renal perfusion rate as a consequence of orthostatic circulatory insufficiency. These shifts, however, were statistically not significant, and on day 30 the profiles were identical in both groups.

The late sequelae of early mobilization were evaluated by follow-up of half of the patients in each group. After an average of one-and-a-half years no significant differences were found (table III). Seventeen patients in group 1 had died after an average of 11 months and 15 in group 2 after they had survived for an average of 13 months.

TABLE III—*Follow-up Data*

| | No. of Patients | Average Interval (Months) | Cardiac Aneurysm | Congestive Heart Failure | Severe Angina | Dead |
|---|---|---|---|---|---|---|
| Group 1 | 50 | 19 | — | 6 | 9 | 8 |
| Group 2 | 48 | 18 | 2 | 5 | 6 | 9 |

## Discussion

To our knowledge only two other controlled studies of this kind have been carried out. Groden *et al.* (1967) compared the clinical course after 15 and 25 days of bed rest. They allocated patients at an early stage. A number of patients could not be mobilized according to schedule because of complicating events. Thus the two groups became unequal in size and a statistical bias was introduced. The rate of complication did not differ between the two groups. Harpur *et al.* (1971) ran a trial on patients who were mobilized on the 8th and 21st days and found no differences in clinical course. A complete clinical comparison was not possible because patients in the first group were discharged on the 15th day. At follow-up after eight months, however, patients from the former group appeared to have fared no worse than those from the latter group.

The results of these studies and the present one indicate that patients with an uncomplicated myocardial infarction may safely be mobilized after one to two weeks and discharged after about three weeks.

We are indebted to Sister A. J. Alblas-Goedegebuure, Sister J. A. v.d. Krans, Miss B. L. Spildooren, Miss A. H. v.d. Hoest, Miss J. A. Spijkman, Miss J. W. Schouls, Miss M. A. Poessé, Miss J. E. Schot, and Mr. R. O. Hatt for invaluable help.

Requests for reprints should be addressed to Dr. W. H. Birkenhäger, Department of Internal Medicine, Zuiderziekenhuis, Groeneveld 15, Rotterdam, Netherlands.

## References

Groden, B. M., Allison, A., and Shaw, G. B. (1967). *Scottish Medical Journal*, 12, 435.
Harpur, J., *et al.* (1971). *Lancet*, 2, 1331.

# Efficacy of Whooping-cough Vaccines used in the United Kingdom before 1968

## Final Report to the Director of the Public Health Laboratory Service by the Public Health Laboratory Service Whooping-cough Committee and Working Party

*British Medical Journal*, 1973, 1, 259–262

## Summary

**The efficacy of pertussis vaccines was investigated in 33 areas in the United Kingdom from November 1966 until April 1968 inclusive. Bordetella pertussis was isolated from 1,293 persons, but there were only six isolations of B. parapertussis. Among vaccinated contacts under 5 years in homes in which B. pertussis was isolated 52% developed paroxysmal cough. The corresponding attack rate among unvaccinated contacts was 69%. These findings suggest that much of the pertussis vaccine in use for five or six years before 1968 was not very effective. However, vaccine from one producer was more effective than vaccine from another. Of the cultures of B. pertussis identified 89% were serotype 1, 3 and only about 9% were serotype 1, 2, 3. Serotype 1, 2, 3 was isolated much more frequently from unvaccinated than from vaccinated children, but some cultures identified as type 1, 2, 3 were found on re-examination to contain colonies of type 1, 3. Virological investigations were made in some areas during the first year of the study. Of the wide variety of viruses identified adenovirus and parainfluenza virus were the most common groups. Virus isolation rates were similar in patients and symptomless contacts, but B. pertussis was isolated far more often from patients than from symptomless contacts. The evidence suggests that B. pertussis remained the major cause of whooping cough in the U.K.**

PUBLIC HEALTH LABORATORY SERVICE WHOOPING COUGH COMMITTEE AND WORKING PARTY: Dr. E. H. Gillespie, P.H.L. Sheffield (chairman); Dr. J. D. Abbott, P.H.L. Manchester (secretary); Dr. A. H. Antonis, P.H.L. Colindale; Dr. H. R. Cayton, P.H.L. Bristol; Professor R. Cruickshank, University of West Indies; Dr. L. M. Dowsett, P.H.L. Norwich; Professor J. P. Duguid, University of Dundee; Dr. W. N. Dunnet, D.H.S.S.; Dr. T. F. Elias-Jones, City Laboratory, Glasgow; Dr. J. A. N. Emslie, P.H.L. Middlesbrough; Dr. R. R. Gillies, University of Edinburgh; Dr. J. V. T. Gostling, P. H. L. Portsmouth; Dr. J. H. Hale, P.H.L. Newcastle; Dr. R. J. Henderson, P.H.L. Worcester; Dr. P. G. Higgins, P.H.L. Epidemiological Research Unit, Cirencester; Dr. H. H. Johnston, P.H.L. Oxford; Dr. L. A. Little, P.H.L. Wakefield; Dr. N. S. Mair, P.H.L. Leicester; Dr. E. R. Mitchell, P.H.L. Nottingham; Dr. B. Moore, P.H.L. Exeter; Dr. D. J. H. Payne, P.H.L. Portsmouth; Dr. F. T. Perkins, National Institute for Medical Research, London; Dr. Sheila Polakoff, Epidemiological Research P.H.L. Colindale; Dr. T. M. Pollock, Epidemiological Research P.H.L. Colindale; Dr. Pauline M. Poole, P.H.L. Chester; Dr. N. W. Preston, University of Manchester; Dr. H. G. M. Smith, P.H.L. Bradford; Dr. A. F. B. Standfast, Lister Institute of Preventive Medicine; Dr. I. O. Stewart, P.H.L. Coventry; Dr. I. Taylor, D.H.S.S.; Dr. Mair Thomas, P.H.L. Edmonton; Professor Scott Thompson, P.H.L. Cardiff; Dr. G. C. Turner, P.H.L. Liverpool; Dr. J. F. Warin, M.O.H. City of Oxford; Dr. J. E. M. Whitehead, P.H.L. Coventry; Dr. A. M. M. Wilson, University of Edinburgh; Dr. P. J. Wormald, P.H.L. Salisbury; Dr. A. E. Wright, P.H.L. Gloucester.

Dr. E. C. Armstrong, Dr. D. M. Green, and Dr. W. J. Ryan acted as deputies for Dr. G. C. Turner, Professor J. P. Duguid, and Dr. B. Moore respectively.

## Introduction

In November 1966 a Public Health Laboratory Service working party began an investigation to identify the serotypes of *Bordetella pertussis* currently responsible for whooping cough and to assess the efficacy of the pertussis vaccines in use before and during the period of the study. In some areas an attempt was made to isolate viruses from the patients. A preliminary report (P.H.L.S., 1969) of the first year's results suggested that much of the pertussis vaccine in general use for some years before 1968 was not very effective.

The present report is concerned with the bacteriological and virological findings and with the results of the whole 18-month period of the survey.

## General Plan and Methods

Thirty-three areas in England, Wales, and Scotland* were included in the investigation. The Scottish areas were Dundee, Edinburgh, and Glasgow.†

The survey was co-ordinated and the results were analysed in the Epidemiological Research Laboratory by Dr. Sheila Polakoff.

Sir Austin Bradford Hill advised on the analysis of the findings.

Details of the investigation were given in the preliminary report. In summary, in each of 33 areas widely spread throughout the United Kingdom a nurse or doctor took pernasal swabs from each patient reported by the family doctor to have a paroxysmal cough suggestive of pertussis. During the first year of the study swabs were taken also from any other children of less than 5 years of age in the home. About three weeks later the home was visited again and swabs were taken from any further patients with paroxysmal cough. Vaccination histories of the patients and their home contacts were checked with the records of the health authority or family doctor. The pernasal swabs were examined in the laboratory for *B. pertussis* and *B. parapertussis*. The cultures of *B. pertussis* isolated were serotyped at the area laboratory and again at one of two reference laboratories. In some areas nose and throat swabs were taken and examined for viruses, but in the last six months of the study virological observations were discontinued.

### LABORATORY METHODS

*Bacteriological.*—Methods used to isolate and serotype *B. pertussis* were described in the previous report (P.H.L.S., 1969). In the area laboratories serotyping was carried out on a subculture from one or more colonies from the primary plate or directly from a sweep of colonies from the primary plate. The reference laboratories received for serotyping a subculture from one or more colonies.

*Virological.*—Specimens for virus isolation consisted of a nose and a throat swab broken off in a bijou bottle of transport medium. They were examined in cultures of monkey kidney, the Bristol line of HeLa cells, and in human embryo diploid fibroblasts (W138) as described in the study by the Medical Research Council Working Party on Acute Respiratory Virus Infections (1965). In addition some of the specimens were examined in cultures of human embryo kidney, human amnion or HEp2, or were inoculated into suckling mice less than 48 hours old.

*Definitions.*—The attack rates in contacts which are analysed refer to attacks of paroxysmal cough developing in children of 10 years of age or less living in a household in which there was a patient with a paroxysmal cough and in which *B. pertussis* was isolated from at least one member, though not necessarily the source patient. Children who developed symptoms within one week of the onset of symptoms in the first patient in the household were excluded from the attack rates as being concurrent rather than contact cases.

*In England and Wales the medical officers of health who collaborated in the study were: Dr. M. Watkins, Barnet L.B.; Dr. E. Bebbington, Beeston and Stapleford U.D.C.; Dr. W. Turner and Dr. J. Douglas (rtd.), Bradford C.B.; Professor R. C. Wofinden, Bristol C.B.; Dr. W. P. Phillips, Cardiff C.B.; Dr. T. O. P. D. Lawson, Cheltenham M.B.; Dr. T. M. Clayton, Coventry C.B.; Dr. W. A. Pollitt, Ellesmere Port M.B.; Dr. E. D. Irvine, Exeter C.B.; Dr. P. T. Regester, Gloucester C.B.; Dr. S. Knight, Gloucester R.D.C.; Dr. J. G. Cairns, Halifax C.B.; Dr. W. Cormack, Harrow L.B.; Dr. S. Hewitt, Havant and Waterlooville U.D.C.; Dr. B. J. L. Moss, Leicester C.B.; Professor A. B. Semple, Liverpool C.B.; Dr. Kennedy Campbell and Dr. C. Metcalfe Brown (rtd.), Manchester C.B.; Dr. R. C. M. Pearson (rtd.), Newcastle upon Tyne C.B.; Dr. W. Dodd (rtd.), Nottingham C.B.; Dr. J. F. Warin, Oxford C.B.; Dr. P. G. Roads, Portsmouth C.B.; Dr. R. J. Donaldson, Rotherham C.B.; Dr. C. H. Shaw, Sheffield C.B.; Dr. W. Sharpe, Stretford M.B. and Urmston U.D.C.; Dr. R. Taylor, Teesside C.B.; Dr. G. Firth and Dr. C. G. K. Thompson (rtd.), Wakefield C.B.; Dr. E. W. Wright, Waltham Forest L.B.; Dr. E. H. Moore, Warrington C.B.; Dr. C. D. L. Lycett, Wiltshire C.C.; and Dr. G. M. O'Donnell, Worcester C.B.

†Professor N. R. Grist, Dr. Constance A. Ross and Dr. R. J. Fallon, Ruchill Hospital, Glasgow, and Dr. M. A. Calder, City Hospital, Edinburgh, also took part in the laboratory investigations in Scotland.

## Results

During the first 12 months of the investigation (November 1966 to October 1967) pernasal swabs were taken from persons in 3,564 households; isolations of *B. pertussis* or *B. parapertussis* were made from one or more persons in 792 households (21%). During the final six months (November 1967 to April 1968) isolations of *B. pertussis* were made from persons in a further 197 households. Of the total 989 households in which isolations were made *B. pertussis* was found in 986, whereas *B. parapertussis* was found in only three.

In the summer of 1967 whooping cough notifications increased in England and Wales, and the number of isolations of *B. pertussis* from the laboratories in the survey areas closely followed this trend. There was also a correspondence between the notifications in the survey areas and those in all other areas in the U.K.

*Attack Rates in Household Contacts.*—In 986 households 1,176 children of 10 years of age or less were in contact with a source patient. Of these, 366 had uncertain vaccination histories and 88 had a history of previous whooping cough. There were 195 fully vaccinated children of less than 5 years, and of these 52% developed a paroxysmal cough. Among 223 unvaccinated contacts in the same age group the attack rate was 69%. The corresponding rates for contacts of 5-10 years were 24% in the fully vaccinated and 32% in the unvaccinated children (table I). The attack rate (32%) in contacts of less than 5 years given vaccine produced by Burroughs Wellcome was substantially less than that (58%) in contacts in the same age group given vaccine produced by Glaxo Laboratories; although the numbers are small this difference attains statistical significance at the 1% level. If attention is paid only to the bacteriologically confirmed cases of whooping cough the resulting attack rates at ages 0-4 years are 38% in the fully vaccinated and 52% in the unvaccinated children. The isolation rates from contacts who developed paroxysmal cough were similar for vaccinated and unvaccinated children (table II). In both

TABLE I—*Attack Rates from Paroxysmal Cough in Vaccinated and Unvaccinated Contacts according to Age*

| History of Vaccination | Age at Contact (Years) | | | | | |
|---|---|---|---|---|---|---|
| | 0-4 | | | 5-10 | | |
| | No. Exposed | Attacked | | No. Exposed | Attacked | |
| | | No. | % | | No. | % |
| Fully vaccinated: | | | | | | |
| Complete course Glaxo | 139 | 81 | 58·3 | 151 | 38 | 25·2 |
| Complete course Burroughs Wellcome | 34 | 11 | 32·4 | 7 | 1 | 14·3 |
| Others* .. .. .. | 22 | 10 | 45·4 | 3 | 0 | 0·0 |
| Total .. .. .. | 195 | 102 | 52·3 | 161 | 39 | 24·2 |
| Not vaccinated .. .. | 223 | 154 | 69·1 | 115 | 37 | 32·2 |

*Other makes of vaccine or courses with more than one make of vaccine.

TABLE II—*Isolation Rates in Home-contact Patients in Households in which* B. pertussis *was isolated from a Source Patient. Results according to Age and Vaccination History*

| Age at Contact (Years) | Vaccination History | Isolation of *B. pertussis* | | |
|---|---|---|---|---|
| | | No. Swabbed | No. of Isolations | % Isolations |
| 0-4 | Not vaccinated | 55 | 43 | 78 |
| | Fully vaccinated | 46 | 33 | 72 |
| 5-10 | Not vaccinated | 16 | 4 | 25 |
| | Fully vaccinated | 27 | 5 | 19 |

groups the organism was more readily isolated from the younger patients.

*Serotypes.*—Most of the 1,293 isolates of *B. pertussis* were serotyped independently at two laboratories. The same serotype pattern was reported by both laboratories for 1,084 cultures. Most of these cultures were of type 1,3 (89%) and a much smaller proportion were of type 1,2,3 (9%) (table III). Very few cultures were types 1 or 1,2.

TABLE III—*Bacterial Isolations:* B. parapertussis *and all Cultures of* B. pertussis *for which Serotyping Results at Two Laboratories were in Agreement*

| | *B. pertussis* Serotype | | | | *B. parapertussis* | Total Cultures |
|---|---|---|---|---|---|---|
| | 1 | 1,2 | 1,2,3 | 1,3 | | |
| No. | 2 | 6 | 103 | 967 | 6 | 1,084 |
| % | <1 | <1 | 9·3 | 89·2 | <1 | 100 |

There were in addition 209 cultures of *B. pertussis*. These included cultures that were typed at one laboratory only (126), cultures reported by the area and reference laboratories as different types (82), and one culture that was not typed.

*Differences in Serotypes.*—Isolations of *B. pertussis* were made from two or more persons in 198 households. The cultures from 136 of these households were identified as the same serotype but in 22 households the serotypes differed. In the remaining 40 households there was some uncertainty about the serotype of one or more of the isolates. In 21 of the 22 households in which different serotypes were identified the types were 1,2,3 and 1,3; in the remaining household they were 1,2,3 and 1,2. The area and reference typing laboratories reported different serotype results for 82 cultures of *B. pertussis*, in 52 of which the differences concerned antigen 2—that is, whether the serotype was 1,3 or 1,2,3. To study the origin of these differences 18 cultures that had been shown by two laboratories to contain antigen 2 (type 1,2,3) were retested and a varying number of single colonies of each culture were examined. Fifty-two serotype 1,3 cultures chosen at random were similarly re-examined. The results (table IV) show that in all of the 52 cultures originally identified as serotype 1,3, colonies of type 1,3 were found again and antigen 2 was found in colonies of only three cultures (6%). On the other hand, in two of the 18 cultures originally identified as serotype 1,2,3, antigen 2 could not be detected in any of the colonies examined and colonies which did not contain antigen 2 were found in all of the 18 cultures originally identified as serotype 1,2,3. Thus some of these cultures were found to contain colonies of serotypes which differed from those originally identified; in particular, cultures that had been identified as serotype 1,2,3.

TABLE IV—*Serotypes of* B. pertussis *according to Results of First Tests on Cultures and of Subsequent Tests of Separate Colonies obtained from Freeze-dried Samples of These Cultures*

| Original Serotype Classification | No. of Cultures Examined | Serotypes Subsequently Identified among Separate Colonies of Each Sample | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | All type 1,3 | Types 1,3 and 1 | Types 1,2,3; 1,2; and 1,3 | Types 1,2,3 and 1,3 | Types 1,2,3; 1,3; and 1 | Types 1,2 and 1 | Types 1,2 and 1,3 |
| 1,3 | 52 | 42 | 7 | 0 | 2 | 0 | 0 | 1 |
| 1,2,3 | 18 | 2 | 0 | 2 | 11 | 2 | 1 | 0 |

*Serotypes in Vaccinated and Unvaccinated Patients.*—Of the total of 418 cultures isolated from unvaccinated children 70 (17%) were identified as serotype 1,2,3 or 1,2 (table V). In contrast, of the 272 cultures isolated from vaccinated children only 12 (4%) were identified as serotype 1,2,3. Thus antigen 2 was identified more often in isolates from unvaccinated than from vaccinated children. This difference is statistically significant at the 1% level.

TABLE V—*Serotypes, agreed by two Laboratories, of Cultures obtained from Vaccinated and Unvaccinated Patients of 10 Years or Less*

| Serotype | Not Vaccinated | | Vaccinated | |
|---|---|---|---|---|
| | No. | % | No. | % |
| 1,2 | 4 | 1·0 | 0 | 0·0 |
| 1,2,3 | 66 | 15·8 | 12 | 4·4 |
| 1,3 | 348 | 83·2 | 258 | 94·8 |
| 1 | 0 | 0·0 | 2 | 0·7 |
| Total | 418 | 100 | 272 | 100 |

*Virological Findings.*—During the first 12 months of the investigation in 21 of the 33 health authority areas swabs for virological examination were taken from patients and from home contacts of less than 5 years of age in 1,646 households. Viral isolations were made from persons in 188 households (11%). As shown in table VI adenoviruses (25%) and the parainfluenza viruses (21%) accounted for almost half of the 207 isolations. Between November 1966 and January 1967 respiratory syncytial virus and the parainfluenza viruses formed 37% of the total viruses isolated, compared with 5% for the remainder of the survey year. No relation was found between any virus and a particular area. In households where both bacteriological and virological investigations were made (table VII) the frequency of virus isolations was the same in those in which *B. pertussis*

TABLE VI—*Groups and Types of Viruses isolated from Patients and Contacts*

| Total | Adenovirus Type | | | | | | | | Coxsackie Type | | | | Echovirus Type | | | | Herpes Simplex | Mumps | Parainfluenza Type | | | Polio Type 2 | R.S.V. | Rhinovirus | | | Not Identified |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 5 | 6 | 7 | 17 | N.K. | A9 | B1 | B2 | B3 | 3 | 6 | 11 | 30 | | | 1 | 2 | 3 | | | H | M | N.K. | |
| No. 207 | 17 | 10 | 6 | 7 | 3 | 3 | 3 | 2 | 4 | 1 | 3 | 6 | 2 | 1 | 2 | 2 | 30 | 5 | 23 | 2 | 18 | 1 | 17 | 25 | 2 | 3 | 9 |
| % 100 | 24·6 | | | | | | | | 6·8 | | | | 3·4 | | | | 14·5 | 2·4 | 20·8 | | | 0·5 | 8·2 | 14·5 | | | 4·3 |

N.K. = Not known. R.S.V. = Respiratory syncytial virus.

TABLE VII—*Viruses isolated from Patients aged 10 Years or less who had both Bacteriological and Virological Investigations. Results according to whether or not* B. pertussis *was isolated from at least One Person in Household*

| Patients | Adeno-virus | | Cox-sackie | | Echo-virus | | Herpes Simplex | | Mumps | | Para-influenza | | R.S.V. | | Rhino-virus | | Other and not Identified | | Total* No. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | |
| In households in which *B. pertussis* was isolated | 9 | 33 | 3 | 11 | 0 | 0 | 5 | 19 | 2 | 7 | 3 | 11 | 1 | 4 | 3 | 11 | 1 | 3 | 27 |
| In households in which *B. pertussis* was not isolated | 35 | 22 | 13 | 8 | 5 | 3 | 25 | 16 | 3 | 2 | 34 | 22 | 10 | 6 | 23 | 15 | 9 | 6 | 157 |

*The remaining 23 isolations were from persons of more than 10 years of age or from children in households that were not revisited or from children in hospital.
R.S.V. = Respiratory syncytial virus.

was isolated—that is, 27/321 (8%)—as in those in which *B. pertussis* was not detected—that is, 157/1,949 (8%). The range of viruses isolated was also similar. Viruses were isolated with similar frequency from patients who yielded *B. pertussis*—that is, 18/227 (8%)—as from patients who were their household contacts but from whom *B. pertussis* was not isolated—that is, 9/94 (10%). The virus isolation rate from all patients of less than 5 years—10% (142/1,390)—was slightly greater than that from symptomless contacts in the same age group—6% (11/182)—but the difference is not statistically significant. In contrast, the isolation rates of *B. pertussis* for similar groups were 22% (710/3,301) and 2% (21/870) respectively; a difference that is statistically significant at the 0·1% level.

## Discussion

In this survey the efficacy of pertussis vaccine was judged mainly on the susceptibility of children who had received a full course of vaccine as part of the normal immunization scheme and who subsequently came into contact with *B. pertussis* infection in their homes. The preliminary results of the first 12 months of the investigation (P.H.L.S., 1969) showed that more than half of such children aged less than 5 years developed whooping cough after exposure; this suggested that much of the pertussis vaccine in general use for some years up to and including 1967 was not very effective. The results for the entire 18 months of the survey are in keeping with the preliminary findings. All of the vaccine fulfilled the provisions of the Amendment Regulations 1964 made under the Therapeutic Substances Act (Statutory Instruments, 1964) and the requirements of the *British Pharmacopoeia* (1963), but the vaccine from one source—the Wellcome Laboratories—was throughout of greater potency (Cameron, 1970), in keeping with the Requirements for Pertussis Vaccine (W.H.O., 1964), and it is noteworthy that this vaccine was more effective than those from other sources. However, as well as fulfilling more stringent potency requirements it also differed from other vaccines in that it included cultures of *B. pertussis* containing antigen 3.

Since the preliminary report the following steps have been taken to attempt to increase the efficacy of the vaccines. The *British Pharmacopoeia* requirements for the potency of pertussis vaccine have been increased (*B.P.*, 1968) to those of the Requirements for Pertussis Vaccine (W.H.O., 1964). All current vaccines now include cultures containing antigen 3, and mineral adjuvants are again being incorporated in some. The effect of these changes will, of course, take time to become fully apparent, and the new vaccines are being kept under surveillance in certain areas by the P.H.L.S. in co-operation with medical officers of health and family doctors.

The present findings confirm the observation of Preston (1963) that the predominating serotype in the population is now type 1,3, in contrast with the early days of pertussis vaccination when antigen 2 could be identified in most of the cultures. It became evident that different serotypes were isolated from patients in the same household more often than might have been expected. All of the 18 freeze-dried cultures of type 1,2,3, when re-examined, were found to contain some colonies which lacked antigen 2. It is evident that a single culture may contain more than one serotype and that this is more common in cultures in which antigen 2 (type 1,2,3) was identified. Serotype tests of cultures give a good indication of the relative prevalence of various serotypes, but to detect the presence of differing serotypes in one culture it is necessary to examine a number of colonies separately. Cultures in which antigen 2 (types 1,2 and 1,2,3) was identified were isolated more frequently from unvaccinated than from vaccinated children, whereas strains which did not appear to contain antigen 2 were isolated with similar frequency from both vaccinated and unvaccinated children. The presence of different serotypes in some cultures makes it difficult to assess the full implication of this observation.

In this survey adenoviruses and parainfluenza viruses accounted for a large proportion of the viral isolates. However, no difference could be shown between the types of virus or the rate with which they were detected in patients in households where *B. pertussis* was isolated and those where it was not. Furthermore, the virus isolation rate from patients from whom *B. pertussis* was also isolated was similar to that from patients who were their household contacts but whose swabs failed to yield *B. pertussis*.

These findings, like those of the Combined Scottish Study (1970), provide little evidence that viruses are a common cause of paroxysmal cough, but the nature of the illness and the arrangements for the collection of samples resulted in at least 80% of the cases being swabbed after the first week of illness. By this time the chance of isolating many of the common respiratory viral pathogens is substantially reduced, so that viruses which persist for a long time—for example, enteroviruses and adenoviruses—or those that may be reactivated from latency—for example, herpes simplex virus—could form a larger proportion of the total isolates than they would have done if swabs had been taken at the onset of the illness.

Thus, in all, the evidence suggests that *B. pertussis* remains the major factor in the causation of whooping cough in the U.K. Certainly *B. pertussis* was isolated from a large number of patients—over 1,000—during the survey, and an association was evident between the number of notifications and the number of isolations of *B. pertussis* during the epidemic period of the survey. How often viruses are responsible for, or contribute to, the incidence of paroxysmal cough could not be determined, but it seems likely that, in some cases at least, viruses isolated in this study were coincidental rather then causal.

The report was prepared by Dr. J. D. Abbott, Dr. E. H. Gillespie, Dr. P. G. Higgins, Dr. Sheila Polakoff, and Dr. T. M. Pollock.

We are grateful for the detailed information about pertussis vaccines supplied by Glaxo Laboratories Ltd., and the Wellcome Research Laboratories and for the co-operation and support of members of these firms during the study. We thank Mr. G. H. Turner for the preparation of the monospecific typing sera and the Wellcome Research Laboratories for the gift of the sera; Dr. F. W. Sheffield (National Institute for Medical Research, London) and Dr. Jean M. Dolby (Lister Institute) for much help with the serotyping; Dr. J. Cameron (Wellcome Research Laboratories) for freeze-drying strains of *B. pertussis;* Dr. D. R. Gamble (Epsom Public Health Laboratory for typing Coxsackie A viruses; Dr. C. M. P. Bradstreet (Standards Laboratory, Colindale) for supplying all sera for neutralization and complement fixation tests; and the Virus Reference Laboratory, Colindale, for further studies of all unidentified viruses. We are grateful for the interest shown in this investigation by Dr. M. Sterne, Dr. A. H. Griffith (Wellcome Research Laboratories), Dr. P. W. Muggleton (Glaxo Laboratories Ltd.), Dr. L. B. Holt (National Institute for Medical Research, London), and Professor D. G. Evans (London School of Hygiene and Tropical Medicine). We are greatly indebted to the general practitioners who reported suspected cases of whooping cough and in some areas collected specimens, and to the many members of the health departments, especially the health visitors who collected specimens and made repeated home visits.

## References

*British Pharmacopoeia*, 1963, p. 576. London, Pharmaceutical Press.
*British Pharmacopoeia*, 1968, Addendum, 1971, p. 80. London, Pharmaceutical Press.
Cameron, J. (1970). *British Medical Journal*, **1**, 109.
Combined Scottish Study (1970). *British Medical Journal*, **4**, 637.
Medical Research Council Working Party on Acute Respiratory Virus Infections (1965). *British Medical Journal*, **2**, 319.
Preston, N. W. (1963). *British Medical Journal*, **2**, 724.
Public Health Laboratory Service (1969). *British Medical Journal*, **4**, 329.
Statutory Instruments (1964). *Therapeutic Substances. The Therapeutic Substances (Manufacture of Vaccines, Toxins and Antigens) Amendment Regulations* 1964, No. 1434. London, H.M.S.O.
World Health Organization (1964). *Technical Report Series*, **274**, 25.