monkeypox, cowpox and alastrim enzymes were available but attempts to raise corresponding antisera against vaccinia and gerbilpox have remained unsuccessful. The results obtained with these sera are summarized in Table 2. By contrast with the results obtained with the monkeypox antiserum (1976-7 Report), where there was a strong suggestion of useful differences between homologous and heterologous interactions, the results obtained with the cowpox and alastrim antisera show cross reactions throughout the poxviruses tested and no useful separation of the viruses in terms of the magnitude of the cross reaction.

Comment

The results obtained with the additional antisera are not very encouraging. The antiserum to alastrim virus clearly needs testing against a few more virus enzyme preparations. Attempts to make cross-absorbed virus-specific antisera have, so far, been hampered by the low-titre of the available antisera and the difficulty of removing residual enzyme activity added at the absorption stage. Recently, the monkeypox serum has been boosted to higher titre (1/32 against monkeypox and 1/8 against smallpox) and this may offer a better prospect of success.

(b) *DNA polymerase*

No further progress has been made with this work for the moment.

2. *Analysis of Intracellular Virus-specific Proteins*

Comparisons have now been made of 41 different orthopoxviruses, principally by means of the patterns obtained in polyacrylamide gel electrophoresis with specimens labelled by pulse at 16 h post-infection using S³⁵-methionine (Table 3).

Observations of polypeptides in three regions of the gels (MW 177,000, 95–103,000 and 15,000) allow all but three of the viruses to be placed in one of four major groupings. Only the cowpox-like viruses have a prominent band of MW 177,000 while only the monkeypox viruses have a heavily-labelled band MW 15,500. Viruses in these two groups have only a single band in the 95–103,000 region (MW 98,000). By contrast, vaccinia-like and smallpox-like viruses have two bands in the 95–103,000 region but can themselves be distinguished because the bands of vaccinia are of higher molecular weight than those of smallpox and are apparently in reversed order. Thus, the more heavily-labelled band of vaccinia is of lower molecular weight whereas the more heavily-labelled band of smallpox is of higher molecular weight and in each case it is the more heavily-labelled band which disappears on chase while the other band is stable.

The primary groupings made on this basis confirm 1) the position of all 6 whitepox viruses as smallpox viruses; 2) the similarity of monkeypox viruses, whether from monkey outbreaks, humans or tissue culture; 3) the Moscow Zoo rat carnivore virus as a cowpox-like virus and 4) the close relationship between the Lenny isolate, buffalopox, the Bangladesh isolate and strains of vaccinia.

Minor differences have been observed between some of the cowpox-like viruses and between some of the monkeypox viruses. These will be the subject of further study with extended collections of these viruses. For the moment, greatest attention is being paid to the possibility of differentiation within the smallpox group. Most interesting are differences in the 25–27,000 region. The viruses labelled A in Table 3 have a band at 27,000 but none at 25,000, whereas those labelled B have a band at 25,000 and none at 27,000. Time-course studies show that in each case the protein is made throughout the growth cycle but more early than late. The proteins are also stable on chase, but an additional band appears in this region on chase (? derived from the precursor at 28–29,000 which disappears on chase) which confirms the distinction between A and B viruses, that of the A viruses being of slightly lower molecular weight (26,000) than that of the B viruses (26,500). Chase studies have, however, been made on only 2A and 2B viruses so far.

Comment

The differentiation of smallpox viruses appears to us to be of great interest. The genuine smallpox viruses of the B group appear, so far, to be linked with origins in the Middle East and Pakistan, whereas the A viruses include all African isolates, alastrim and some variola major strains of less certain origin, although some (e.g., T. Levell) possibly originated from India. It is clearly necessary to extend this survey with further smallpox strains, particularly from known Asiatic sources, and the help of Professor Keith Dumbell is being sought in this connexion.

Meanwhile, the existence of the same two types among the whitepox viruses strongly supports the view that these must be regarded as smallpox viruses. It is difficult, at the moment, to assess the significance of these findings in terms

of the original source of the whitepox viruses but it is interesting that the two Dutch whitepox viruses which were of possible Asiatic origin are those which are of type B and that the African whitepox viruses are all of type A.

The finding that Algeo and 6128—two strains from the London School of Hygiene outbreak—are of type A confirms Professor Dumbell's observation that these derived from the Harvey strain of variola major and not the Dutch whitepox viruses.

Very recently, chase studies have suggested that further subdivision may be possible amongst the viruses grouped as A. It will therefore be important to re-examine all the smallpox-like viruses with chase specimens, not only to confirm the A-B grouping, but also to look for further differences of this kind.

A further aspect which is being studied derives from the Kuwait viruses, two of which (K5/67 and K1628) do not produce diffusible LS antigen. Both these viruses lack a band which is present in the other Kuwait isolate and all other smallpox viruses examined. While K5/67 and K1628 therefore represent a subvariety of the B type of smallpox virus, their co-existence with K1629 in a single circumscribed outbreak due to importation from Pakistan (Arita, Shafa and Kader, 1970) suggests that the LS-lacking virus arose during the course of the outbreak and not elsewhere. The possible tie up between the LS antigen and the missing band is being pursued.

TABLE 1
INHIBITION OF THYMIDINE KINASE ACTIVITY BY
THYMIDINE TRIPHOSPHATE

Virus	Strain	Residual % Activity*	
		at TTP Concentration 4 uM	8 uM
Smallpox	Kuwait 5/67	15	9
	Kuwait 1628	14	7
	Kuwait 1629	14	5
Vaccinia	Bangladesh '76	85	71
Cowpox	Whipsnade	99	96
	Moscow Zoo (anteater)	134	91

*Enzyme preparations, all from LTK cells.

TABLE 2

Neutralization of Thymidine Kinase Activity by Poxvirus Antisera

Group	VIRUS Strain	ANTISERUM TO POXVIRUS		
		Monkeypox	Cowpox	Alastrim
COWPOX	Brighton	2*	4	8
	Whipsnade	—	2	—
	Moscow Zoo (anteater)	—	4	—
MONKEYPOX	Denmark	4	2	—
	Holland	4	1	4-8
	Washington	2	2	—
	Congo 5	4	2	—
	LIB. 1	4	2-4	—
	64-9411	4	4	—
SMALLPOX	Hinden	1	1	16
	Congo 5	1	2	—
	Kuwait 1628	1	1	—
	Iran 2602	1	1	—
	Butler	1	1	16
	Brazil 1	1	2	—
	EA 12/61	1	2	—
	EA 17/61	1	1	—
WHITEPOX	Chimp 9	1	2	16
	MK 7	1	1	—
	64-7255	1	4	—
	64-7275	1	4	—
	RZ38	1	2	—
	RZ10	1	1	8
VACCINIA	Connaught Lab	2	—	—
	Rabbitpox—Utrecht	1	2	16
	Lister	—	1	8
GERBILPOX	(Lourie et al.)	2	1	16

*Figure is reciprocal of highest dilution giving 50% or greater neutralization of enzyme activity.

TABLE 3
Viruses Examined by PAGE

Virus	Strain	PAGE Grouping
COWPOX	Brighton	Cowpox
	Brighton-White	"
	Whipsnade	"
RAT CARNIVORE	Moscow Zoo (anteater)	"
MONKEYPOX	Denmark	Monkeypox
	Denmark-White	"
	Washington	"
	Congo-8 (human Isolate)	"
	LIB.1 (human Isolate)	"
	64-9411 (tissue culture Isolate)	"
	VACCINIA	Lister WR
BUFFALOPOX	Indian Isolate (Baxby)	"
LENNY	Human Isolate	"
MK10	Primate Isolate Zaire	"
BANGLADESH	Human Isolate 1976	"
SMALLPOX	Harvey—var. major	Smallpox A
	Hinden—var. major	" A (chase studies conf.)
	Congo 5	" A
	T. Levell—(Merseyside 1958),	" A
	EA 17/61	" A
	Butler—Alastrim	" A (chase studies conf.)
	Brazil 1—Alastrim	" A
	Iran 2602	" B
	Shuka Mia— (UK 1962)	" B
	Kuwait 5—(1967)	" B
	Kuwait 1628—(1967)	" B
	Kuwait 1629—(1967)	" B (chase studies conf.)
	Botswana 21	" A
	Botswana 89	" A
	Algeo (Lond. Sch. Hyg. 1973)	" A
	1628 (Lon. Sch. Hyg. 1973)	" A
WHITEPOX	Chimp 9	Smallpox A
	MK 7	" A
	64-7255	" B (chase studies conf.)
	64-7275	" B
	RZ-38	" A
	RZ-10	" A
ECTROMELIA	Mill Hill	} Individual patterns each distinguishable from 4 major virus groups.
GERBIL POX	(Lourie)	
CAMELPOX	CM-S	

4/5/78

VARIOLA LABORATORY FACILITIES CHECKLIST

NAME OF LABORATORY: DEPT OF MEDICAL MICROBIOLOGY
ORGANISATION UNIVERSITY OF BIRMINGHAM
ADDRESS B' HAM B15 7TJ
DIRECTOR'S NAME: H. S. BEDSON
TITLE PROFESSOR

PHYSICAL SECURITY OF LABORATORY

Separate building _____
Controlled area within a building
Method of access control to laboratory Lock + Key
Is list of personnel authorised entry to lab posted? YES

INVENTORY OF STRAINS

Variola # STRAINS V. major 19 ± V. minor 135 # vials 300+
White pox # " 6 # " INCLUDED IN ABOVE TOTAL
Monkey pox (Y) / N
Other ortho pox viruses (Y) / N

Are smallpox and whitepox viruses stored within the laboratory? YES

If no, complete column 3 checklist.

Variola + Whitepox
AUTHORISATION TO MAINTAIN AND WORK WITH VIRUSES ~~INDICATED ABOVE~~
National DHSS / LONDON
Other UNIV SAFETY + EH Comm. Advisory GP on Pathogenic Organisms & Infectious Materials

Variola + Whitepox
PRIMARY FUNCTION OF LABORATORY INVOLVING USE OF VIRUSES ~~INDICATED ABOVE~~

Archival _____
Diagnostic: (2) Regional Dx facility
Research: (1)

FACILITY DESCRIPTION AND WORK PRACTICES

	Variola Laboratory		Lab Animal* Facility		Variola/Whitepox* Respiratory	
	YES	NO	YES	NO	YES	NO
1. Walls, floors and ceilings sealed and impervious to water	✓					
2. Air locks for entry of supplies and materials		✓				
3. Contiguous change room and shower for entry-exit access to laboratory		✓				
4. Double doored autoclaves						
Autoclave doors interlocked to prevent opening of outer door unless chamber has undergone heat cycle						
5. Biowaste treatment system if contaminated liquid wastes are discharged from laboratory		✓				
a. Heat						
b. Chemical						
c. Other						
6. Separate ventilation system	✓					
Air pressure in laboratory negative to adjacent areas	✓					
Directional airflow in laboratory	✓					
Recirculation of air within laboratory						
7. Prefiltration of supply air						
8. Filtration of exhaust air through 2 HEPA filters in series						
9. All primary access doors to laboratory locked	✓					
10. Who controls keys? <u>Prof. Badson / Dept Safety Officer</u>						
① <u>air exhausted via BSC to single HEPA</u>						

	Varicella Laboratory		Lab Animal Facility		Varicella/Whitepox Repository	
	YES	NO	YES	NO	YES	NO
11. Is Biohazard Warning Sign Posted?	✓					
12. Are signs posted indicating that smallpox vaccination is a condition of entry into building or controlled access area?	✓					
13. Are biological safety cabinets used in laboratory? Specify type(s) <u>CO-1 (negative pressure BSC)</u> Other primary containment equipment <u>Centrifuge safety cups opened in BSC</u>	✓					
14. Does laboratory have view windows from which all areas can be seen?	①					
15. Does laboratory design and operational procedures preclude the entry of insects, rodents, and other pests?	✓					
16. Are laboratory animals used in diagnostic or research procedures? Indicate species _____	✓					
17. Are infected laboratory animals maintained in: Laboratory (), in separate animal facility () If animal facility is separate from laboratory, complete Column 2 checklist.						

*Complete if Laboratory Animal Facility or Varicella Whitepox Repository is not within the Varicella Laboratory

① Isolation Room has window

VACCINATION PRACTICES

Are all personnel working in laboratory vaccinated with WHO approved vaccine? YES
 At what intervals? 1 (years)
 Are vaccinations read and recorded by a physician? YES Records in Dept of Micro.
 Are personnel evaluated for antibody levels? only if "take" is questionable
 What test(s) are used? HA () ; HI () ; SN ()
 At what intervals are serologic evaluations performed?
 Are demonstrated antibody levels required for lab. personnel, 1:256H
 If laboratory is not in a separate building, are all persons working in building
 vaccinated? 2 yrs in Dept of Micro. household contacts At what intervals? and maintenance personnel
 Are family members of laboratory personnel vaccinated? ye commended - not required

SAFETY

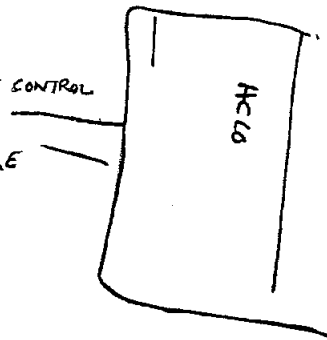
- * " " " " " INSTITUTION: YES
- Is there a safety committee for the variola laboratory? NO
 Is it part of the administrative structure of lab.: NA
 Does this committee: make periodic inspections of laboratory operations _____ ;
 prepare written reports? Inspections made by & not Safety Comm.
 Last report made: _____
 - Are personnel provided written safety procedures? YES: specific to Variola lab
 - How are personnel entries into laboratory recorded? Day book work record identifies personnel in lab on given day.
 - How are accidents reported and recorded? Dept Chairman + Safety officer.
(Dr Skinner) advised immediately:
and household contacts
 - Who is responsible for health surveillance of personnel? Personnel call in if ill - Dr. Redmon will visit if rash or other suggestion of lab. associated illness.
 - Has a laboratory operations manual been prepared? YES
 - What action would be taken in the event of a suspect case in lab:
 COMMENTS: Item 5 + immediate notification of safety officer + local Health authorities.

SITE VISIT TEAM R. NETTER / J. RICHARDSON 4 MAY 78
WAHBA

- Dept Safety Manual also available
- Health alert card & notification of nature of lab work made available to physician.

SUGGESTIONS.

1. NO MOUTH PIPETTING (ml pipettes)
2. WEAR GLOVES.
3. Do a McCLARTY - TYPE EFFLUENT CONTROL IN SINKS.
4. ENSURE THAT LAB COATS ARE CHANGED ON LEAVING LABS.



APPENDIX 22

SAFETY ARRANGEMENTS AT BIRMINGHAM UNIVERSITY

As a result of the requirements of the Health and Safety at Work Act etc. 1974, Birmingham University compiled in April 1975 a document entitled "Safety" and provided each member of staff with a copy.

The full document is reproduced here.

THE UNIVERSITY OF BIRMINGHAM SAFETY

One of the requirements of the Health and Safety at Work etc. Act 1974, is that employers should prepare and bring to the notice of all their employees a statement of their safety policy and arrangements.

The following account, "Safety Arrangements in the University", was prepared by the University Safety and Environmental Health Committee and has been approved by the Council and Senate of the University, and is being distributed in order to fulfil the above requirement of the Act.

Also under the above Act employers are required to provide their employees with such information as is necessary for their health and safety at work. The accompanying paper, "Accident and Emergency Procedure", is being issued to meet this obligation, and information covering other aspects of health and safety will be issued in the future if considered necessary.

Safety arrangements in the University

Each individual carries a responsibility for his own safety and the safety of others around him. It is realised however that to leave safety entirely in the hands of the individual is unsatisfactory, and that safety advice and assistance must be provided. The following account describes the safety arrangements at this University.

Arrangements at Departmental Level

1. Individuals and their safety responsibility

Ultimate responsibility for safety rests firmly with the individual. Individuals have at all times a duty to conduct themselves and to do their work in a safe manner so as not to endanger themselves and others around them. Clearly the degree of such responsibility carried by particular individuals will depend on the nature and extent of their work. Should any individual feel concerned over the safety aspects of his or her work, the advice of a competent person should be sought immediately.

2. Supervisors

Persons in supervisory positions have special duties with regard to safety when in charge of students, research workers, junior staff, technicians, etc.,

either individually or in groups. Such persons must give consideration to the safety aspects of the work in hand and must ensure that all reasonable precautions are taken. In cases of uncertainty, expert advice should be sought.

3. *Heads of Departments*

The Head of a Department has the duty to ensure that proper safety arrangements are made in conformity with University policy. This should not be taken to imply that the Head of Department is personally responsible for each and every detailed aspect of safety. However, included for example among his duties should be to ensure:

- (a) that a safety conscious attitude is encouraged, particularly with regard to technical operations;
- (b) that safety information and instructions are adequately disseminated in his Department;
- (c) that a proper mechanism exists within the department for raising safety matters and that this is well publicised.
- (d) that proper arrangements are made for the disposal of hazardous wastes.

In discharging his duties, of which the above are only some examples, a Head of Department may, but need not, decide to delegate some of his duties to one or more Departmental Safety Officers who should be experienced persons with professional knowledge of the equipment, processes and materials used in the department. If this course is taken, then it is essential that the duties of the Departmental Safety Officer should be agreed between him and the Head of Department. In order that no misunderstandings can arise it is necessary that a list of specific duties be given in writing.

In some situations, for example in the Faculties of Arts and Commerce, where safety problems are likely to be fewer than elsewhere, or where individual departments are small, it might be appropriate for Safety Officers to be appointed either on a Faculty or Building basis rather than departmentally. In this case, the Dean or Sub-Dean of the Faculty should assume the responsibilities of a Departmental Head and the duties delegated to the Safety Officer should be agreed with him and specified in writing.

4. *Departmental, Faculty and Building Safety Officers*

Departmental, Faculty or Building Safety Officers must, in performing their duties, be given recognition for their work, as is the case when staff undertake other administrative work not directly connected with research or teaching.

Depending on the nature and extent of the work in the various departments, the duties of Departmental, Faculty or Building Safety Officers may differ very considerably. Such Safety Officers do not carry any special legal responsibility for safety, and certainly cannot be held responsible for errors made by others. They are however expected to be administratively competent, and to be persons who will perform their duties in a responsible manner and with reasonable care. It is appreciated that a Departmental, Faculty or Building Safety Officer may

not feel competent to advise on all specialist safety problems that may arise, but if situations of this sort do occur it is his duty either to seek appropriate advice from a competent expert, or to ensure that the persons concerned are in touch with such experts.

5. *Persons allocated specific safety duties*

Departmental, Faculty, or Building Safety Officers might, with the consent of the Head of Department, Dean or Sub-Dean concerned, wish to delegate particular and well defined duties to other persons. Such a duty might be checking the contents of First Aid Boxes on a regular basis and making good any deficiencies. Other examples could be in relation to fire precautions and emergency evacuation procedures. Such duties could be arranged on a departmental basis, but need not be e.g. a person could be responsible for a particular duty in an entire building or a floor of a building.

In such cases, the persons to whom such duties are delegated should receive clear written statements of their duties.

Committee Structure

At the present time there exists considerable legislation concerning safety, some of which applies to the University. Regardless of whether or not the University is subject to particular pieces of legislation, it is University policy to ensure that high standards of safety are achieved. The body that has been charged with this duty on behalf of the University is the University Safety and Environmental Health Committee (USEHC) which is a joint committee of the Finance and General Purposes Committee and the Senate. This Committee advises the Finance and General Purposes Committee and the Senate on safety policy and is also responsible for ensuring that University safety policy is properly implemented. It must also ensure that an adequate safety structure is established, that safety information is circulated, and that advice on safety matters is available.

The University Safety and Environmental Health Committee is therefore a committee which is concerned with broad issues affecting safety and which co-ordinates the activities of various other committees involved with safety.

More detailed consideration of specific safety problems is given by a number of other committees and sub-committees, and so problems of this sort should be notified in the first instance to these other committees. These committees are:—

Committee for the Control of Pathogenic Organisms and Infectious Materials—this is a sub-committee of USEHC.

Committee for the Control of Radiation Exposure—this is also a sub-committee of USEHC and the University Radiation Protection Officer is its executive officer.

Faculty of Science and Engineering Safety Committee—this committee considers all aspects of safety for the Faculty and issues a Safety Handbook.

Faculty of Medicine and Dentistry Joint Services Board Safety Sub-Committee—this committee considers all aspects of safety in the Faculty.

Works and Maintenance Committee—this is a committee of the Finance and General Purposes Committee and is responsible for such matters as fire precautions, emergency lighting, safety of Maintenance and Grounds personnel, design and construction of petroleum and solvent stores, security, traffic control and safety policy in Halls of Residence. The Estates and Buildings Officer is responsible for implementing the policy of this committee and does so through the appropriate officers.

Safety Advice and Information

The University Safety Adviser acts as Secretary to USEHC and is also responsible for communicating safety information to departments. Such communications are sent by the University Safety Adviser to Departmental Heads and Departmental, Faculty and Building Safety Officers. Some safety items are given wider publicity in the 'Bulletin'. The University Safety Adviser is also available to advise departments or seek advice from outside bodies on safety problems. Advice on legal aspects of safety may be obtained from the Secretary to the University, and advice on electrical and mechanical aspects of safety may be obtained from the Estates and Buildings Officer.

The Committee of Vice-Chancellors and Principals has recently issued Part 1, 'General Principles' of a Code of Practice for Safety in Universities. This forms the basis of University Safety Practice and copies have been distributed to Heads of Departments and Safety Officers.

In the above Code of Practice, it is stated that the University must set up a clearly defined chain of responsibility for safety and this document is intended to meet that need.

Legal

The legal responsibility for safety in the University lies ultimately with the governing body, and in law the University is responsible for the actions, within the scope of their employment only, of members of its staff. Heads of Department are responsible to the Council of the University for safety in their department. Individuals are liable jointly with the institution for their own negligence towards colleagues or members of the general public.

Insurance

The University's insurers state that there is no distinction between a Safety Officer and any other employee. They confirm that the University's relevant policy recognises the fact that an employee might be sued instead of or in conjunction with the University and gives an indemnity up to the limit of liability, which has recently been raised to £1,000,000 in respect of cover against injury, and loss of or damage to property. A proviso has been added to the effect that this indemnity would not extend to the consequences of "wilful negligence"—this is a standard exclusion clause in all liability policies.

Accident and Emergency Procedure

1. Fortunately because the majority of people working in this University are safety-conscious and the precautions and preventive measures adopted throughout the University are effective, the incidence of accidents is low and those that occur tend to be of a minor character.

2. However, this note is intended to outline the various procedures that can be adopted in the event of an accident or medical emergency.

3. In the event of a minor cut, scratch or abrasion occurring, the wound should be cleaned if dirty, bleeding stopped by firm pressure, and if necessary a dressing applied. There are first aid boxes in most buildings, and it is suggested that you enquire where the nearest one to your place of work is situated.

4. Weekdays

- (a) If it is felt that such a minor injury needs more careful treatment, or that a Tetanus Toxoid injection should be given, then the patient should come or be brought to the Health Centre and medical and/or nursing attention can be given between 9.00 a.m. and 5.0 p.m. during the term time, and similar facilities will usually be available during the vacation.
- (b) Between about 5.0 p.m. and 10.0 p.m. there is a nurse on duty at the University Health Centre who will give advice and can, if necessary, contact the duty doctor, (ring 472 0731).
- (c) Between 10.0 p.m. and 9.0 a.m. in emergency ring 472 0731 and the telephone answering machine will give the telephone number of the duty doctor available.

Weekends

During term, from 9.0 a.m. to 10.0 p.m. the arrangements described in (b) above apply.

During vacations, the Health Centre is not manned at weekends but the telephone answering service described in (c) above is available.

5. In the event of a more serious injury, then a decision needs to be made by the injured person or a colleague as to whether the person should be transported by car to the University Health Centre, or by car or ambulance to the Accident Hospital, which deals with all cases of injury including burns, or to the Eye Hospital for eye injuries. In the case of radiation exposure accidents, contact Mr. D. Bush, Radiation Protection Officer (Internal No. 5115, or PABX 3546) if possible for advice. If Mr. Bush is not available, then radiation exposure accidents should be taken to the General Hospital Casualty Department.

6. The University Health Centre is not equipped to deal with other than minor injuries. Cases of injury will of course be seen speedily at the Health Centre, but it is suggested that if it is thought that an X-ray or more than simple treatment is going to be required, the patient can then be taken directly to the Accident Hospital rather than to the Health Centre.

7. If the injury is not so severe that immediate action is necessary, then if there is any doubt as to procedure, please ring the University Health Centre and discuss the problem with a member of the staff.

8. If it is obvious that the injury necessitates hospital care, then order an ambulance by dialling the emergency telephone number (usually PO or internal 5555) and explain exactly where you are and what the problem is, and where you wish the ambulance to be sent.

9. If having ordered an ambulance you feel that the injured person is in need of immediate medical care, then ring the Health Centre and if a doctor is available the problem will be discussed and the appropriate action initiated.

10. If in doubt ring the emergency number.

11. In the case of serious injury:—

- i. Avoid moving the injured person if possible.
- ii. Maintain a clear airway, and if necessary apply mouth to mouth artificial respiration.
- iii. Stop bleeding by firm pressure to the bleeding area, whilst waiting for the ambulance and/or doctor to arrive.

12. Acute medical emergencies can be seen at the University Health Centre, or if obviously severe may be taken straight away by ambulance or car to the nearest appropriate hospital.

13. If in doubt about the appropriate action in a medical emergency, please ring the University Health Centre (472 0731). (Reception 9.0 a.m. to 5.0 p.m., Internal 432; Sanatorium about 5.0 p.m. until 10.0 p.m. Internal 5427).

April 1975

APPENDIX 23

POX VIRUS STRAINS HELD IN THE DEPARTMENT OF
MEDICAL MICROBIOLOGY

COWPOX	Brighton	
	Brighton White	
	Whipsnade	
	Moscow Zoo	
MONKEY POX	Denmark	
	Holland	
	Washington	
	Congo 8	
	Lib 1	
	64-G411	
SMALLPOX	Hinden	EA 17/61
	Congo 5	Iran 2602
	Kuwait 1628	Shuka Mia
	Iran 2602	Kuwait 5
	Butler (Alastrim)	Kuwait 1628
	Brazil 1 (Alastrim)	Kuwait 1629
	EA 12/61	Botswana 21
	EA 17/61	Botswana 9
	Harvey	Algeo (L.S. Hygiene)
	Mimin	1628 (")
	Congo 5	Jumma
	Calcutta 1	W. Java
	Bombay	Bandung
	Hawa	
	Botswana 88	
	Ethiopia 7-8-9-23	
	Iran 9866, 9883, 9879	
	Karachi 72, 74	
	Taj	
	Abid	
	Nasar	
	Tjiandora	
Nurbaity		
VACCINIA	Lister	
	Connaught Lab	
WHITE POX	Chimp 9	
	Mk 7	
	64-7255, 7275	
	RZ 38, 10	
OTHERS	Gerbil pox	Lenny
	Camel pox	Mk 10
	Buffalo pox	Bangladesh
		Electromelia

APPENDIX 24

SEQUENCE OF EVENTS

February 1973	Escape of smallpox virus from a laboratory in the London School of Hygiene and Tropical Medicine resulting in the death of two persons.
June 1974	Cox Committee Report on the above incident published Interim Code of Practice suggested for safety in laboratories handling smallpox virus.
May 1975	Godber Working Party on the Laboratory Use of Dangerous Pathogens publishes its Report. The report recommends the setting up of a Dangerous Pathogens Advisory Group and proposes a code of practice for use in laboratories holding Category A pathogens.
November 1975	Dangerous Pathogens Advisory Group meets for the first time.
February 1976	Birmingham Smallpox Laboratory inspected on behalf of DPAG.
August 1976	DPAG advises the Department of Health and Social Security that the Birmingham Smallpox Laboratory is suitable to continue work with smallpox virus.
September 1976	DHSS writes to Professor Bedson notifying its approval of his laboratory for work with smallpox virus.
October 1976	DPAG publishes its Safety Code.
September 1977	WHO informs Professor Bedson that his laboratory is not to be made a Collaborating Centre. This implies that his work with smallpox virus will soon have to end.
October 1977	WHO agrees that the Birmingham laboratory should discontinue work with smallpox virus at the end of 1978.
May 1978	WHO inspects the Birmingham Smallpox laboratory. They criticise the facilities but do not alter the timetable for the discontinuation of smallpox work. The laboratory receives 22 variola strains from the laboratory at St Mary's Hospital Medical School. The pace of work increases.
July 1978	Mrs. Parker infected with smallpox.

11th August 1978	Mrs. Parker unwell.
15th or 16th August 1978	Mrs. Parker develops rash, seen by her doctor on 16th August.
21st August 1978	Mrs. Parker transferred to her parents' home in her father's car.
24th August 1978	Mrs. Parker taken to hospital. Her illness diagnosed as smallpox. The Birmingham Smallpox laboratory ordered to be closed the following day.
7th September 1978	Mrs. Whitcomb develops smallpox.
11th September 1978	Mrs. Parker dies.
22nd September 1978	Mrs. Whitcomb discharged from hospital.

HER MAJESTY'S STATIONERY OFFICE

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