

births or died in early infancy, compared with 36% (8 of 22) who were first-born.

**Aetiological Factors.**—In consecutive admissions to the Fountain Hospital of 46 individual twins and 100 singletons, the most striking difference was in the percentage incidence of mongolism—six times commoner in the singleton than in the twin series.

**Clinical Findings.**—In consecutive admissions to the Fountain Hospital of 44 individual twins and 100 singletons (mongolism excluded) over three-quarters of the patients in each series had physical abnormalities. Differences in incidence of individual clinical findings between the two groups were not statistically significant.

**Necropsy Findings.**—In nine of the Fountain Hospital twin series who had died since admission, none of the brains showed gross malformation suggesting origin in embryonic life, though all nine had pathological changes. The origin of these changes could not be timed precisely, though all were consistent with damage late in pregnancy, at birth, or post-natally.

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## A STUDY OF THE AETIOLOGY OF RESPIRATORY DISEASE IN A GENERAL HOSPITAL

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The main objects of this investigation were to determine (1) the prevalence of viral and bacterial infections in *all* patients admitted to hospital suffering from a respiratory illness, their clinical picture, and the effect of admission to hospital on the course of the illness; and (2) the number and cause of acute respiratory illnesses arising in patients already in hospital suffering from some other disease.

### Materials and Methods

The survey covered the period September 29, 1958, to March 31, 1959, and comprised 117 children and 179 adults. The following were included: (1) *All* patients with symptoms of respiratory disease admitted to all the adult medical wards of St. Thomas's Hospital; (2) all children with symptoms of respiratory disease admitted to the medical children's ward at St. Thomas's Hospital and the children's ward of the Royal Waterloo Hospital; (3) patients developing symptoms of respiratory disease while in these wards. These were ascertained by daily visits to each ward by one of us.

All patients were seen and examined by one of us within 24 hours of admission. The history and results of physical examination were recorded on a standard form, which also included the results of x-ray examination. Patients were re-examined at intervals, usually of two to three days, throughout their stay in hospital. Serological results were regarded as significant only when there was a fourfold or greater rise between suitably paired specimens. Results are expressed as statistically significant only when  $P < 0.05$ .

**Specimens Examined.**—At the first examination 5–10 ml. of venous blood was taken from all patients. A further specimen was obtained 10 to 28 days later from as many patients as possible. Serum was separated immediately from all samples and stored at  $-20^{\circ}$  C. Throat swabs for virus isolation were taken from all children at the first examination, and from adults with symptoms of less than five days' duration before admission. Swabs were broken off into bijoux bottles containing 2 ml. of Hanks's solution with 0.5% lactalbumin hydrolysate and placed immediately in a vacuum flask

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containing solid carbon dioxide for transport to the laboratory. Nose and throat swabs for bacteriological examination were taken by the nurses immediately after admission and placed in test-tubes containing blood-agar. These swabs were plated out within 36 hours of being taken. Samples of sputum were obtained from all adult patients producing phlegm.

*Follow-up Specimens.*—Nose and throat swabs were taken at intervals of two to four days from all children in St. Thomas's Hospital who remained in the ward for more than three days, and from adults for the first two weeks of their stay, or until discharged, whichever was the shorter, providing there was no history of chronic bronchitis. Further samples of sputum were also obtained from patients developing pneumonic complications. In addition, specimens were obtained for virus and bacteriological examination from any patient in the survey on whom a necropsy was performed.

*Control Nose and Throat Swabs.*—Nose and throat swabs were obtained in a similar manner from medical and surgical patients admitted without respiratory symptoms in the period January 1, 1959, to March 31, 1959. As too few babies without respiratory symptoms were admitted to hospital to produce the same number of controls, the majority of "control" swabs for children of less than 1 year were obtained from normal babies attending a child-welfare clinic at the hospital.

*Virus Isolation.*—Specimens: throat swabs in Hanks's solution were inoculated in 0.1-ml. amounts into duplicate tubes of HeLa cells, monkey-kidney cells, and human amnion cells. HeLa cells were grown and maintained as described by Pereira and Kelly (1957) and examined for cytopathic change on alternate days for a period of 28 days. Monkey-kidney cells were grown as described by Pereira (1958). Tubes were examined on alternate days for any cytopathic effect and tested for haemadsorption on the fifth and tenth days of incubation by the methods used by Chanock *et al.* (1958) for the isolation and identification of viruses. Human amnion cells were prepared and maintained as described by Lane and Marshall (1957).

Adenoviruses were identified by complement-fixation followed by serum neutralization with type-specific rabbit antisera; Coxsackie B and Echo viruses by serum neutralization; parainfluenza viruses by serum neutralization. The isolation of influenza virus in fertile hens' eggs was not in general attempted except from lungs from fatal cases, as it was realized that as a cause of respiratory infection it would be revealed by the complement-fixation tests on paired sera.

*Serology.*—*Complement-fixation tests*, except those for the parainfluenza group of viruses, were carried out in plastic haemagglutination plates (World Health Organization, 1953), using volumes of 0.1 ml. (Holland *et al.*, 1960). Specimens of serum taken at the convalescent stage were first screened at a dilution of 1/10 against: influenza viruses A, B, and C; Sendai virus; psittacosis virus; adenovirus; and *Rickettsia burnetii*. Titrations of paired sera were carried out as indicated by the screening tests. Complement-fixation tests for the parainfluenza group of viruses were done, using the method described by Pereira (1956) with monkey-kidney-tissue-culture fluid as antigens. *Serum neutralization tests* were used to detect the presence of antibodies to Coe virus (Pereira and Pereira, 1959). *Agglutination tests* for antibodies to *Streptococcus M.G.* were carried out also (Thomas *et al.*, 1945).

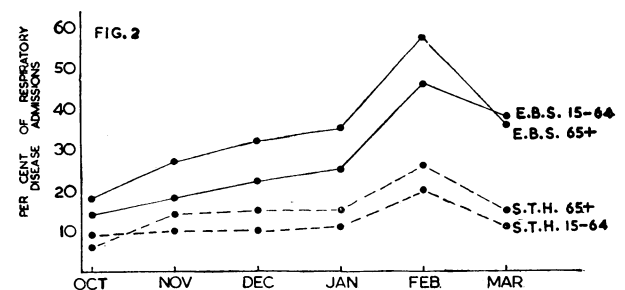
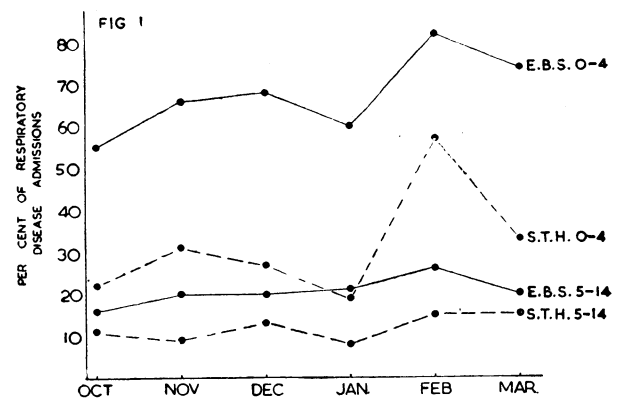
*Bacteriological Methods.*—Specimens of sputum and nose and throat swabs were cultured on blood-agar and heated blood-agar. All strains of *Staphylococcus aureus* isolated were tested for their sensitivity to penicillin, streptomycin, chloramphenicol, tetracycline, erythromycin, and novobiocin by the ditch-plate method (Barber *et al.*, 1958) and phage-typed by Dr. Patricia Jevons at the Central Public Health Laboratory, Colindale.

## Results

*Number of Samples Available for Testing.*—From patients aged 1 year and over, 91–94% of satisfactory samples of paired sera were obtained for testing. From those aged less than 1 year we could get only 75% of satisfactory pairs of sera owing to the difficulty in obtaining sufficient blood. There was usually a longer interval between the onset of symptoms and admission to hospital in adults, which accounted for the lower proportion of throat swabs for virus isolation taken then.

*Prevalence of Respiratory Illnesses.*—Figs. 1 and 2 show the proportion of patients in each age-group who were admitted to St. Thomas's Hospital because they were suffering from respiratory disease, compared with those, over a similar period, arranged by the Emergency Bed Service (E.B.S.) in London. Table I shows the actual number of patients with respiratory disease during this period. It should be noted that the E.B.S. figures are classified as total respiratory disease—that is, they include such cases as carcinoma of the bronchus—whereas the St. Thomas's Hospital cases are only those with an acute respiratory illness.

*Clinical Diagnosis.*—Table II represents the clinical diagnoses made by one of us as a result of physical and radiological examination in conjunction with the opinion of the physicians in charge of the patients. It also shows the number of deaths that occurred in each group.



FIGS. 1 and 2.—A comparison of the proportion of patients admitted with acute respiratory disease to St. Thomas's Hospital (S.T.H.) with those admitted by the Emergency Bed Service (E.B.S.) over the period October, 1958, to March, 1959, in the different age-groups.

TABLE I.—Age Distribution of Patients with Respiratory Diseases Admitted to St. Thomas's Hospital (S.T.H.) or by the Emergency Bed Service (E.B.S.) in the Period October, 1958, to March, 1959

|             | Age in Years |        |        |        |        |        |        |        |        |        |
|-------------|--------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|             | <1           |        | 1-4    |        | 5-14   |        | 15-64  |        | 65+    |        |
|             | E.B.S.       | S.T.H. | E.B.S. | S.T.H. | E.B.S. | S.T.H. | E.B.S. | S.T.H. | E.B.S. | S.T.H. |
| October ..  | 45           | 4      | 58     | 4      | 63     | 6      | 321    | 17     | 221    | 3      |
| November .. | 66           | 2      | 85     | 13     | 74     | 5      | 440    | 20     | 393    | 6      |
| December .. | 109          | 6      | 112    | 4      | 74     | 7      | 570    | 18     | 594    | 9      |
| January ..  | 160          | 4      | 136    | 5      | 88     | 4      | 722    | 19     | 747    | 9      |
| February .. | 284          | 12     | 265    | 15     | 120    | 5      | 1,695  | 39     | 1,578  | 12     |
| March ..    | 151          | 8      | 162    | 7      | 75     | 6      | 639    | 21     | 640    | 6      |
| Total ..    | 815          | 36     | 818    | 48     | 494    | 33     | 4,387  | 134    | 4,173  | 45     |

TABLE II.—Clinical Diagnoses Made in Each Age-group of Patients Admitted During the Survey

|  | Age-group   |    |           |    |            |    |             |    |           |    |
|--|-------------|----|-----------|----|------------|----|-------------|----|-----------|----|
|  | 0-11 Months |    | 1-4 Years |    | 5-14 Years |    | 15-64 Years |    | 65+ Years |    |
|  | No.         | %  | No.       | %  | No.        | %  | No.         | %  | No.       | %  |
| Acute infections of upper respiratory tract .. | 11          | 31 | 19        | 40 | 22         | 67 | 24          | 18 | 0         |    |
| Bronchitis ..                                  | 14          | 39 | 14        | 29 | 2          | 6  | 26          | 19 | 15        | 33 |
| Localized pneumonia ..                         | 6           | 17 | 3         | 6  | 5          | 15 | 33 (2)      | 25 | 10        | 22 |
| Diffuse pneumonia ..                           | 3           | 8  | 12        | 25 | 4          | 12 | 32 (6)      | 24 | 11        | 24 |
| Cor pulmonale ..                               | 0           | 0  | 0         | 0  | 0          | 0  | 19 (2)      | 14 | 9 (2)     | 20 |
| Bronchiolitis ..                               | 2           | 6  | 0         | 0  | 0          | 0  | 0           | 0  | 0         |    |

Figures in parentheses represent number of deaths.

Evidence for Virus Infection in Patients Admitted

The seasonal distribution of the different viruses isolated is shown in Fig. 3. Table III illustrates the relation of the various clinical diagnoses and evidence of virus infection. The clinical diagnoses were divided into three main groups, as shown in this table, because no helpful differentiation in aetiological diagnosis could be made by further subdivision. A diagnosis of virus infection was made more often in the children than in the adults admitted, and in infections of the upper respiratory tract than in the lower respiratory tract. Of 33 babies aged less than 1 year from whom satisfactory samples were available for testing only 4 (12%) had evidence of virus infection. This is in contrast to the evidence of virus infection in 22 (45%) children aged 1

to 4 years, 9 (29%) children aged 5 to 14 years, and 38 (21%) patients aged more than 15 years.

**Influenza A, B, and C Viruses.**—Three strains of influenza A virus, all of the Asian variety, were isolated, and serological evidence of infection was obtained in 28 patients. Four strains of influenza B virus were isolated and serological evidence of infection was obtained in 12 patients, one of whom also had evidence of infection with influenza C. These infections were found in all age-groups.

**Parainfluenza Viruses.**—Three strains of parainfluenza 1 virus were isolated in children aged 1 to 14 years. Five further patients, including two adults and one baby aged less than 1 year, had serological evidence of parainfluenza virus infection—three with parainfluenza 3 virus and two with parainfluenza 1 virus. There was no evidence of infection with parainfluenza 2 virus.

**Adenoviruses.**—Two strains of adenovirus type 1, one strain of adenovirus type 2, one strain of adenovirus

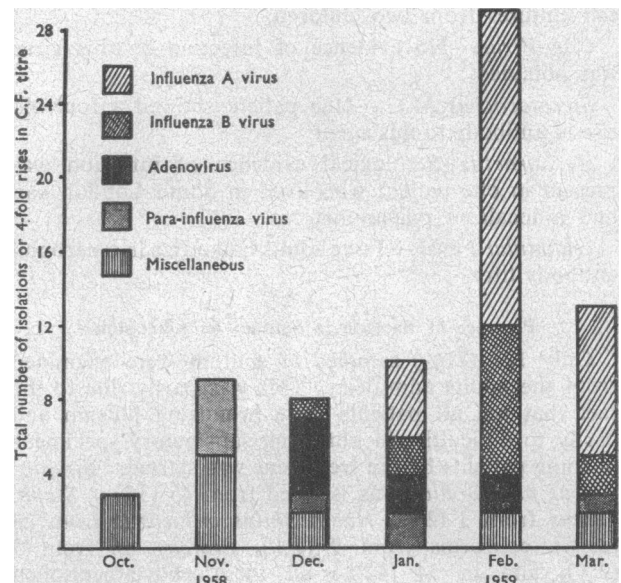


FIG. 3.—Distribution of respiratory virus infections during the period October, 1958, to March, 1959, diagnosed by isolation or fourfold rise in complement-fixing antibody titre.

TABLE III.—Clinical Diagnosis and Evidence for Virus Infection in Patients Admitted to Hospital

|   | Infection of Upper Respiratory Tract |    |           |    | Bronchitis; Bronchiolitis; Cor pulmonale |     |           |    | Localized and Diffuse Pneumonia |    |           |    | Total |
|---|--------------------------------------|----|-----------|----|--|-----|-----------|----|---------------------------------|----|-----------|----|-------|
|   | 0-14 Years                           |    | 15+ Years |    | 0-14 Years                               |     | 15+ Years |    | 0-14 Years                      |    | 15+ Years |    |       |
|   | No.                                  | %  | No.       | %  | No.                                      | %   | No.       | %  | No.                             | %  | No.       | %  |       |
|   | No.                                  | %  | No.       | %  | No.                                      | %   | No.       | %  | No.                             | %  | No.       | %  |       |
| Total No. of patients ..  | 52                                   |    | 24        |    | 32                                       |     | 69        |    | 33                              |    | 86        |    | 296   |
| No. of paired sera ..   | 46                                   | 89 | 23        | 96 | 28                                       | 85  | 59        | 86 | 28                              | 85 | 70        | 81 | 254   |
| „ „ throat swabs tested for viruses ..                                  | 47                                   | 90 | 22        | 92 | 32                                       | 100 | 49        | 71 | 32                              | 97 | 52        | 60 | 234   |
| Influenza virus A, B, and C ..  | 5                                    | 11 | 9         | 39 | 7*                                       | 25  | 9         | 15 | 2                               | 7  | 10        | 14 | 42    |
| Parainfluenza viruses ..  | 4                                    | 9  | 0         | 0  | 0  | 0   | 0         | 0  | 2                               | 7  | 2         | 3  | 8     |
| Adenoviruses ..   | 3                                    | 7  | 0         | 0  | 3  | 11  | 0         | 0  | 0                               | 0  | 2†        | 3  | 8     |
| Psittacosis virus, Echo virus, Coxsackie virus, R. burnetii             | 4                                    | 9  | 2         | 9  | 1  | 4   | 0         | 0  | 0                               | 0  | 1         | 2  | 8     |
| Unidentified cytopathic agents  | 2                                    | 4  | 0         | 0  | 0  | 0   | 0         | 0  | 0                               | 0  | 0         | 0  | 2     |
| Streptococcus M.G. ..   | 0                                    | 0  | 0         | 0  | 0  | 0   | 0         | 0  | 0                               | 0  | 1†        | 2  | 1     |
| Glandular fever ..  | 0                                    | 0  | 4         | 17 | 0  | 0   | 0         | 0  | 0                               | 0  | 0         | 0  | 4     |
| Total No. of positive isolations or fourfold rises in antibody titre .. | 18                                   | 40 | 15        | 65 | 11                                       | 40  | 9         | 15 | 4                               | 14 | 16        | 24 | 73    |

\* One patient had a fourfold rise in antibody titre to both influenza virus B and C.  
 † One patient had a fourfold rise in antibody titre to both adenovirus and Streptococcus M.G.  
 The percentages in the table are percentages of satisfactory specimens tested.

type 3, and one strain of adenovirus type 5 were isolated. All these were isolated from children except the type 2 strain, which came from a man aged 64. Serological evidence of adenovirus infection was obtained in three additional patients. In some of these a fourfold rise in agglutination titre to *Streptococcus M.G.* was observed.

*Psittacosis Virus*.—Serological evidence of infection was present in one patient, a vagrant, who habitually slept on the Thames Embankment, in the company of pigeons.

*Coxsackie B Virus*.—Three strains of Coxsackie B4 virus and one strain of Coxsackie B3 virus were isolated. None of these patients had an increase in antibody titre. One strain of Coxsackie B4 virus was isolated from the lesions of a woman, aged 50, with herpetiform stomatitis.

*Echo Type 3 Virus*.—Two strains were isolated in children, both of whom showed a fourfold rise in antibodies to this agent.

*Unidentified Cytopathic Agents*.—Two strains of an unidentifiable cytopathic agent were isolated in HeLa cell cultures from two children.

*Coe Virus*.—No evidence of infection by this virus was obtained.

*Streptococcus M.G.*—One patient showed a fourfold rise in antibody to this agent.

*R. burnetii*.—Serological evidence of infection was present in one patient who lived in South London and had a localized pneumonia.

*Glandular Fever*.—Four adults had a rise in heterophil antibody titre.

#### Presence of Bacteria in Sputum on Admission

Only 127 (71%) samples of sputum were examined from the adults admitted. This was partly due to the fact that not all patients were producing phlegm and partly to difficulties in obtaining satisfactory specimens in some patients before treatment was started. *Streptococcus pneumoniae* was isolated from 45 (36%), *Staph. aureus* from 3 (2%), *Haemophilus influenzae* from 28 (22%), coliforms from 9 (7%), *Proteus sp.* from 3 (2%), and in 54 (42%) all these above-mentioned organisms were absent. It is not known if any of these organisms was the primary cause of the illness. The relationship with virus infection is shown below.

From 33 (77%) of 43 cases of localized (lobar) pneumonia in adults, sputum was obtained for testing. *Str. pneumoniae* only was isolated from the sputum of 11 (33%); no evidence of virus infection was present in any of these patients. Of 19 (58%) from whom no pathogens were isolated from the sputum, four showed evidence of virus infection. *Staph. aureus* was isolated from the sputum of one patient (she did not, clinically, have a staphylococcal pneumonia), and *Proteus sp.* was isolated from the sputum of another patient who had a long history of chronic bronchitis. One patient with a localized pneumonia had evidence of a primary tuberculous infection. Of 43 cases with diffuse pneumonia, sputum was tested in 35. *Str. pneumoniae* only was grown in 7 (20%); two of these also had evidence of influenza A virus infection. The sputum from seven contained *H. influenzae* and *Str. pneumoniae*, and sputum from two contained a mixture of coliforms and *Str. pneumoniae*. From three patients *H. influenzae* only was grown, from one patient coliforms only, and from another *Staph. aureus*. No pathogens were grown

in 14 patients (40%). The relationship of bacterial flora in the nasopharynx to the cause of illness is discussed below.

#### Comparison of Aetiology of Acute and Chronic Illnesses

The respiratory illnesses of 105 of the children admitted could be regarded as acute; in three the respiratory-tract symptoms were probably due to cardiac failure complicating congenital heart disease, three were secondary to leukaemia, and six had a long history of asthma.

Among the adults admitted to hospital the illnesses of 87 could be regarded as primarily respiratory and not precipitated by any other condition, and 92 illnesses were secondary to an underlying abnormality. Of the latter patients, 12 suffered from heart disease (rheumatic or hypertensive) and were admitted with cardiac failure as well as illnesses of the respiratory tract, 7 had leukaemia or generalized sarcoidosis, 13 had a history of asthma, and 60 showed evidence of chronic bronchitis and emphysema.

Evidence of virus infection was obtained more commonly in children and adults admitted with an acute illness (33%) than in those with a "chronic" illness (18%).

#### Relationship of Sputum Findings to Evidence of Virus Infection

There was no relation between the isolation of various pathogens from the sputum and evidence of virus infection in patients admitted with a respiratory illness. This is also borne out by Fig. 4, which shows the seasonal

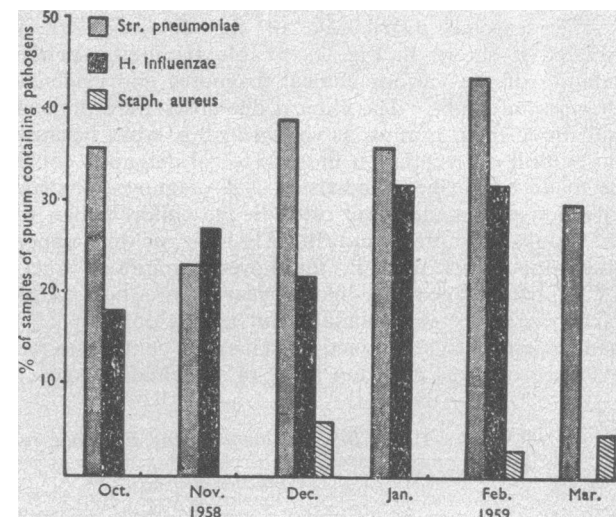


FIG. 4.—Percentage of specimens of sputum containing bacterial pathogens in the period October, 1958, to March, 1959.

distribution of *Str. pneumoniae*, *H. influenzae*, and *Staph. aureus* in the sputum; the seasonal incidence of these bacteria in sputum has not varied, or has followed the pattern of virus infections shown in Fig. 3.

#### Importance of Nasopharyngeal Flora

No association between any one virus and the presence of a particular kind of organism or combination of organisms in the nasopharynx was found. There was also little seasonal variation in the isolation of bacteria from the nasopharynx (Fig. 5). There was, however, a considerable difference in the rates of isolation of *H. influenzae*; both in adults and in children a signi-

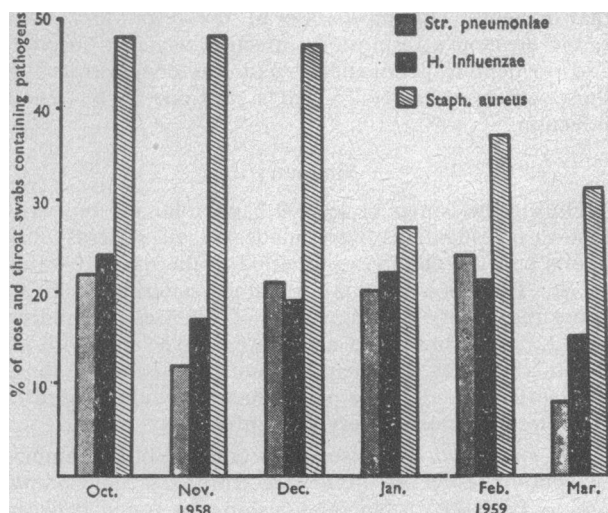


FIG. 5.—Percentage of nose and throat swabs containing bacterial pathogens in the period October, 1958, to March, 1959.

ificantly greater proportion of patients with infections of the lower respiratory tract had strains of *H. influenzae* present in the nasopharynx (Table IV).

TABLE IV.—Incidence of Pathogens in Nasopharynx on Admission of Patients With and Without Respiratory Infection

|                                    | 0-14 Years              |    |                         |    |          |    | 15+ Years               |    |                         |    |          |     |
|------------------------------------|-------------------------|----|-------------------------|----|----------|----|-------------------------|----|-------------------------|----|----------|-----|
|                                    | Upper Respiratory Tract |    | Lower Respiratory Tract |    | Controls |    | Upper Respiratory Tract |    | Lower Respiratory Tract |    | Controls |     |
|                                    | No.                     | %  | No.                     | %  | No.      | %  | No.                     | %  | No.                     | %  | No.      | %   |
| Total No. of patients ..           | 82                      |    | 35                      |    | 163      |    | 66                      |    | 113                     |    | 191      |     |
| No. of nose and throat swabs taken | 77                      | 94 | 34                      | 97 | 163      |    | 62                      | 94 | 108                     | 95 | 191      |     |
| <i>Str. pneumoniae</i> ..          | 15                      | 19 | 7                       | 21 | 29       | 18 | 8                       | 13 | 21                      | 19 | 20       | 10  |
| <i>Str. pyogenes</i> ..            | 11                      | 14 | 2                       | 6  | 19       | 12 | 1                       | 2  | 3                       | 3  | 1        | 0.5 |
| <i>Staph. aureus</i> ..            | 34                      | 44 | 14                      | 41 | 85       | 52 | 23                      | 37 | 37                      | 34 | 71       | 37  |
| <i>H. influenzae</i> ..            | 16                      | 21 | 13                      | 38 | 21       | 13 | 5                       | 8  | 21                      | 19 | 22       | 12  |
| Coliforms ..                       | 18                      | 23 | 2                       | 6  | 30       | 18 | 6                       | 10 | 22                      | 20 | 19       | 10  |
| <i>Proteus sp.</i> ..              | 1                       | 1  | 2                       | 6  | 7        | 4  | 5                       | 8  | 10                      | 9  | 10       | 5   |
| None of above                      | 5                       | 6  | 4                       | 12 | 33       | 20 | 21                      | 34 | 30                      | 28 | 71       | 37  |

Fatal and Other Complications in Patients Admitted to Hospital With Respiratory Illness

No deaths occurred among the children in the study. In two a staphylococcal pneumonia developed after admission ; from one of these a strain of *Staph. aureus* resistant to penicillin and tetracycline was isolated, though no such strain had been found in the nasopharynx on admission. From the other child the same phage type of *Staph. aureus* was isolated at the time of the pneumonia as was isolated from the nasopharynx on admission.

Among the adults 12 deaths occurred. Post-mortem examinations were performed on six of these, and material from five was available for virological and bacteriological examination. One influenza virus A (Asian) and one influenza virus B strain was isolated from these. *Str. pneumoniae* was isolated from one patient, and staphylococci from three. In these three patients the strain of *Staph. aureus* isolated at post-mortem examination was either not present in the sputum or nasopharynx on admission or was of a different phage type. These three strains were resistant

to three or more antibiotics, as were the majority of the "acquired" strains (see below).

In five adult patients a staphylococcal pneumonia developed after admission. In all cases the strain isolated from the sputum was of a different type from that present in the nasopharynx or sputum on admission and was resistant to three or more antibiotics.

Acquisition of Staph. aureus by Patients with Respiratory Illnesses

Nose and throat swabs were taken at intervals of two to three days from 62 (53%) of the children and 103 (61%) of the adults. The children were followed for an average of six days, the adults for nine days ; this reflects the duration of stay in hospital. Six of the children

TABLE V.—Sensitivity Characteristics of Staph. aureus in Nasopharynx of Patients Admitted with Respiratory Disease, Including Strains Isolated at Necropsy

|   | Staph. aureus Isolated on Admission |    | Staph. aureus Acquired in Hospital |    |
|---|-------------------------------------|----|------------------------------------|----|
|   | No.                                 | %  | No.                                | %  |
| Total No. of strains ..   | 109                                 |    | 51                                 |    |
| Sensitive to all antibiotics ..   | 52                                  | 48 | 7                                  | 14 |
| Resistant to penicillin ..  | 53                                  | 49 | 43                                 | 84 |
| "    " streptomycin ..  | 16                                  | 15 | 23                                 | 45 |
| "    " one or more of: tetracycline, chloramphenicol, erythromycin, novobiocin .. | 23                                  | 21 | 42                                 | 82 |
| Not known ..  | 2                                   | 2  | 0                                  |    |

(10%) and 17 of the adults (17%) retained the same phage type throughout their stay. Thirteen of the children (21%) and 11 of the adults (11%) lost the original strain without acquiring a new phage type. Fifteen of the children (24%) and 32 of the adults (32%) acquired a new strain of staphylococcus in the nasopharynx. 28 children (45%) and 43 adults (42%) did not acquire a strain of *Staph. aureus* throughout their stay. The pattern of antibiotic sensitivity of strains isolated on admission compared with that of strains acquired in hospital is shown in Table V: it may be seen that those acquired were usually resistant to more than one antibiotic.

Analysis of the figures concerning bacteria acquired in the nasopharynx by patients with evidence of virus disease and those without did not reveal any significant difference.

Respiratory Infections Arising in Patients Already in Hospital

Post-operative Respiratory Illnesses.—345 operations under general anaesthesia were performed in the six adult medical wards and 39 in the one children's ward at St. Thomas's Hospital. Eight adults and one child developed fever of 99° F. (37.2° C.) or over, lasting more than 24 hours, with symptoms of respiratory tract involvement within one week of operation. No evidence of virus infection was found in any of these patients. *Str. pneumoniae*, *Staph. aureus*, *H. influenzae*, and coliforms were isolated from the sputum of five of the adults. *Str. pyogenes* was isolated from the throat swab of the child.

Other Patients Developing Respiratory Illnesses.—Five adults and three children developed a respiratory illness while in hospital with some other disease. No evidence of virus infection was obtained in any of the adults, nor were samples of sputum examined before antibiotics were administered. In one child with hypercalcaemia a strain of adenovirus type 2 was isolated from

a throat swab, and there was a fourfold rise in complement-fixing antibody titre to adenovirus. Parainfluenza type 1 virus was isolated from the throat swab of one other child. From the third, a boy with fibrocystic disease of the pancreas, no virus was isolated, but moniliae were grown from the sputum; he died, but necropsy was not performed.

### Discussion

This study confirms the importance of infections of the respiratory tract as a cause of admission to hospital. The seasonal pattern during the period of the survey showed a slow rise in adult admissions, with a peak in February; a similar picture was seen in the children, but in these a rise had already occurred in November. The peak in the second half of the period was due to influenza A and B viruses.

It was hoped that this investigation might reveal an association between particular clinical syndromes and different aetiological agents. This aim was not realized. Evidence of virus infection was found more often in patients with an acute disease of the respiratory tract than in those in whom the acute infection was complicating some pre-existing respiratory disease. Evidence of virus infection was obtained also much more commonly in patients with disease of the upper respiratory tract than with that of the lower, and in children as compared with adults. It is possible that both these findings are related to the time interval between onset of the illness and admission to hospital, since children come to hospital much earlier than adults.

The results suggest that 28% of the illnesses in children and 22% in adults were caused by an identifiable virus. In the period studied 12% of illnesses in children and 16% of illnesses in adults were due to influenza A and B viruses. Thus, despite the identification of a large number of viruses capable of causing acute respiratory illness in recent years, the majority of illnesses remain unidentified. A certain proportion may, of course, have been streptococcal sore throat and pneumococcal pneumonias, but, according to the figures presented, this would account for only about another 5% of illnesses.

A striking finding was the relative paucity of evidence for the cause of infection in babies aged 0-11 months. No explanation for this is available, as similar methods were used in all groups. This finding is very different from the investigation of respiratory illnesses in babies undertaken in Washington, D.C., where isolation rates for parainfluenza viruses 1 and 3 were highest in the 0-1 age group (B. E. Andrews, 1959, personal communication; Parrott *et al.*, 1959).

It is difficult to compare our results with those of other workers in view of the differences in the populations studied and in the methods used. Crofton *et al.* (1951) obtained serological evidence of virus or rickettsial infection in 26 out of 110 cases of pneumonia, and pneumococci were isolated from the sputum in 29 (26%) of them. These results were similar to those obtained in our investigation of all respiratory illnesses. Evans (1957) was able to make an aetiological diagnosis in 18% of 710 Wisconsin students admitted to hospital, and Griebel *et al.* (1958) made an aetiological diagnosis in 29 out of 122 adults with acute respiratory infections seen at a clinic, but not needing admission to hospital.

In the development of complications of disease of the respiratory tract, the danger of acquiring a highly resistant strain of *Staph. aureus* was evident. It appears

that patients without disease of the respiratory tract rarely develop a respiratory infection while in hospital, and no definite aetiological agent was demonstrated in those adults who contracted a post-operative "chest infection."

### Summary

During the winter of 1958-9 bacteriological and virological investigations were made on all patients—179 adults and 117 children—admitted to the medical wards of St. Thomas's Hospital, London, suffering from an acute respiratory illness. 28% of illnesses in children and 22% of illnesses in adults were associated with an identifiable virus. Influenza A and B viruses were those most often found. The parainfluenza groups of viruses were responsible for very few infections.

*Str. pneumoniae* was isolated from 36% of the samples of sputum tested, *H. influenzae* from 22%, and *Staph. aureus* from 2%. No relationship was found between the presence of particular bacteria in the nasopharynx or sputum and evidence of virus infection.

No deaths occurred among the children, but among the adults there were 12 (6.7%). Seven patients (two children and five adults) developed a staphylococcal pneumonia after admission, and in six of these patients the pneumonia was due to a strain of *Staph. aureus* acquired from the hospital environment. Of the patients studied it was found that 24% of the children and 33% of the adults acquired a new strain of *Staph. aureus* during their stay in hospital. Most of these strains were resistant to more than one antibiotic.

This survey illustrates that respiratory disease accounts for more than one-third of all child and at least 15% of all adult admissions to a general hospital in the winter. The aetiology of these infections could be determined in about a quarter of the patients admitted.

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