THE ASSOCIATION OF PNEUMOCOCCI, HEMOPHILUS INFLUENZAE, AND STREPTOCOCCUS HEMOLYTICUS WITH CORYZA, PHARYNGITIS, AND SINUSITIS IN MAN

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In a previous paper (1) it was reported that persons harboring pneumococci in their noses and throats were relatively subject to coryza, pharyngitis, and sinusitis, and conversely that persons not harboring these organisms were relatively free of these diseases. Moreover, it was stated that the occurrence and degree of symptoms were associated to some extent with variations in the numbers of pneumococci obtained from the nose and throat cultures. These relationships are described in more detail in the present paper.

Technique

The general scheme of study has been described previously (1). The group on which the observations were made comprised adults working at The Rockefeller Institute and in some instances their children. Each individual was questioned every 2 or 3 days to ascertain the presence of fever, chill, malaise, headache, nasal discharge, sore throat, sneezing, cough, etc., and was requested to report whenever such symptoms occurred. Cultures of the nasal passages and throat were usually made weekly; when symptoms were present, however, cultures were taken daily, if possible. Material obtained by means of a sterile swab was streaked over one or two freshly prepared 15 cm. rabbit blood agar plates. The resultant aerobic growth was classified into Gram-positive and negative cocci and bacilli. Pneumococci, *S. hemolyticus*, and *H. influenzae* were identified with care (1).

RESULTS

The present analysis is based on the protocols of the individuals studied most intensively. Since considerable information about each case is needed in order to judge the degree of association of upper respiratory tract symptoms and potential pathogens, the selected

group constitutes less than 20 per cent of the entire number studied. This association, moreover, became increasingly apparent with the amount of care exercised in obtaining full histories, in taking frequent cultures, and examining them minutely.

The protocols are divided into those of individuals not carriers of pneumococci, *H. influenzae*, and *S. hemolyticus*, and individuals who were transient, periodic, and chronic carriers of these organisms. Illustrative cases are described in the following paragraphs.

Non-Carriers.—Two in number. Were free of symptoms 2½ years and 1 year respectively.

Transient Carriers.—

Case 1, free of upper respiratory tract symptoms and pathogens on 25 tests from Sept. 4, 1928, to Nov. 27, 1928, suffered an influenzal attack from Nov. 26, 1928, to Dec. 10, 1928, during the epidemic. At this time, 6 of 32 cultures contained large amounts of *H. influenzae* and 2 contained pneumococci of an unnumbered, specific type. Subsequently, tests were negative and remained so during a 9 day period of sore throat from Feb. 1, 1929, to Feb. 10, 1929. Thereafter no symptoms were reported and 34 cultures contained none of the above mentioned organisms. On Nov. 17, 1930, the individual reported sore throat lasting 24 hours and yielded *H. influenzae* on this date and 1 week later. The succeeding 17 cultures were free of these organisms and no further symptoms were noted until Apr. 20, 1931, at which time chills, weakness, sneezing, nasal discharge, and sore throat were experienced for 2 days and *H. influenzae* was recovered on Apr. 20, 1931. 7 tests thereafter were negative; 1 on Aug. 27, 1931, contained *H. influenzae*; 5 tests then proved negative. On Oct. 19, 1931, chills, fever, malaise, and sore throat developed, lasting 5 days. During this time and thereafter to Nov. 1, 1931, 5 cultures were taken, all negative for the organisms.

Case 55 was a carrier of pneumococci Type XIII on 14 tests from Oct. 11, 1929, to Feb. 7, 1930. During this time one 6 day period of nasal discharge preceded by malaise, nasal obstruction, and sore throat was noted. Tests were negative from Feb. 7 to Apr. 15, 1930. From Apr. 11 to Apr. 22, 1930, the individual suffered a relatively severe attack of prostration, irritability, and general aching sensations, accompanied by sneezing, nasal obstruction, and slight discharge. On Apr. 15 and 16, *S. hemolyticus* was recovered from the throat. Subsequent tests were negative. On Oct. 14, 1931, malaise and nasal congestion were reported, but 5 tests from Sept. 24 to Oct. 27, 1931, were negative. Commencing Oct. 30, 1931, a moderately severe attack of coryza, lasting 8 days, was experienced, and 2 weeks later, a second attack, lasting 10 days, was reported. 7 of 9 cultures taken during this period contained *S. hemolyticus*. Shortly after the symptoms disappeared, the tests became negative and remained so for 2½ months, during which time a 48 hour period of nasal discharge and sore throat

occurred. On Feb. 13, sore throat and nasal discharge were reported, lasting 5 days, and on Feb. 14 and 16 *H. influenzae* was obtained. No further symptoms were reported and subsequent tests were negative for these organisms[1] (Text-fig. 1).

These cases are examples of individuals who, on brief and infrequent occasions, carry a few pneumococci, *H. influenzae*, or *S. hemolyticus*. Their appearance is usually associated with the presence of upper respiratory tract symptoms, although symptoms may occur during a period of negative cultures. The organisms usually decrease in numbers or disappear at varying intervals after the symptoms have subsided.

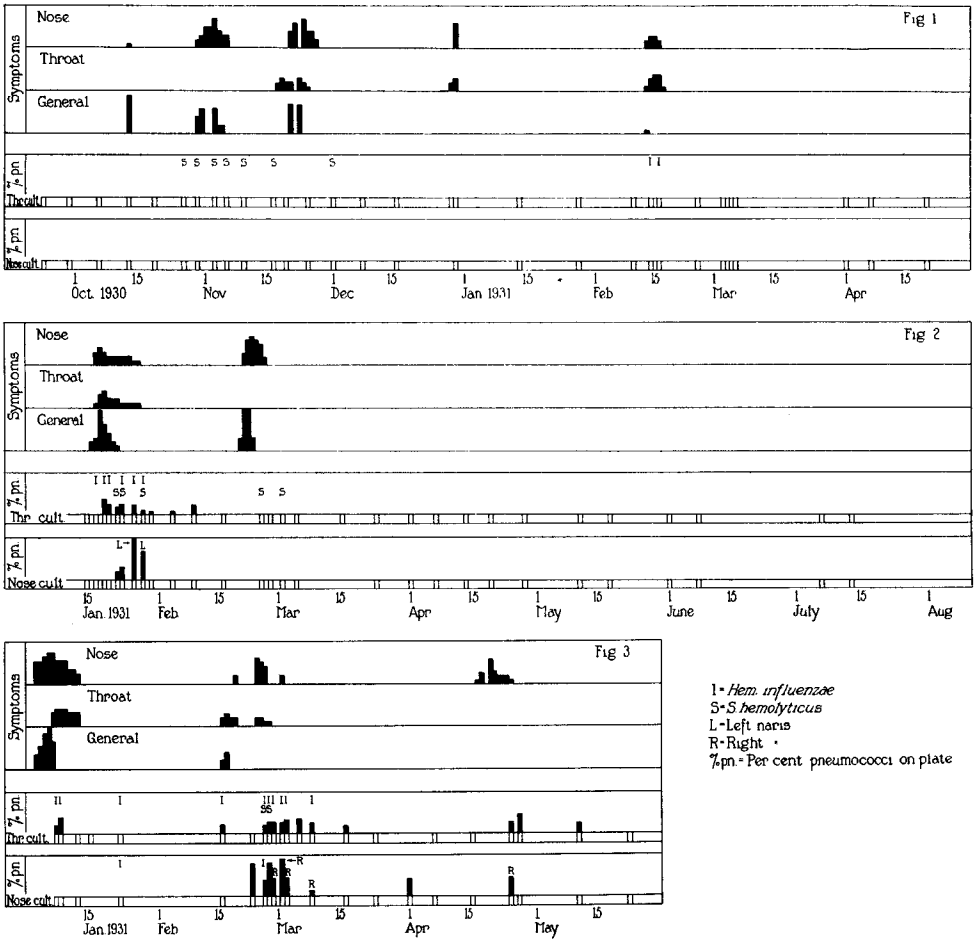
Periodic Carriers.—

Case 17, free of pneumococci on 34 tests, from January, 1929, to Jan. 17, 1931, and free of upper respiratory symptoms, save for one 6 day attack of coryza and cough which was not studied, developed on Jan. 16, 1931, chill, nasal discharge, sore throat, and cough which persisted 11 days. Cultures taken the day after the onset of symptoms were negative; those taken daily thereafter, to Jan. 30 and Feb. 4 and 9, contained abundant pneumococci of a single, unnamed type, together with *H. influenzae* and *S. hemolyticus*. A second similar attack was reported from Feb. 20, 1931, to Feb. 24, 1931, but only 1 test was made and this proved to be negative. Thereafter, no further symptoms were noted and 21 tests were negative (Text-fig. 2).

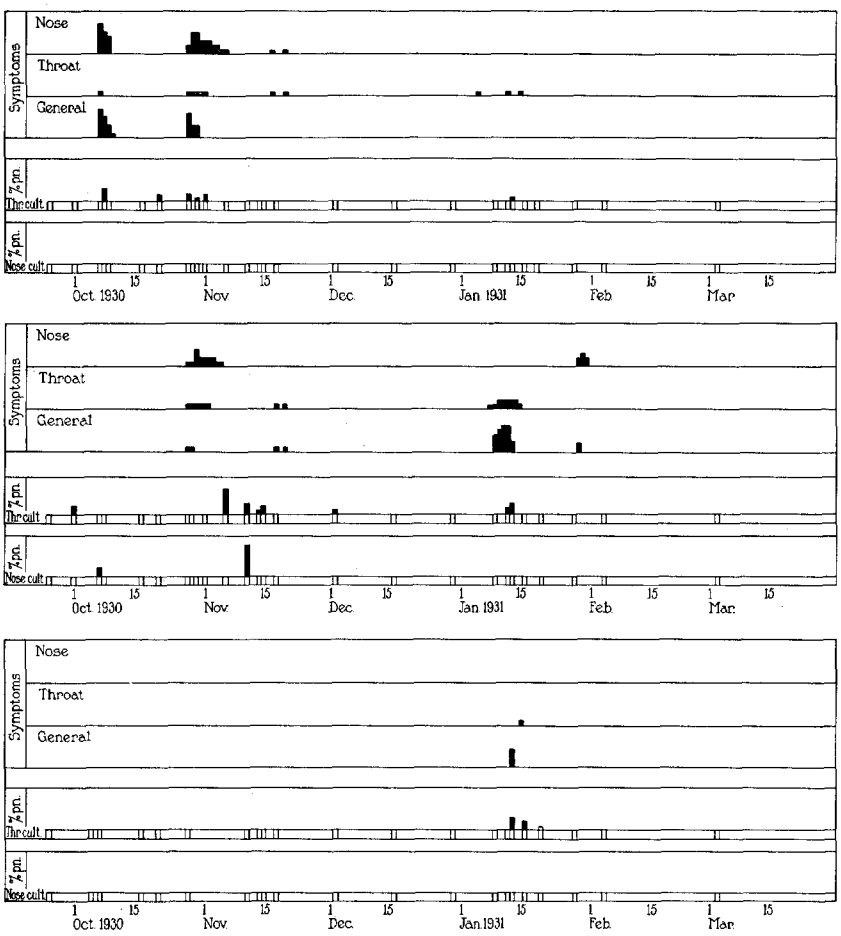
Case 50, free of the organisms on 8 cultures over a 5 months' period, developed on Mar. 3, 1931, chills, malaise, headache, and sore throat, lasting 72 hours. Tests Mar. 30, 1931, Apr. 1, Apr. 7, and Apr. 14 revealed pneumococci Types VIII and XXII and *H. influenzae*. 10 subsequent cultures were free of these organisms and no further symptoms have been reported.

Case 51, suffering a severe attack of fever, chills, malaise, nasal obstruction and discharge, sore throat, and cough from Jan. 3, 1931, to Jan. 13, 1931, was first cultured Jan. 8 and 9. Pneumococcus Type V and *H. influenzae* were present. A second attack, with nasal discharge and sore throat, lasted from Feb. 16, 1931, to Mar. 8, 1931, during which time 6 cultures were taken, and was accompanied by the presence of Pneumococcus Type X, *H. influenzae*, and occasional *S. hemolyticus*. During a third 7 day period of coryza, 11 cultures were taken which contained these same organisms. 4 subsequent tests were negative, with the exception of 1 instance, when pneumococci Type X appeared in the culture from

[1] During the past 17 weeks, Oct. 15, 1931, to time of writing, typical meningococci Type II have been recovered in large numbers and it is not known how long these organisms had been present but unrecognized.



TEXT-FIGS. 1, 2, and 3


Symptoms
Nose
Throat
General
Throat cult.
Nose cult.
1 15 1 15 1 15 1 15 1 15 1 15
Oct. 1930
Nov.
Dec.
Jan. 1931
Feb.
Mar.

TEXT-FIG. 4

the right naris. From Apr. 17, 1931, to Apr. 25, nasal congestion and discharge were reported; on Apr. 25 and 27 and May 11, Pneumococcus Type X was recovered. 1 culture taken May 23, 1931, contained none of these organisms (Text-fig. 3).

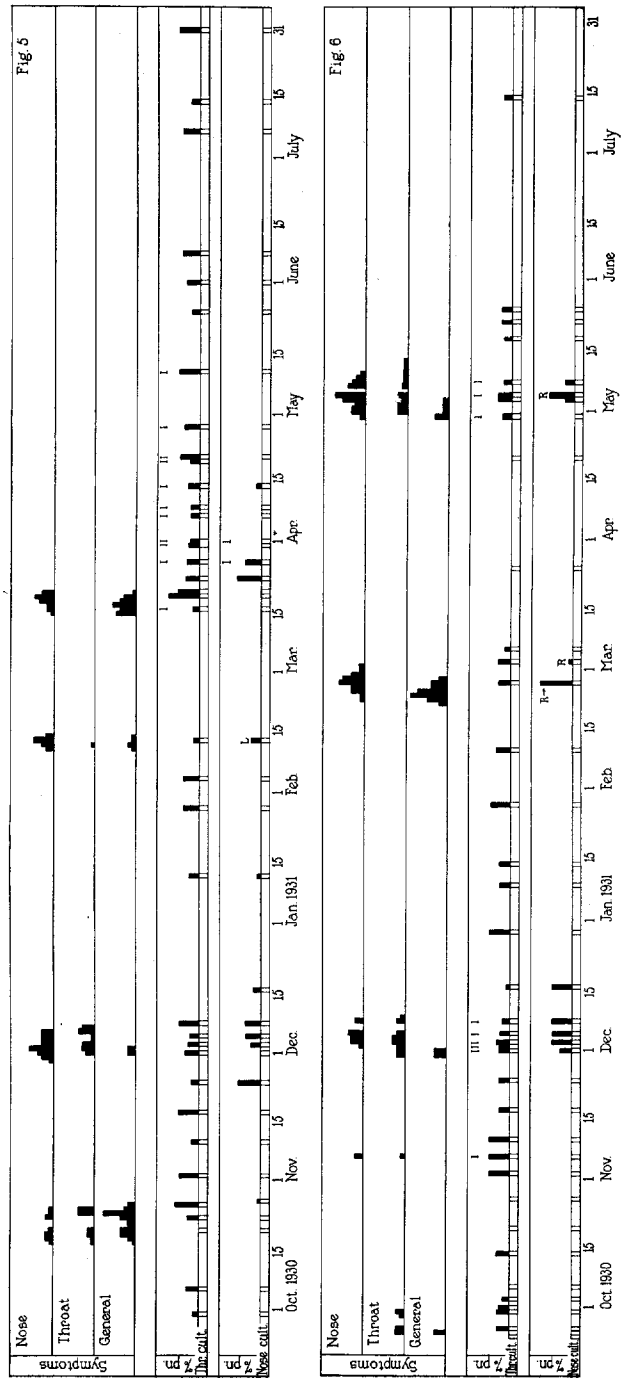
Cases 33, 34, 35, and 36 are members of a family. The father, No. 36, has been free of pneumococcus with the exception of 1 brief period, and free of upper respiratory tract symptoms for 3 years. The mother, No. 35, has been a transient carrier of pneumococci on 3 occasions, during the past 3 years, associated with the appearance of upper respiratory tract symptoms. The 2 children, Nos. 33 and 34, have carried the same type of pneumococci during 3 winter periods and have experienced 2 or 3 mild attacks of coryza and cough. The present study was made during the winter of 1930–1931. One child, No. 33, after 2 negative cultures in September, became a carrier of pneumococci of a specific, unnumbered type on Oct. 10, 1930. The other child, No. 34, after 3 negative cultures, suffered a mild 3 day attack of coryza, during which pneumococci of the same type appeared on culture. Subsequently, both children continued to carry this organism on 21 cultures for the remainder of the winter. They experienced simultaneous attacks of coryza and cough for 2 to 10 days on 3 separate occasions. During the most severe attack, the mother, No. 35, came down with malaise and sore throat, and yielded pneumococci of the same type as found in the children. Thereafter, tests became negative and no symptoms were noted until October, 1931 (Text-fig. 4).

In this group of individuals, the organisms appeared during illness and disappeared at varying intervals after the symptoms ceased.

Chronic Carriers.—

Case 15 has been a carrier of Pneumococcus Type XIII for at least 4 years and Case 52 a carrier of an unnumbered specific type of pneumococcus for at least 1 year. Each has experienced during the winter months 4 to 6 attacks of frontal headache, malaise, nasal discharge, and sore throat. On these occasions, roentgenographs have shown extensive clouding of the antra, cultures from the throat show a great increase in numbers of organisms, and cultures from the nares, previously free, show the organisms present often in nearly pure culture. Moreover, in instances when the individual's pain was localized to one antrum, this localization corresponded to the localization of clouding in the roentgenogram and to the localization of the organisms in right or left nares. When symptoms subsided, the nasal cultures became free of pneumococci, the throat cultures contained them in fewer numbers, and the roentgenographs showed some clearing of the antra (Text-figs. 5 and 6).

In brief, chronic carriers of pneumococci proved subject to respiratory tract symptoms and antrum disease. There appeared, moreover, a direct relation between the degree of symptoms, amount of



TEXT-FIGS. 5 and 6

clouding of antra in roentgenographs, and numbers of organisms contained on throat and nose cultures.

A relationship between the presence of these pathogens and symptoms, although demonstrated in all cases of this special series, may not invariably exist. Indeed, in three cases studied with less care during 1928 and 1929, no such organisms were found during attacks of upper respiratory tract disease. The limits of this relationship therefore must be decided by painstaking study.

DISCUSSION AND CONCLUSIONS

Pneumococci, *H. influenzae*, and *S. hemolyticus* are known to be frequent inhabitants of the upper respiratory tract, but most workers have not recognized any definite relationships between their presence and coryza, sore throat, influenzal, and sinusitis attacks (2–5). Dochez, Shibley, and Mills, however, in their experimental studies of common cold, state that in both the spontaneous and experimentally induced "colds" in anthropoid apes, the "most significant change observed has been the increase of activity on the part of the potential pathogens habitually present in the throat flora. Coincident with the appearance of symptoms, pneumococci, *S. hemolyticus*, and *B. pfeifferi* have developed in greatly increased numbers and have spread over a wide area of the nasopharyngeal mucous membranes. These organisms became at this time conspicuous even in the nose, where they are seldom or never present under normal conditions. The same phenomena have not been observed in human beings" (6, 7).

The essential facts of the present observations are that persons free of pneumococci, *H. influenzae*, and *S. hemolyticus* are in general free of coryza, sore throat, influenzal and sinus attacks; that persons who are occasional or periodic carriers of these organisms may be negative on tests over long healthy periods, but generally become positive during or following attacks and subsequently become negative again; finally, that persons who are chronic carriers show during these illnesses increasing numbers of organisms in the throat and extension of the organisms to the nose.

That these organisms may be the actual incitants has been claimed by Park (8); that they are secondary invaders is the view of Shibley,

Mills, and Dochez who state as a result of their experimental work on this subject that "the most important significance of viruses of this type [common cold] seems to lie in their capacity to incite activity on the part of the more dangerous pathogenic organisms that infect the upper respiratory tract" (7). The present observations bring out the intimate relationship between these pathogens and upper respiratory tract symptoms, but do not disclose the nature of this relationship.

Finally, an addition has been made to the knowledge of the mode of spread of these organisms. A focus of growth and dissemination has been determined in the nasal passages and throat of individuals with chronic upper respiratory tract disease and increases in numbers of the organisms at the focus and their spread to contacts have been related to the winter season and to the occurrence of symptoms in the carrier. The observations suggest that the dosage of these organisms in a community is controlled by the resistance of the carrier and of the contacts. This view is in agreement with the facts derived from studies of native animal infections (9).

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