THE EPIDEMIOLOGY OF PNEUMOCOCCUS INFECTION

THE INCIDENCE AND SPREAD OF PNEUMOCOCCI IN THE NASAL PASSAGES AND THROATS OF HEALTHY PERSONS

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Present knowledge of the epidemiology of human pneumococcus infection is incomplete and confused. In the first place, it is uncertain whether the pneumococcus group of bacteria consists of one, two, perhaps three specific organisms, Types I, II, and III, each with an undetermined capacity for variation, or of a relatively large collection of definite entities, each with general similarities but with specific differences in variability, in ability to spread in a population, to grow in human tissues at the normal portal of entry, and to incite the phenomena of disease. A further question then arises as to what is the respective ability of each type or strain of pneumococcus to vary, to spread, and to incite disease. Finally, it may be asked, what are the respective rôles of the microorganism and of the host in determining the various phases of individual infection on the one hand—the healthy carrier state, the localization of infection in the pharynx, sinuses, and middle ear, and the generalization of infection in the lungs, peritoneum, meninges, and blood-stream—and population infection on the other hand—epidemic, sporadic, and endemic prevalence?

Answers to similar questions in the field of animal infections have been obtained by controlled experimentation under natural conditions (1), but in the case of human pneumococcus infection such procedures are not feasible. Consequently, a survey has been made of the incidence of pneumococci in healthy persons in the hope that the resulting findings, although lacking the degree of control necessary for drawing precise conclusions, will be useful in reaching an understanding of (*a*) the specificity and stability of pneumococci, (*b*) the different capacities of pneumococci to infect and give rise to disease, and (*c*)

the differences and variability of the response of individuals to exposure to pneumococci. The results of these studies are described in the present paper.

Technique

Clinical observations and nose and throat cultures were made on four separate groups of normal people. The first group consisted of 33 adults connected with The Rockefeller Institute, together with six children and adults in their respective families. These individuals, living under relatively similar environmental conditions, were chosen to represent a typical cross-section of an urban population. Each person was questioned at 2 or 3 day intervals to ascertain the presence of coryza, sore throat, headache, malaise, or fever, and at the same time was instructed to report voluntarily whenever such symptoms were present. As a rule, bacteriological cultures of the nasal passages and throats of these people were made every 7 days; during periods of illness, however, a report was made and one to three cultures were taken daily. Individuals of this group have been under observation for periods of 7 months to 3½ years. The second group consisted of 19 children at the New York Foundling Hospital. These boys and girls, 5 and 6 years old, lived in two relatively isolated units comprising playroom, dining room, and bedroom, and were each under the care of one special nurse. Nasal passage and throat cultures were made bimonthly from November, 1929, to March, 1930. The third group of individuals consisted of 25 children, aged 3 to 54 months, living in their respective homes in New York City. They were brought to the clinic of the New York Nursery and Child's Hospital about once a month for physical examination. On these occasions, from February to June, 1930, cultures were made from their nasal passages and throats.[1] The fourth group consisted of 22 children, aged 5 and 6 years, attending the Bethlehem Day Nursery in New York City. These children were studied during May and June, 1930.

In making a culture from the nasal passages the individual was requested to exhale forcibly and a sterile swab was then passed into each nasal orifice. In making a culture from the throat a swab was passed over the entire posterior pharyngeal wall and the surface of the tonsils. The swabs were then streaked over the surfaces of media contained in 10 and 15 cm. Petri dishes.

Media were prepared according to the method of Avery, Chickering, Cole, and Dochez (2). The best grade of fresh beef was employed and heating was reduced to a minimum. Slants and plates made with fresh agar plus 5 per cent whole, citrated, rabbit blood were kept moist and were used within a few hours after their preparation.

The inoculated plates were incubated in a moist atmosphere at 37.5°C. for 18 hours, after which the resulting bacterial growth was classified into the relative

[1] The authors wish to express their thanks to Dr. Dorothea Moore for assistance which made possible the observations on this group of children.

numbers of Gram-positive cocci, Gram-negative cocci, Gram-positive bacilli, diphtheroids, Gram-negative bacilli, hemolytic, green-producing, and indifferent streptococci, hemoglobinophilic bacilli, and pneumococci. The procedure for identifying pneumococci was to transfer representative, small, green-producing colonies suggestive of pneumococcus to blood agar plates or slants and after 6 to 8 hours' incubation to reseed this pure culture growth to broth. The broth cultures, incubated 6 to 9 hours, were then tested for solubility in bile, fermentation of inulin, autolysis in saline, agglutination in acid buffers (1 *a*), agglutination in pneumococcus sera of Types I to XXV,[2] and virulence for mice. The virulence of the cultures for mice was tested by injecting 1 cc. of the 8 hour broth culture in dilutions of 10^0 to 10^{-6} intraperitoneally into a total of 14 mice, each dilution of culture being given to two mice. The result was expressed in terms of dilution of culture killing all mice within 48 hours.

GENERAL RESULTS

Observations on the 39 individuals of Group I were made for periods averaging 11 months, during which an average of 39 cultures were secured from the nasal passages and 27 from the throats of each individual. Pneumococci were obtained from 86 per cent of the group at some time during the period, from the nasal passages of 35 per cent, and from the throats of 86 per cent. Cultures from the throats of individuals of this group contained pneumococci more frequently than cultures from the nasal passages—249 of 913 cultures from the throat, 27.3 per cent, as compared to 71 of 1,330 cultures from the nose, 5.3 per cent.

Observations on the 19 children of Group II were made from November, 1929, to March, 1930, during which time five cultures from nasal passages and throat were secured from each individual. Pneumococci were obtained from 69 per cent of the group, from the nasal passages of 69 per cent and from the throats of 38 per cent. Cultures from the throats of members of this group contained pneumococci less frequently than cultures from the nasal passages—6 of 101 cultures from the throat, 6 per cent, as compared to 40 of 101 cultures from the nose, 40 per cent.

Observations on the 25 children of Group III were made from February to June, 1930, during which time 4 cultures were taken from the nasal passages and throat of each individual. Pneumococci were obtained from 80 per cent of the group, from the nasal passages of 72 per cent and the throats of 72 per cent. Pneumococci were obtained on cultures from the throat and nasal passages with equal frequency—33 of 111 cultures from the throat, 30 per cent, and 35 of 111 cultures from the nose, 31 per cent.

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[2] Diagnostic sera of Types I, II, and III were kindly furnished by Dr. Mary B. Kirkbride of the New York State Department of Health Laboratories; sera of Types IV to XXV by Dr. G. Cooper of the New York City Department of Health Laboratories.

Observations on the 22 children of Group IV made during May and June, 1930, were as follows: 4 cultures taken from the nasal passages and throat of each individual showed pneumococci in 41 per cent of the group. The organisms were found in nasal cultures of 37 per cent and throat cultures of 23 per cent. Cultures

TABLE I

Incidence of Pneumococci on Nose and Throat Cultures of 105 Normal Persons

Serum type of pneumococcus	Number of individuals positive	Individuals positive	Duration of positive period in different individuals	Mouse virulence of strains from different individuals[1]
		per cent		
I	1	0.9	1± day	6
II	2	1.9	1±, 1± day	5−, 5, 6
III	9	8.5	1, 1, 1, 1, 1, 1, 1 day±, 3, 8 mos.	6−, 6−, 6−, 5−, 6−, 5−, 5, 5, 6−, 5, 6
VII	1	0.9	7 mos.	1 cc., 1 cc., 1 cc.
X	2	1.9	1, 1 day±	1
XIII	9	8.5	1, 1 day±; 2+, 4+, 4+, 5, 5 mos.; 1+, 3½+ yrs.	Avir.−, 1−, 2, 1, Avir.−, 3, 4, 3−, 2, 3−, 5, 5, 5−, 3, 3, 4, 3−, 3, 4, 3, 2, 2, 2, 4, 4, 5, 3, 4
XIV	5	4.7	1, 1, 1 day±; 2+, 3+ mos.	1−, 1−, 1−, 1, 0, 1, 2, 2−
XVII	1	0.9	3+ mos.	2, 1, 2, 2
XVIII	3	2.8	1, 1 day±; 7+ mos.	2−, 1 cc.−, 5, 5, 5
XIX	2	1.9	1 day ±; 4+ mos.	1 cc.−, 1, 1, 1, 1, 1
XXIII	1	0.9	1 day±	1 cc.
x[2]	9	8.5	4+, 4+, 4+, 5, 5 mos.; 1½+, 2+ yrs.	4, 3, 3−, 1, 2−, 3, 3, 1 cc., 4−, 1, 1, 2, 2, 1, 2, 2, 1 cc., 1, 2, 1−, 2, 2, 2, 1 cc., 1, 2, 1, 1, 1, 1−, 3, 3, 3, 4, 3−, Avir. (14 strains tested)
Group IV[3]	51	48.5		
Non-type-specific	13	12.4		

[1] Results of tests on consecutive strains from a given individual are given together between dashes and are expressed exponentially. Avir. = avirulent; 1 cc. = 1 cc. killed in 48 hours; 1 = a dilution of 10^{-1} killed; etc.

[2] Strains from each individual agglutinated in a homologous serum and in no other sera.

[3] Strains agglutinated in no available sera. No homologous serum prepared.

from the throats of individuals of this group contained pneumococci less frequently than cultures from the nasal passages—6 of 84 cultures from the throat, 7 per cent, as compared to 11 of 84 cultures from the nose, 13 per cent.

To recapitulate, pneumococci were found at one time or another in cultures from the nasal passages or throats of about 80 per cent of the 105 healthy adults and children studied. In adults they occurred chiefly on cultures from the throat, while in children, they occurred more frequently on cultures from the nasal passages.

Specificity of Pneumococci Found in Healthy Persons

Of about 500 strains of pneumococci obtained from the four groups of individuals, 97 per cent proved to be serologically specific. They formed smooth colonies, were bile-soluble, were for the most part virulent for mice, did not flocculate in acid buffers, but agglutinated in specific antipneumococcus serum. The incidence of the various type-specific strains among the 105 individuals is given in Table I. Types III, XIII, XIV, and XVIII were obtained most frequently. Sixteen atypical strains from 13 persons were soluble in bile, fermented inulin, failed to kill mice in 1 cc. doses, did not flocculate in normal salt solution, but flocculated over a wide range of acid buffer solutions, pH 3.6 to 4.7 (1 *a*), and agglutinated in all types of antipneumococcus serum employed. The colony morphology of these strains differed markedly; some colonies were disc-shaped, others flat, others pinhead, and still others granular. These cultures are defined in the present paper as non-type-specific strains.

Stability of Pneumococci in Normal Persons

Evidence of the stability of pneumococci growing in the nasal passages and throats of normal people was secured by comparing strains obtained on successive cultures from the same individual. Strains of pneumococci isolated from a single carrier on successive tests proved with rare exceptions to be of the same serological type and were uniform in colony morphology, bile solubility, tendency to autolyze, inulin fermentation, agglutinative properties, and virulence for mice.

Thus, 11 strains from the 3 month carrier of Type III pneumococci were alike (Table I), and 29 strains from the 8 month carrier of Type III pneumococci were alike; moreover, 18 strains from the 7 month carrier of Type VII pneumococci, 14 strains from a 5 month carrier of Type XIII organisms, 17 strains from the 1 year carrier of Type XIII, and 52 strains from the 3½ year carrier of Type XIII pneumococci were alike; 18 strains from a 5 month carrier of an unnamed specific

TABLE II

Incidence of Non-Type-Specific Pneumococci in Normal Persons

Identity of individual	Results of nose and throat cultures															
		1929		1930												
	Date of culture	Dec.		Jan.				Feb.			Mar.	April		May	June	
		14	18	4	9	10	22	4	11	27	28	17	29	21	4	
5	Type of pneumococci	A	0	0	A	GIV	0	III	0	0	0	GIV	GIV	A	0	

		1928				1928	1929		1930	
	Date of culture	Nov.		Nov. to Dec.		Dec.	Jan. to Feb.	Feb.	Feb. to June	
		2	8	14	13	4	17 4	18	26	26
20	Type of pneumococci	x	x	18 tests x		A	6 tests x	A	179 tests x	

		1929									1930									
	Date of culture	Oct.		Nov.			Dec.				Jan.		Feb.					Mar.	Apr.	May
		21	28	4	11	25	10	23	27	30	10	22	4	5	6	7	19	26	15	19
24	Type of pneumococci	0	II	0	0	GIV	GIV	II	GIV	GIV	A	0	0	0	0	0	0	0	0	0

		1929 1930	1930								
	Date of culture	Dec. to Jan.	Jan.			Feb.			Mar.		Apr. to May
		14 19	21	22	24	4	13	27	18	27	17 21
31	Type of pneumococci	4 tests 0	x	x	x	x	A	x	x	x	3 tests 0

		1928			1928 1929	1929 1930					1930		1930 1931	
	Date of culture	Sept. to Oct.		Oct.	Nov.	Nov. to Jan.	Jan.				Jan. to Jan.		Jan. to May	June to Jan.
		3	28	28	3	4 4	5	6	7	8	9	11	21 12	13 31
35	Type of pneumococci	17 tests 0		GIV	GIV	17 tests 0	A	0	0	A	50 tests 0		12 tests x	45 tests 0

A = Atypical pneumococcus.
GIV = Strains agglutinated in no available sera. No homologous sera prepared.
x = All strains from the individual agglutinated in homologous serum but in no other available sera.
0 = Pneumococci absent.

type of pneumococcus, 20 strains from another 5 month carrier of pneumococci of the same type, 32 strains from an 18 month carrier of a different unnamed specific type of pneumococcus, and 51 strains from a 2 year carrier of still another unnamed specific type, were uniform respectively. On rare occasions, these carrier strains were accompanied by small numbers of pneumococci of a different serological type, but there was no evidence suggestive that any carrier strain was undergoing a type-transformation.

This degree of uniformity in successive strains of pneumococci recovered from a given carrier indicates that pneumococci growing in the upper respiratory tract of healthy humans are relatively stable.

A further measure for testing the stability of pneumococci in healthy people was suggested by the observations of Griffith (3) and Dawson and Avery (4) that type-transformation and virulence-enhancement of pneumococci *in vitro* take place not in the type-specific smooth colony forms but in the degraded or rough variants. An attempt was made, therefore, to determine whether the presence of non-type-specific pneumococci obtained in nose and throat cultures of the 13 persons referred to previously (Table I), was associated in any way with type-transformations or virulence changes *in vivo*. In each case non-type-specific pneumococci were secured infrequently and in very small numbers. They were found during periods in which no other pneumococci were present, and during or at the end of periods of 1 month to 3 years in which the same type-specific and stable pneumococcus was present. These relationships are shown in the partial protocols of 4 cases (Table II). There is nothing in these observations to indicate that the occurrence of non-type-specific pneumococci was associated with a type-transformation or virulence-enhancement process *in vivo*.

Relative Capacity of Pneumococci of Different Types to Survive and Spread in Healthy People

It is known that pneumococci of Types I and II are found most frequently in cases of lobar pneumonia and relatively infrequently in healthy persons (5, 6, 7). In the present group of 105 individuals from whom a total of more than 3,000 cultures has been taken, Type II pneumococci were found on but three single cultures from two individuals and Type I was obtained on but one occasion from a single

individual. This strain, virulent for mice in dilutions of 10^{-6}, was introduced into the nasal passages and throat of another person known to be free of pneumococci. Nasal cultures taken 3 hours later contained fully virulent Type I pneumococci; later nasal passage cultures

TABLE III

Incidence of Type III Pneumococci in Normal Persons

Room number	Number persons tested	Number persons positive	Identity of positive cases	Duration of carrier period							
				1928		1929					
				Oct.	Dec.	Feb.	Apr.	June	Aug.	Oct.	Dec.
1	5	2	12								
			23								
2	7	3	7								
			30								
			6								
3	5	2	4								
			5								

TABLE IV

Incidence of Type XIII Pneumococci in Normal Persons

Number persons tested	Number persons positive	Identity of positive cases	Duration of carrier period																			
			1927		1928						1929						1930					
			Oct. 1	Dec. 1	Feb. 1	Apr. 1	June 1	Aug. 1	Oct. 1	Dec. 1	Feb. 1	Apr. 1	June 1	Aug. 1	Oct. 1	Dec. 1	Feb. 1	Apr. 1	June 1	Aug. 1	Oct. 1	Dec. 1
7	6	15																				
		22																				
		36																				
		33																				
		20																				
		52																				

and all throat cultures were negative. In contrast with these findings are the observations that Type III pneumococci and others included in Group IV occur frequently in normal people (5, 6, 7). Types III and XIII, for example, were each found in nine of the present group of 105 individuals (Table I), and under circumstances suggestive that

they were actually spreading from individual to individual (Tables III and IV).

Of the nine persons yielding Type III pneumococci, seven were working in three adjacent rooms (Table III). Of five persons tested in one of these rooms, two were positive, one for 3 months and one throughout an 8 months' period of observation. Of seven persons tested in an adjacent room, three were positive on four, one, and one isolated occasions respectively; and of five persons tested in another adjacent room, two were positive on one occasion. It is important to note again that these strains of Type III pneumococci killed mice uniformly within 48 hours when injected intraperitoneally in dilutions of 10^{-5} and 10^{-6} (Table I).

Of the nine persons positive for Type XIII pneumococci, six were working whole or part time in a single laboratory room and one in an adjacent room (Table IV). Case 15 has been a carrier for 3½ years; her husband is likewise a carrier of Type XIII. Case 22, working within a few feet of Case 15, became a carrier of Type XIII in January, 1929, and remained so until April, 1930. Cases 36, 20, and 52, working in the same room, have each been positive on one occasion; Case 33, a part time assistant, and No. 10, working in an adjacent laboratory, became carriers of Type XIII in the autumn of 1929 and remained so until the spring of 1930.

Apparently the types of pneumococci which are more commonly associated with cases of serious disease (Types I and II) survive and spread with relative infrequency in normal persons, and conversely, the types of pneumococci less commonly associated with cases of severe disease (Types III, XIII, etc.) are those which tend to survive and spread in these individuals.

Thus far it has been shown that 97 per cent of pneumococci obtained from about 3,000 cultures from the nasal passages and throats of 105 healthy persons were serologically specific, that these specific strains, especially those obtained from chronic carriers which could be studied more carefully, proved to be stable in colony morphology, bile-solubility, tendency to autolyze, acid and serum agglutination characteristics, and intraperitoneal virulence for mice. Atypical strains, on the other hand, found in a few individuals on single and scattered occasions, appeared not to be undergoing type-transformation into Types I, II, or other serologically specific strains. Finally, Types I and II pneumococci, rarely encountered in the present group of healthy persons, showed little tendency to survive or spread, while Types III and XIII, present in 10 per cent of the group, showed a decided tendency both to survive and spread.

Individual Differences in the Incidence of Pneumococci on Nose and Throat Cultures

During the course of these studies it became apparent that there were consistent differences in the bacterial flora of the nasal passages and throats of different individuals. With respect to the presence or absence of pneumococci on these cultures, the 39 individuals of Group I were divided into non-carriers, transient, periodic, and chronic carriers (Table V). *Non-carriers* comprised eleven of the group, of which five were negative whenever tested and six were positive on only one or two occasions. *Transient carriers*, twelve in number, were positive for pneumococci on single and scattered occasions between

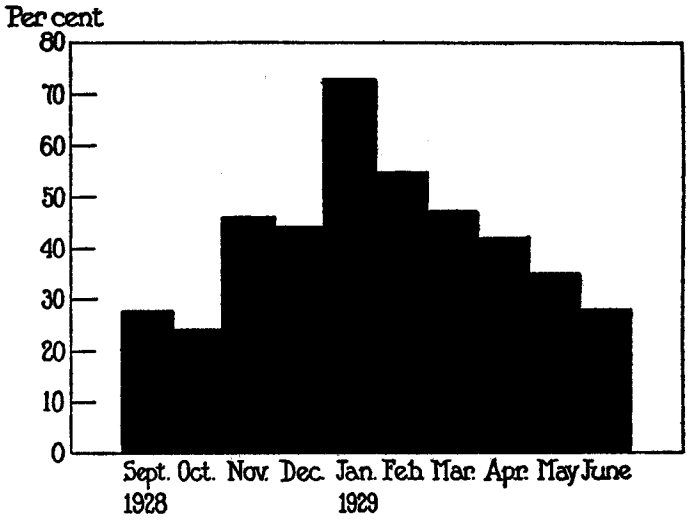
TABLE V

Individual Differences in the Incidence of Pneumococcus on Nose and Throat Cultures

Class	Description	Number	Per cent
Non-carriers	Pneumococcus-free	5	13
	Positive 1–2 tests	6	15
Transient carriers	Positive tests; occasional and scattered	12	31
Periodic carriers	Positive tests; 1 week to 3 months	8	21
Chronic carriers	Positive tests; 3 months to 3+ years	8	21

pneumococcus-free periods (Table II, Cases 5 and 22). The strains of pneumococci recovered from an individual of this group on an occasion following a pneumococcus-free period, usually differed from the strains obtained on a subsequent occasion following another pneumococcus-free period. *Periodic carriers*, numbering eight, were those from whom pneumococci of one serological type were obtained for periods of 1 to 12 weeks between pneumococcus-free intervals (Table II, Case 35). *Chronic carriers*, numbering eight, were those from whom pneumococci of one serological type were obtained for periods of 3 months to 3 years or more (Table II, Case 20).

These differences in the incidence of pneumococci in individuals have been too characteristic and consistent to be attributable to chance and too apparent in members of the same family and in individuals working in the same and adjacent rooms to be related to qualitative or quantitative differences in exposure to pneumococci. In the case of 17 persons exposed to a carrier of Type III pneumococcus (page 544), eleven remained consistently negative, four were positive on single isolated occasions, and one became a carrier for 3 months (Table III); in the case of seven individuals exposed to a carrier of



TEXT-FIG. 1. Incidence of pneumococci in cultures from the nose and throat of individuals of Group 1, 1928–1929.

Type XIII pneumococcus (page 544), one remained consistently pneumococcus-free, two were positive on single occasions, and three became Type XIII carriers for 7 and 15 months respectively (Table IV).

Apparently these differences in the incidence of pneumococci were associated with host properties. There is reason to believe that the pneumococcus carriers were infected individuals in the sense that the organisms were growing in the rhinopharyngeal tissues. Five of the eight chronic carriers had sinus or tonsil infections and suffered four

or more attacks of coryza, sore throat, headache, or malaise during each winter. During these attacks the pneumococci on throat cul-

TABLE VI

Incidence and Duration of Coryza and Sore Throat in 30 Persons of Group I, 1928–1929

Identity of case	1928				1929					
	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
12										
13										
14										
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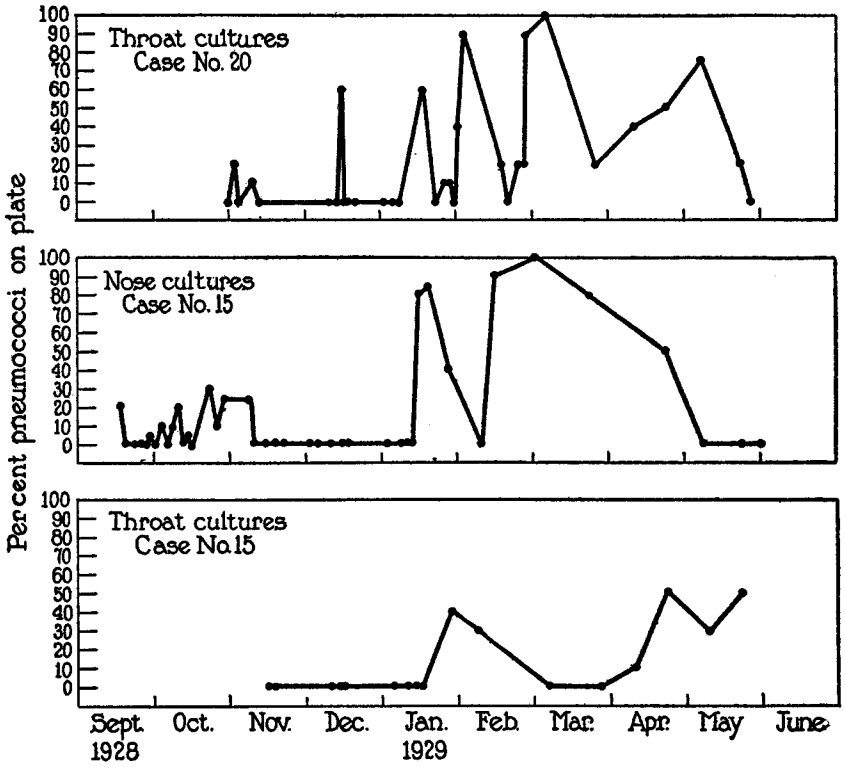
26										
28										
29										
30										
31										
32										
35										
36										
Totals.	0	6	8	11	14	8	5	1	0	0

ture plates increased in numbers markedly, often to the point of being present in pure culture, and were found on nasal culture plates which

previously and subsequently were pneumococcus-free. None of the five non-carriers of pneumococci, on the other hand, had either objective or subjective evidence of upper respiratory tract infection, nor contracted coryza or sore throat during the 7 month to 3 year periods of observation. Finally, it was noted that the incidence of pneumococci in individuals of Group I underwent a seasonal variation (Text-



TEXT-FIG. 2. Incidence of pneumococci in cultures from the nose and throat of Cases 20 and 15, 1928–1929.

fig. 1) similar to that of the incidence of coryza and sore throat in the same individuals (Table VI) and that the incidence of the given type of pneumococcus in each of the chronic carriers was subject to the same sort of variation (Text-fig. 2). These observations are suggestive that the persons studied differed in the amount of their resistance to pneumococcus infection and that this resistance underwent a seasonal fluctuation.

DISCUSSION

The bearing of the foregoing data on the question of pneumococcus epidemiology is threefold. In the first place, most pneumococci in healthy persons proved to be antigenically specific and stable, an observation in agreement with the knowledge that in persons with pneumonia, pneumococci are specific (5 to 11) and stable. Pneumococci kept under highly artificial conditions, however, are reported to undergo profound changes in serological specificity and virulence for mice (3, 4). One is inclined to believe, therefore, that the group of bacteria classified as pneumococci consists of a collection of biological entities with different specific characteristics which, although varying in abnormal environments, are in man relatively unchanging (12). Second, pneumococci of Types I and II were obtained on but three occasions, while pneumococci of Types III and XIII were encountered frequently and under conditions suggestive that they were actually spreading from person to person. These findings are in agreement with the knowledge that pneumococci of Types I and II are relatively common in cases of severe pneumonia and uncommon in healthy persons (6 to 8), and together are supportive of the view that pneumococci differ among themselves in their inherent capacity to spread from host to host and multiply in tissues at the normal portal of entry and in their capacity to incite natural disease. Third, individuals appeared to differ in their response to exposure to pneumococci, some remained consistently pneumococcus-free, some were transient carriers, others, periodic carriers, and still others, chronic carriers. Moreover, the number of pneumococcus carriers and the quantity of pneumococci obtained from each chronic carrier underwent a seasonal variation corresponding to that of the incidence of coryza, sore throat, and other upper respiratory tract disease. The observations are suggestive that pneumococcus carriers are infected individuals in the sense that the organisms are growing in their nasopharyngeal tissues, that the presence or absence of the infected state is dependent on the amount of resistance of the host to the given pneumococcus, and that this resistance is a varying property, decreasing during the winter months and increasing during the warm weather.

These observations may be considered to advantage in the light of

results of experimental epidemiological studies on analogous animal infections. With reference to the question of specificity and stability of the bacterial incitant, it was found that in rabbit and fowl pasteurellosis specific strains of pasteurella from cases of septicemia, pneumonia, sinusitis, and from healthy carriers were on all significant occasions under natural and controlled conditions, relatively fixed in pathogenicity and serological specificity (1 *b*, *c*). With reference to the question of differences in the capacities of strains to survive, spread from host to host, and to give rise to disease, it was determined experimentally that strains of pasteurella most able to incite severe disease were least able to spread from host to host, and *vice versa* (1 *d*, *e*). Finally, regarding the problem of respective rôles of microorganism and host in determining the spread of individual and population infection studies on three populations of rabbits infected with pasteurella under relatively controlled conditions showed that some animals were consistently free of the organisms, others were periodic or chronic carriers, and still others carried pasteurella in association with sinusitis or pneumonia (1 *f*, *g*, *h*). Moreover, controlled groups of rabbits given a fixed intranasal dose of pasteurella reacted similarly according to the above classification (1 *d*), and similar tests with fowls and *P. avicida* gave corresponding results (1 *e*). Finally, similar differences in the response of individual animals to pathogenic microorganisms were shown to depend upon differences in the resistance of the animals (1 *i*). From these studies, it has been concluded that the prevalence of these infections is determined by variations and differences in the resistance of individual animals to the relatively stable bacterial incitant.

The similarity in behavior of these animal infections and human pneumococcus infection is suggestive of the possibility that their incidence and spread are controlled by similar mechanisms, that in the case of pneumococcus infection, the pneumococcus incitants differ in their ability to spread from host to host and grow in tissues at the portal of entry, and to incite severe disease, but that each is relatively unchanging, that the epidemic and endemic spread of infection is determined by differences and variations in host resistance to the given strains of organisms. For the solution of the problem, however, evidence is required which is based on a satisfactory experimental technique involving controlled and natural conditions.

SUMMARY

1. Pneumococci were obtained at one time or another from the nasal passages or throats of 80 per cent of 105 adults and children studied. In adults, they were obtained more frequently from the throat; in children, as often from the nasal passages as from the throat.

2. Of 500 pneumococcus strains studied, 97 per cent proved to be serologically specific. They formed smooth colonies and were for the most part avirulent for mice. Types I and II were obtained from one and two individuals respectively on one occasion only. Type III was obtained from nine individuals; Type XIII from nine individuals; Type XVI and Type XVIII from three individuals, for varying periods in each case. Atypical pneumococci were secured from 13 persons on single and scattered occasions. They varied in colony morphology, did not kill mice, or agglutinate in saline, but flocculated in all types of antipneumococcus sera employed and over a wide pH range in acid buffers. Their occurrence was apparently not associated with any type-transformation or virulence-enhancement process *in vivo*.

3. Strains of pneumococcus obtained on successive cultures from a given carrier were, with rare exceptions, of the same serological type and were similar in colony morphology, virulence for mice, and other tested biological characteristics.

4. Pneumococci of Types I and II were obtained under conditions suggestive that they lacked a capacity to spread readily; pneumococci of Types III and XIII, on the other hand, were obtained under conditions suggestive that they were spreading from person to person.

5. The persons studied differed consistently with respect to the occurrence of pneumococci. Some were pneumococcus-free, some were transient carriers, some periodic, and some chronic carriers. Data are given which suggest that the differences were due to variations in host resistance.

6. The incidence of pneumococci in all individuals studied underwent a seasonal variation paralleling that of coryza and sore throats in the same persons.

BIBLIOGRAPHY

1. Webster, L. T., and associates: (*a*) Hughes, T. P., *Proc. Soc. Exp. Biol. and Med.*, 1930, **27**, 804; (*b*) *J. Exp. Med.*, 1926, **44**, 359; (*c*) *J. Exp. Med.*, 1930, **51**, 219–259; (*d*) *J. Exp. Med.*, 1926, **43**, 555, 573; (*e*) To be published; (*f*) *J. Exp. Med.*, 1924, **39**, 857 and **40**, 109; (*g*) *J. Exp. Med.*, 1927, **45**, 529; (*h*) *J. Exp. Med.*, 1927, **45**, 911; (*i*) *J. Exp. Med.*, 1923, **37**, 231; 1924, **39**, 129, 879; **40**, 397; Pritchett, I. W., 1925, **41**, 195, 209; **42**, 1; 1926, **43**, 161, 173; 1927, **46**, 557; 1930, **52**, 901, 909, 931.
2. Avery, O. T., Chickering, H., Cole, R., and Dochez, A., Acute lobar pneumonia. Prevention and serum treatment, Monograph of The Rockefeller Institute for Medical Research, No. 7, New York, 1917.
3. Griffith, F., *J. Hyg.*, 1928, **27**, 113.
4. Dawson, M. H., and Avery, O. T., *Proc. Soc. Exp. Biol. and Med.*, 1927, **24**, 943.
5. Neufeld, F., and Haendel, L., *Arb. k. Gsndhtsamte*, 1910, **34**, 293.
6. Dochez, A., and Gillespie, L., *J. Am. Med. Assn.*, 1913, **61**, 727.
7. Dochez, A., and Avery, O. T., *J. Exp. Med.*, 1915, **21**, 114; **22**, 105.
8. Stillman, E. G., *J. Exp. Med.*, 1916, **24**, 651; 1917, **26**, 513.
9. Olmstead, M., *J. Immunol.*, 1917, **2**, 425.
10. Cooper, G., Edwards, M., and Rosenstein, C., *J. Exp. Med.*, 1929, **49**, 461.
11. Plummer, N., Raia A., and Shultz, S., *Am. J. Dis. Child.*, 1930, **40**, 557.
12. Neufeld, F., De Lamar Lectures, Baltimore, The Williams and Wilkins Company, 1926–1927.