A Study of Lobar Pneumonia in Massachusetts: Methods and Results of Pneumococcus Type Determination, 1931-1932*

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EARLY in 1931 a study of lobar pneumonia in Massachusetts was begun. This study,[1, 2] financed by the Commonwealth Fund of New York City, comprises a study of the epidemiological factors involved in the spread of the disease; the production of concentrated antipneumococcic serum for treatment; and the organization of various areas of the state, selected by our Advisory Committee on Lobar Pneumonia. In them pneumococcus typing can be carried out so that patients may receive the benefits of early serum treatment.

Eleven selected areas have been organized embracing a population of about 2 million or approximately one-half that of the state. They include urban, rural, industrial, residential, seashore, and upland regions. It was decided to use the laboratories of the one or more centrally located hospitals of each area as the typing center for that area. The present paper will deal with the findings of the 20 laboratories coöperating in this work.

In order to obtain uniform and proficient technic in this work, the technicians were sent to Boston and trained in pneumococcus typing at the Boston City Hospital. Typing is carried out for Types, I, II, III and V (V, because of occasional cross-agglutinations with Type II). Pneumococci other than I, II and III are reported as Group IV. Cultures of Group IV are sent to the State Bacteriological Laboratory where typing is carried out to the full 32 (Cooper[3]) types, to determine their geographical distribution and frequency. Incidentally, this affords a measure of checking the accuracy of the typing in the outlying laboratories, for if a culture is sent in as a Group IV and turns out to be a I, II, or III, it is obvious that an error has been made.

A set of directions was drawn up and copies were supplied to each

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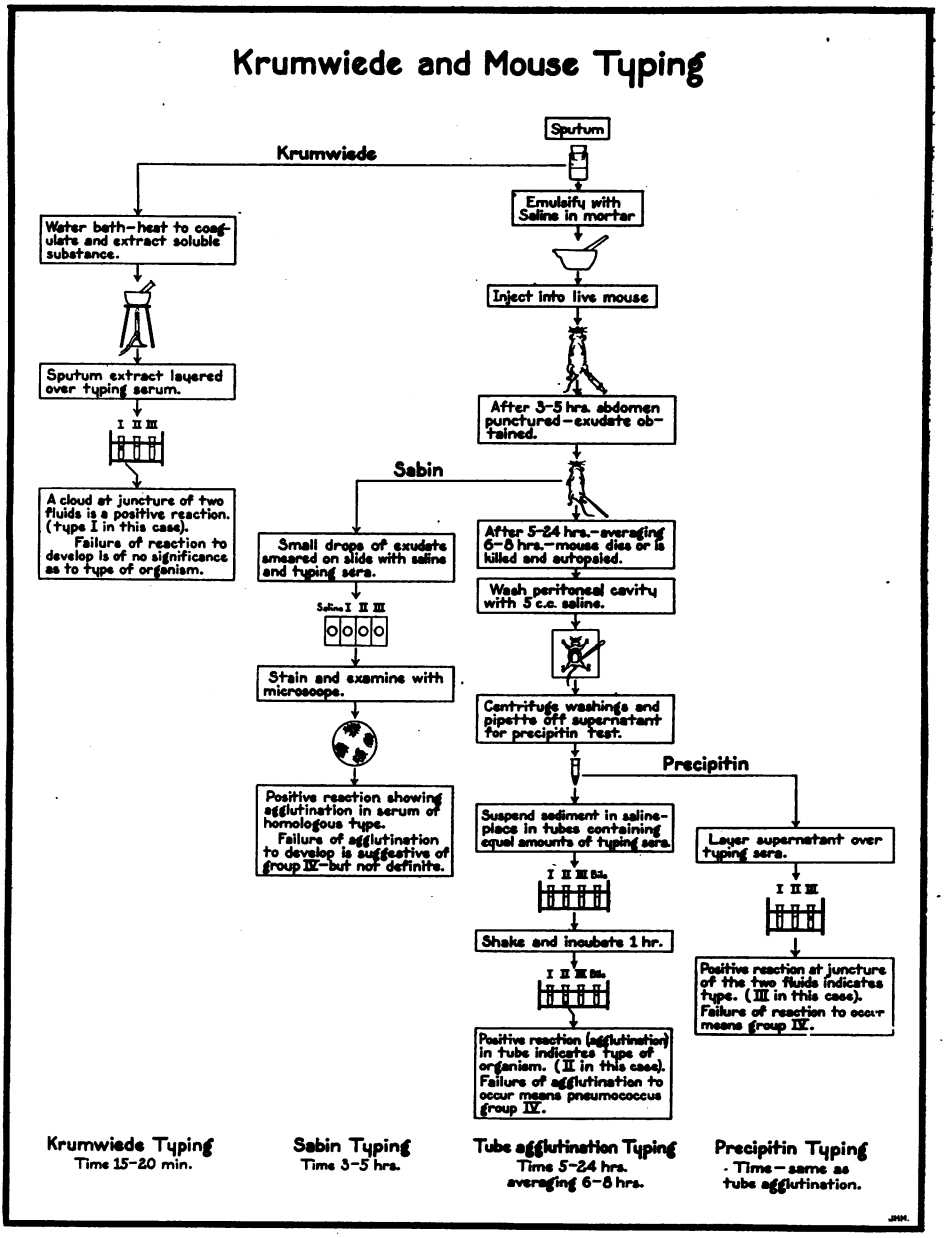

FIGURE I

technician. These give detailed procedure for typing sputum by the Krumwiede,[4] Sabin,[5] tube agglutination and precipitin methods[6]; and for typing material obtained from blood, throat, and other cultures, spinal and chest fluids, pus, and urine. The use of white mice in typing sputum and other suitable material has been adopted.

Given sputum, the technicians have been requested to try on each

specimen the Krumwiede, Sabin, and tube agglutination methods in the order named. Either the Sabin or tube agglutination acts as a check on the result of the previous method employed. An attempt was made to have every typing in these outlying laboratories checked by typing the organisms obtained from cultures of the mouse's heart blood or peritoneal exudate in plain or blood broth or on blood agar plates. This has been done in some laboratories and neglected in others.

To familiarize the physicians of the state with some of the methods of typing sputum and urine, two sheets of illustrations showing schematically the methods used and the usual time necessary to perform each have been distributed at large (Figures I and II).

TYPING RESULTS IN OUTLYING LABORATORIES

The number of typings in the laboratories of the areas over the state during the past fall, winter and spring is as follows:

	Area	*Number of Typings*
(1)	Beverly	30
(2)	Malden	43
(3)	Chelsea	(data not available—small number)
(4)	Newton	45
(5)	Boston	204
(6)	Brockton	19
(7)	New Bedford	13
(8)	Ayer	32
(9)	Worcester	122
(10)	Pittsfield	10
(11)	Great Barrington	3
	Total	521

Areas 2, 7 and 9 were not organized until well into the winter.

The distribution of types was as follows:

Type I		79
Type II		26
Type III		50
Group IV No pneumococci Streptococci Friedländer's bacilli		362
Total		517 *

* This figure is smaller than the total of 521 typings attempted because 5 specimens were urine. These gave negative precipitin reactions.

At first no request was made that cultures of all Group IV be sent to the State Bacteriological Laboratory for further typing. During the early winter such a request was made, and since cultures of most of Group IV have been obtained.

One hundred and seventy-one cultures have been received from the outlying laboratories and typed out to the full 32 types. (Table I.)

TABLE I

RESULTS OF EXAMINING AND TYPING SPUTUM, CULTURES AND OTHER MATERIAL AMONG THE THREE LARGE GROUPS

Type	*Cultures from Outlying Laboratories*	*Sputum Sent in by District Health Officers*	*"Regular" Typings*	*Type*	*Cultures from Outlying Laboratories*	*Sputum Sent in by District Health Officers*	*"Regular" Typings*
I	3 *	9	84	XXII	0	1	6
II	0	2	33	XXIII	1	0	6
III	4 †	6	82	XXIV	0	0	3
IV	8	1	16	XXV	0	0	0
V	13	6	31	XXVI	1	0	4
VI	2	0	4	XXVII	0	0	1
VII	4	4	16	XXVIII	0	0	4
VIII	13	9	40	XXIX	5	1	4
IX	3	4	16	XXX	0	0	4
X	9	2	12	XXXI	3	0	6
XI	2	0	20	XXXII	0	0	0
XII	1	1	5				
				Miscellaneous	60	..	..
XIII	2	0	8	No pneumococci	..	17	134
XIV	2	0	6	"Group IV"	..	4	77
XV	0	0	2	*Strep. hemolyticus*	9	2	31
XVI	0	0	1	Friedländer's bacilli	2	1	7
XVII	2	1	7				
XVIII	8	1	16	Untyped pneumococci	..	..	3
XIX	8	1	15				
XX	6	0	9	Total	172 **	73	716
XXI	1	0	3	Grand total all typings			960

* 1 sent for corroboration
† 3 sent to see if they were VIII
** 1 culture gave cross-agglutination with X and XX serums and is reported in both types.

Among the cultures sent in, only 2 of Type I and 1 Type III were sent in as Group IV.

STATE BACTERIOLOGICAL LABORATORY TYPINGS

During the past year typing has been carried out to the full 32 known types at the State Laboratory on all material sent there for this purpose. In the spring the demand became so great that an additional bacteriologist was taken on for this work.

The typings at this laboratory during the past year may be divided into 3 groups: (1) those done on Group IV cultures sent in from the outlying laboratories, (2) those on sputa sent in by the District Health Officers associated with this department, from

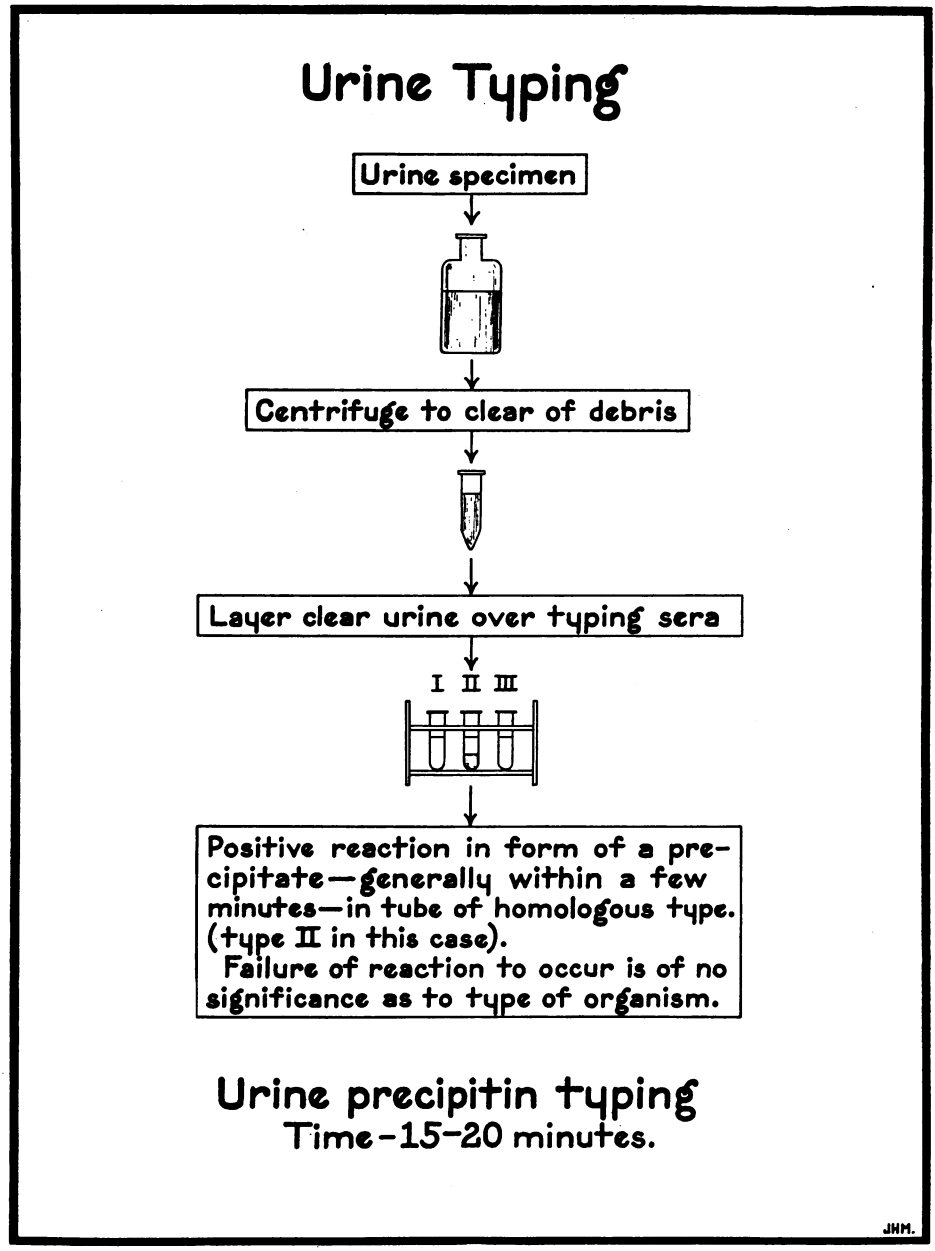

FIGURE II

patients with lobar pneumonia cared for at home, and who are not receiving antipneumococcic serum, (3) the group of "regular" typings carried out on material of various sorts sent directly by physicians at large. (Table I.) The specimens in this last group have not all come from cases of lobar pneumonia; many are from cases of broncho-pneumonia and other respiratory diseases; conse-

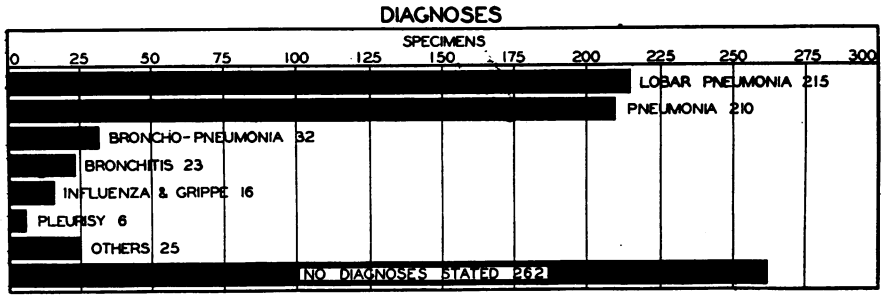

FIGURE III

quently, the frequency with which any particular type is observed cannot be compared with the reported occurrence of various types as the etiological agents in cases of lobar pneumonia alone. (Figure III.) This group represents a true picture of the variety of materials from hundreds of cases sent for typing by physicians of this state, and probably yields a picture similar to that which may be found by other state laboratories undertaking such work, and gives definite evidence that in Massachusetts, nearly every known type of pneumococcus can be found associated with respiratory disease.

Every specimen of sputum, chest or spinal fluid, or pus, received for typing which has yielded good pneumococci has been typed by one or more methods, and a vigorous attempt made to check each by cultures from the heart's blood of the mouse in plain or blood broth or on blood agar plates.

The routine methods employed on sputa have been (1) Krumwiede, (2) Sabin, and (3) tube agglutination, with or without precipitin test. (The final report to the physician on the result, if not previously rendered, was given here.) (4) In a few cases, typing has been done from heart's blood cultures, where the above methods have failed, (5) Occasionally, typing has been done from individually fished colonies.

The Sabin and tube agglutination (with or without the precipitin test) methods were used on chest or spinal fluids and pus. They were also cultured in broth and on blood agar plates directly.

On sputa, frequently the first 3 were done before checking from cultures, in order that an attempt might be made to evaluate the speed, accuracy and applicability of these various methods. The results will be discussed later.

A list of the organisms found in the sputa obtained from patients with lobar pneumonia who were cared for at home will be seen in Table I. These specimens were sent by the District Health Officers, and came from widely separated areas of the state. Data

concerning the case fatality rates, incidence of complications, and so forth, are being gathered upon this series which will give definite information upon this particular group of little known and much debated cases.

In Table I it will be noted that the term " Group IV " appears near the bottom of the table. In all such instances the specimens were inoculated into mice. Pneumococci could be seen in the mouse peritoneal exudate, but due to the overgrowth of other organisms, which increased in numbers upon further cultivation and exterminated the pneumococci, they could not be classified as to type. Unfortunately, the number of such was rather large.

If no pneumococci could be seen in direct smear of the mouse exudate, the report was " No pneumococci found." Hemolytic streptococci and Friedländer's bacilli were never reported, the former because they occur so often in normal throats their significance is uncertain, and the latter because there was no diagnostic serum available for the types known to be pathogenic for man. Such agglutinating serum has been obtained and henceforth Friedländer's bacilli will be reported. Records were kept where they were found and these findings are included here. No record has been made of *S. viridans,* nor of *B. influenzae,* when found. These organisms have occurred in varying numbers and there is great doubt of their clinical significance in the numbers found.

The third and last group of typings is the so-called " regular " done on sputum and other specimens sent directly to the laboratory. The results give an excellent gross picture of the variety of organisms likely to be encountered.

Among the " regular " typings the specimens upon which typing was requested were as follows:

	Number
Sputa	691
Chest fluids	8
Urines	7
Spinal fluids	5
Cultures of blood or pus	5
Total	716

It must be emphasized that the above specimens did not all come from cases of lobar pneumonia, but from many sorts of respiratory disease. The organisms reported are given in Table I.

The group of " regular " typings in Table I includes 15 instances where 2 types were isolated from the same specimen or definite cross-agglutination between 2 types occurred. These are reported under both types. The results of examination of 7 urines negative for I,

II and III, and of 8 specimens in which too few pneumococci were found to be typed are not included.

Summarizing the results of the "regular" typings noted in Table I, the distribution of the specimens as to organisms found is:

	Number	*Per Cent*
Pneumococci Types I to XXXII	464	64.7
Reported as "No pneumococci found"	134	18.7
Reported as "Group IV" pneumococci	77	10.8
Streptococcus hemolyticus	31	4.3
Friedländer's bacilli	7	1.0
Pneumococci—typical—but could not be typed with any of the 32 diagnostic sera available	3	0.4
Total	716	99.9

SEASONAL INCIDENCE

In an effort to determine the relative frequency with which the various types of pneumococci and other organisms occurred during the different seasons a series of charts have been prepared on which their monthly incidence has been recorded for 11 months, September 1, 1931, to July 31, 1932. Two groups of specimens have been combined. The results from sputa sent in by the District Health Officers have been added to those of our "regular" typings, as all of these specimens were sent to the laboratory directly from patients. (No Group IV cultures from outlying laboratories are included.)

The following charts (Figures IV to VII) give occurrence by months of the various organisms found in percentages, and show the

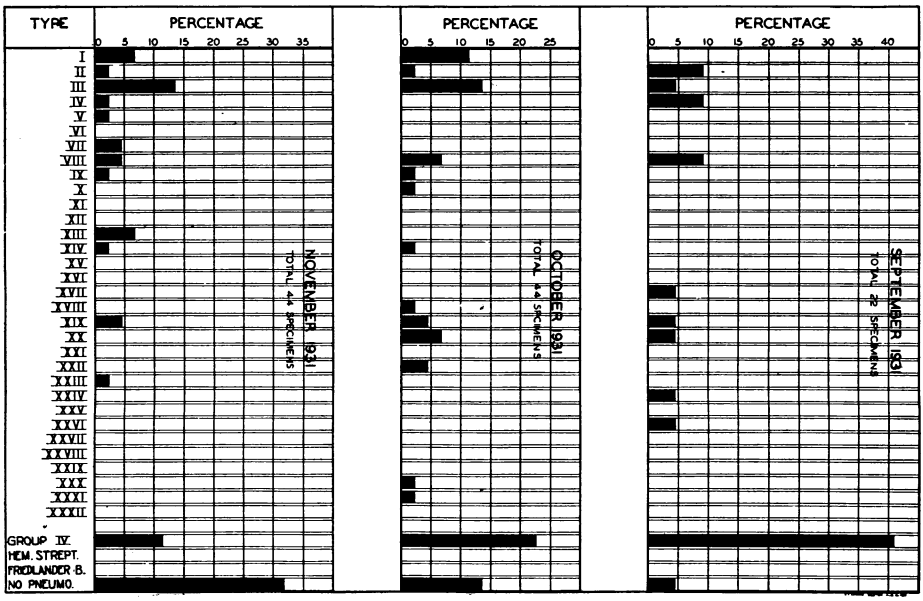

FIGURE IV

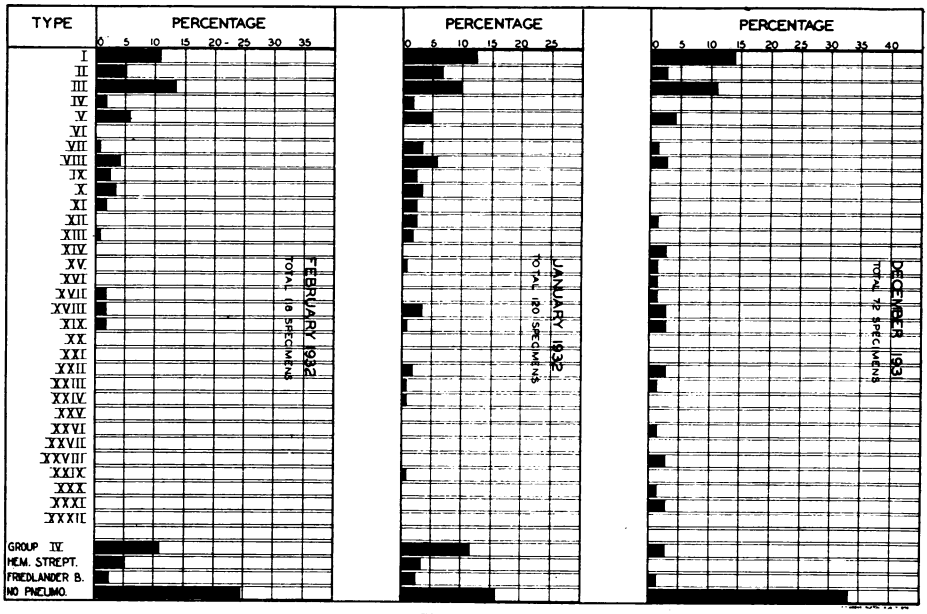

FIGURE V

results of typing 789 specimens. The various sub-types (IV to XXXII) were found more frequently during the winter and spring months December to May, than during the warmer months.

The approximate figures for this may be found in Table II. It will be noted that the percentage incidence of the sub-types (IV to

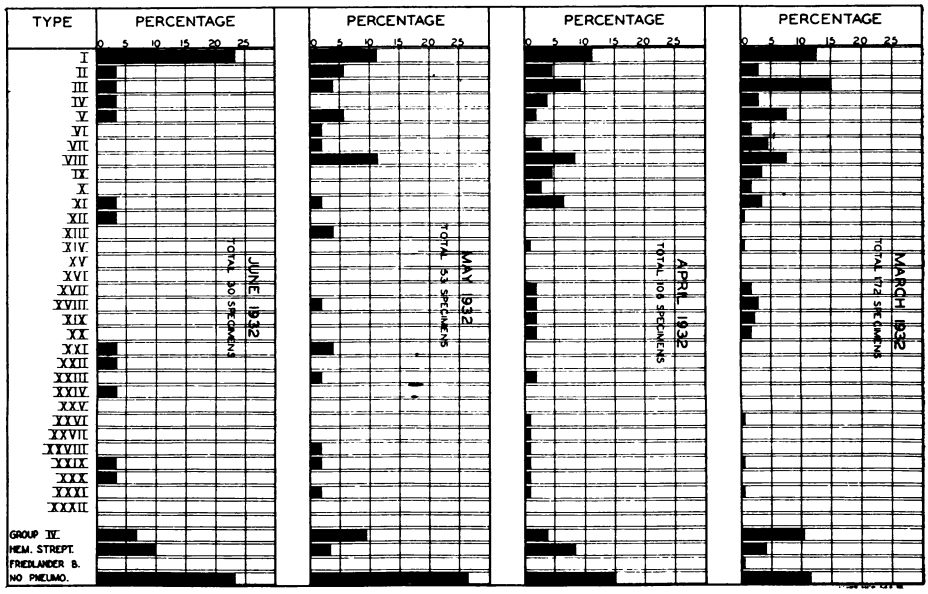

FIGURE VI

XXXII) remains more constant than does the actual number of different sub-types found; also, that Types I, II, and III comprise less than a quarter of the total 11 months' yield at the State Laboratory. There is every reason to believe that the figures for I, II, and III would be much greater were these typings done on consecutive cases of lobar pneumonia only.

TABLE II

Month	Percentage of Types Found (Approximate)		Percentage of Group IV and Other Organisms (Approximate)	Actual Number of Different Sub-types Found
	I, II and III Per Cent	IV to XXXII Per Cent	Per Cent	
Sept., 1931	13.6	40.7	45.4	7
Oct.	27.3	36.2	36.3	10
Nov.	22.6	31.7	43.2	9
Dec.	27.8	35.0	37.5	16
Jan., 1932	29.2	37.3	33.2	16
Feb.	30.5	26.1	43.2	11
Mar.	30.7	43.1	26.8	17
April	25.4	46.4	27.4	19
May	20.8	39.8	39.6	12
June	29.9	29.7	40.0	9
July	0.0	37.5	62.5	3
Approximate average for all 11 months	23.4	36.6	39.5	11.7

The lower chart in Figure VII summarizes the results for 11 months and shows the percentage incidence of the various organisms found September 1, 1931, to July 31, 1932—a total of 789 specimens including 764 sputa, a few chest and spinal fluids, a few urines, and blood cultures.

GEOGRAPHICAL DISTRIBUTION OF TYPES FOUND

There has been no especial geographical distribution among any of the 30 types of pneumococci found. The same type was isolated from individuals ill at the same time in widely separated regions of the state without apparent contact having occurred between the hosts.

Every type of pneumococcus (Cooper types), excepting XXV and XXXII, has been found among the specimens sent to the State Laboratory.

MULTIPLE FAMILY CASES OF LOBAR PNEUMONIA

Instances where 2 or more members of the same family have had lobar pneumonia within a few days or weeks of each other due to the same type of pneumococcus, have been decidedly uncommon and occurred only four or five times among nearly 1,000 cases typed either by our collaborators or at the State Laboratory.

ACCURACY OF TYPING METHODS

It is difficult, if not impossible, for us to give other than an estimation of the accuracy of the various methods of typing used. It is our experience that when the results of a typing by the Krumwiede, Sabin, or tube agglutination method are definitely positive, they are over 99 per cent accurate. The reporting of indefinite results leads to error and is to be discouraged.

The following figures throw light upon this attempt to estimate accuracy. The number of typings by the method used and the number of these checked by another method or by culture is indicated. Where a definite type has been determined and later yields a different one (not including cross-agglutinations and specimens with 2 types) on culture, such findings are indicated as discrepancies and for all practical purposes may be counted as errors in typing.

		Total No. of Typings Checked	
Typing Method	*No. of Specimens Yielding Types*	*Those in Agreement with Original Type Found*	*Those NOT in Agreement with Original Type Found*
Krumwiede	57	53	3
Sabin	380	360	4
Tube agglutination	150	143	2

The Krumwiede takes from 30 to 60 minutes. The Sabin usually gives positive results in 5 to 8 hours. The tube agglutination and/or the precipitin method can be done from 6 to 24 hours after inoculation of the mouse.

ADVANTAGES AND DISADVANTAGES OF METHODS

Krumwiede method of typing sputa: This method, when positive, yields a very speedy result. Usually, however, it has been found that the sputa sent to the State Bacteriological Laboratory for typing are insufficient in amount for this method, or when boiled become cloudy or otherwise unsatisfactory. For these reasons the usefulness of the Krumwiede has been greatly decreased. With some attention paid to the gathering of suitable specimens in satisfactory amounts it should be possible to increase greatly the number of positive typings by this very valuable rapid method.

Figure VIII shows the small number of positive Krumwiedes obtained from 683 sputa, being only 7.9 per cent of the whole (Krumwiedes were not done for Types IV to XXXII). The method yielded 30 per cent positives for I, II, and III among those sputa

from which a satisfactory supernatant fluid for layering was obtained. For any individual laboratory, in close association with patients, it should be possible to better this record with ease.

The results of the Krumwiede method of typing among sputa later proved to contain Type I, II, or III pneumococci are shown in Table III.

TABLE III

RESULTS OF TYPING BY VARIOUS METHODS

Results with specimens containing	Krumwiede				Sabin				Tube Agglutination			
	No. of specimens available	No. tried	No. positive	Per cent positive among those tried	No. of specimens available	No. tried	No. positive	Per cent positive among those tried	No. of specimens available	No. tried	No. positive	Per cent positive among those tried
Type I	89	31	24	77	83	73	69	95	44	44	40	91
Type II	35	14	12	86	27	25	24	96	12	12	11	92
Type III	74	27	18	67	63	54	51	95	34	34	31	91
Types IV to XXXII inclusive	...	...	...	...	255	253	232	92	93	74	66	89

Sabin method of typing specimens: In our experience this method will give a positive result on the largest number of specimens (sputa, chest, or spinal fluids, pus, and so forth) in the shortest period of time of any used; and is readily learned by new technicians.

Figure IX shows the results with this method. A total of 778 specimens were received which might have been put into mice, but due to the character and age of some this procedure was not always followed out though seven hundred and thirty-one were inoculated into mice. Sabins were not done on all of these for various reasons, the principal one being that in a large number of cases examination of the mouse exudate showed a very mixed growth or no pneumococci. Of the 731 specimens, 448 were tried with typing sera (this number includes 43 which never yielded a pneumococcus of any kind and 7

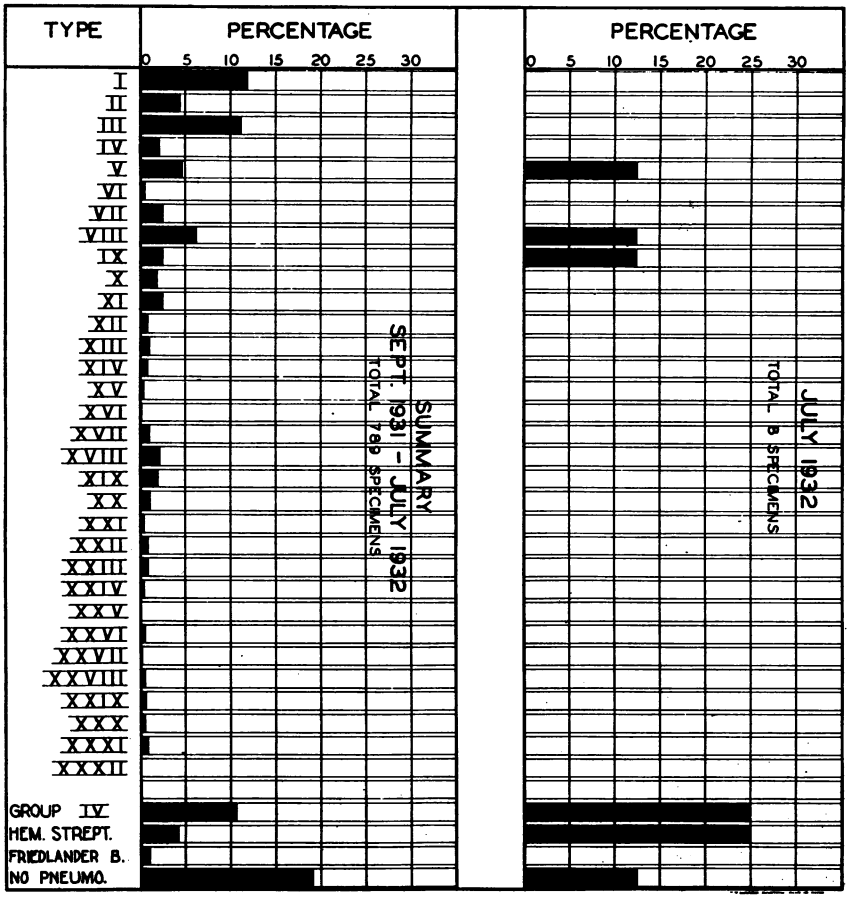

FIGURE VII

tried only for I, II, and III which later yielded a higher type). Of the 778 specimens, 376, or 48.3 per cent, gave a positive result for some type, or 83.9 per cent of those tried. Of those tried, 22 were negative and later on culture or tube agglutination yielded some definite type.

In estimating the efficiency of the Sabin method it is found that

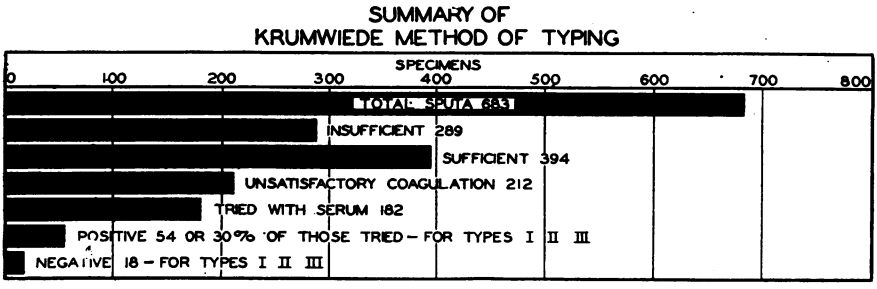

FIGURE VIII

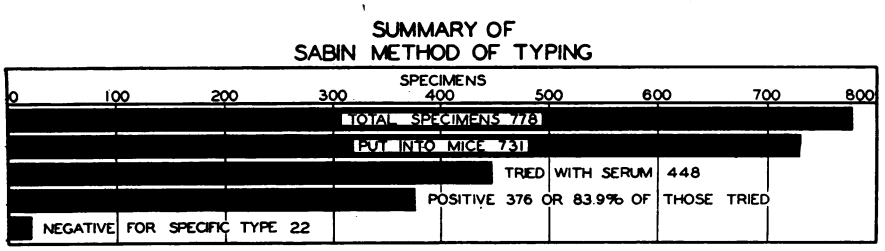

FIGURE IX

among 398 specimens that contained some definite type of pneumococcus, 376 or 94.5 per cent gave a positive result.

The results of the Sabin method among specimens proved to contain pneumococcus of some definite type (from I to XXXII) may be seen in Table III.

Tube agglutination method of typing: This method offers no particular advantage except in occasional instances where the Sabin has been negative, due chiefly to the presence of mixed culture. Of course, the tube agglutination is an old and well tried method and as such has rendered, and still does render, invaluable service. The great disadvantage lies in the fact that so much time is required for its performance.

Owing to the lack of time during the past year tube agglutinations were omitted on some specimens when satisfactory results were obtained by the Krumwiede or Sabin. These were checked by cultures, usually heart's blood cultures from the mouse. There were 273 specimens on which our records for tube agglutinations are complete. (See Figure X.) Of these, all 273 were tried. One hundred and forty-eight or 54.2 per cent were positive which is also 54.2 per cent of those tried. Sixteen of the negatives contained some specific type. Of the remaining 109, 90 never yielded a definite type by any method and the others were not typed out far enough to include the specific type later obtained from culture.

The results of tube agglutinations among specimens proved to contain pneumococci of some definite type (I to XXXII) are shown in Table III.

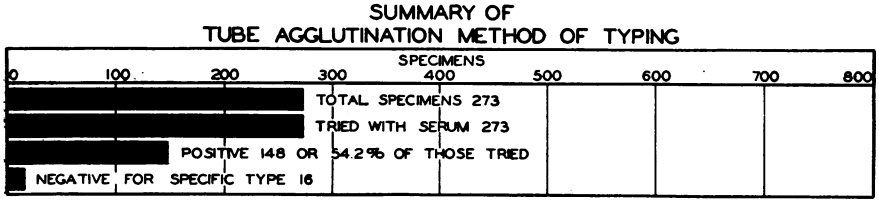

FIGURE X

Other methods of typing: The precipitin test as an aid to typing (using the supernatant of centrifuged mouse peritoneal exudate washings) has been used occasionally and was most useful where the mouse peritoneal exudate contained other organisms with the pneumococcus.

Occasionally Avery broth cultures (the so-called artificial mouse method of typing) have been made simultaneously with mouse inoculations, using the same specimen. Such data are being collected and will be reported later.

CHECKING BY CULTURES

Efforts were made to check every type previously determined from a culture of the organism. Among 789 typings only 43 or 5.4 per cent were not checked by either some other method of typing or by culture, and most of these were checked from cultures of the organism. The majority of such cultures were made from the heart's blood of the mouse in plain or blood broth or on blood agar plates. Most of those not checked could not be typed by any rapid method due to the presence of other organisms; the type was ascertained from cultures of individually fished colonies or cultures of the heart's blood of the mouse.

MISCELLANEOUS FINDINGS

Two distinct types of pneumococci have been isolated from 4 specimens, culture of the mouse's heart blood yielding a different type from that obtained by one or more of the rapid methods of typing. In each case both types were obtained by more than one method. In 3 other instances pneumococci have been found in conjunction with another organism, both in the mouse's peritoneum and in the heart's blood culture. The list follows:

PNEUMOCOCCUS TYPES OR OTHER ORGANISMS

Number	*Type*	*Type*
1	III from peritoneal exudate;	XX from heart's blood
1	III from peritoneal exudate;	V from heart's blood
1	IX from peritoneal exudate;	V from heart's blood
1	I from peritoneal exudate;	II from heart's blood
2	III with Friedländer's bacilli	
1	IV with Friedländer's bacilli	
1	XXVI with *Streptococcus hemolyticus*	

Many of the above findings were also verified by culture of individually fished colonies. Due to the great amount of time which must be used in carrying out this type of work little has been done in this direction.

Since the figures in this article were compiled, a single Type I

colony has been isolated from the heart's blood culture of a reported Type XXII (by Sabin). The heart's blood broth culture gave a negative I and a positive XXII macroscopic agglutination. The heart's blood was also streaked on to a blood agar plate from which colonies of Type XXII and a single colony of Type I were isolated. Similarly, a strain agglutinating with both X and XI sera has been isolated from a reported Type I.

In seven other instances cross-agglutination occurred in the Sabin. Two of these strains were never obtained in pure culture. Two lost their dual characteristics upon cultivation and later agglutinated only with 1 type serum. The other 3 (isolated by single colony fishing) maintained the property of cross-agglutination for as long as they were kept, agglutinating with 2 sera both in the tube and by stirring on the slide. The types showing cross-agglutination were as follows:

Types II and XIX
Types IV and IX (never obtained in pure culture)
Types VIII and XI (later, only XI)
Types XI and XV
Types XVI and XXVIII (never obtained in pure culture)
Types XXVI and XXIX
Types XXIII and XXX (later, only XXX)

DISCUSSION

A review of the bacteriological findings show that there has been a large amount of work done on sputum examination and pneumococcus typing. Perhaps the major difficulty encountered was that of obtaining a satisfactory specimen of sputum (or other material) of suitable quality and quantity for typing. In the outlying laboratories less difficulty has been experienced as they are in much closer association with physicians and patients than is the State Laboratory, where over 90 per cent of the specimens come by mail. Roughly, one-half of the specimens sent for typing were 24 hours old on arrival, and most of the remainder were older. Among such old specimens, as is well known, pneumococci tend to be over-grown by other organisms and die out, thus making typing difficult if not impossible, and the isolation of pneumococci in pure culture very laborious and wasteful of time. Sputa received by ordinary mail during the warm months are especially difficult to type. Specimens of satisfactory quality and quantity should be specifically requested and if specimens cannot be brought by messenger they should be sent by special delivery mail.

To carry out pneumococcus typing on a large scale, a 24-hour service is, of course ideal, but is seldom obtained. In lieu of such an ideal service, arrangements have been made in the coöperating laboratories (in the areas organized for the serum treatment of cases of lobar pneumonia) to have all specimens arriving at night for typing, injected into mice at once in order that the typing may be done in the morning by the technician. Mice dying during the night should be placed in the refrigerator so that their peritoneal exudate will not be over-grown with *B. coli*. In most instances specimens arriving in the early evening have been typed that night.

At the State Laboratory the specimens for typing are taken from cases of all sorts of respiratory diseases, of many days' duration, so that with the majority of specimens the acute need of saving a few hours of time has not arisen. Even so, there was a sufficiently large number of specimens, from early cases of lobar pneumonia in which serum treatment was contemplated, to keep the laboratory force (2 workers) very busy during the pneumonia season, often working 12 to 16 hours a day during that period (January through April). An attempt was made to check every typing by cultures of the organism, obtained chiefly from the mouse's heart blood. In some instances as many as 5 different methods of typing have been done upon a specimen to ascertain the value of each method and afford data for a comparison of the methods. Typings are now reported to physicians as "Type I," "Type II," "Type III," "Group IV—type V," or whatever the sub-type happens to be, or "Group IV—type undetermined—advise another specimen."

When 2 types are obtained from a single specimen or cross-agglutination occurs, several things can be done to clear up the problem. Another specimen of sputum should be requested and the urine typed. From the clinical standpoint, cultures of blood and/or lung puncture, with the typing of any pneumococci found, will usually settle the matter.

The Krumwiede is a very valuable method of typing in that it is a great time saver. A negative Krumwiede is of no significance and neither a tentative nor final report of Group IV should be made upon this finding. A slight hazy ring or indefinite cloudiness at the line of juncture of the two fluids in the tube is not significant and should not be reported. About one-half of these "suggestive" reactions have later proved to be some other type. Seventy-five per cent of those sputa yielding a clear liquid for layering have been positive and about 25 per cent negative, for Types I, II, and III, some one of which was later found in the specimen.

The Sabin method is the most generally satisfactory and useful for accurate and rapid determination of type. Where pneumococci are seen in the mouse exudate but show no agglutination with Types I, II, or III sera, a tentative report of "Group IV" may be made and is nearly always correct. Considering Types I, II, and III only, the Sabin has failed while the tube agglutination has yielded a type, in about 1 of 75 instances. From observations made in various laboratories this proportion of failures might be expected to be greater, as most technicians do not stir the mixture of organisms and serum sufficiently before drying it.

Usually good pneumococci give a clear-cut result with the Sabin, and in such cases it has proved safe to assume the result correct. "Naturally occurring clumps" do sometimes occur, however, in one smear only and not in the others. In such cases experience is necessary for an accurate diagnosis. If there is any question as to the reading of the Sabin, it should be repeated. The reporting of indefinite results leads to error.

If the typing is being done out to the full 32 types, all should be tried on every specimen. At the State Laboratory during the rush season, we did not always adhere to this policy and were led into some difficulty with supposed cross-agglutinations which later turned out to be clearly one of the higher types not tried at the first typing. Subsequent checking with mouse's heart blood cultures confirmed these results. (Only those cross-agglutinations which were very definite in both types are recorded in the earlier part of this paper.)

A final report of "Group IV" should not be made until after the tube

agglutination method has been carried out, with incubation and frequent shaking of the tubes for 1, or preferably, 2 hours. Both undiluted and diluted sera should be set up. Freshly isolated organisms of high virulence occasionally do not agglutinate in diluted serum; sometimes they do not agglutinate in the undiluted, probably due to the " pre-zone " phenomena.

The tube agglutination method has not proved as sensitive as the Sabin and fewer positives were obtained with it than with the Sabin.

Considering Types I, II, and III only, as these are the predominating and the ones of greatest immediate or potential interest regarding the specific treatment of illness caused by them, it is found that among a total of 216 such types found, 9 errors were made. In 6 instances the report was " Group IV " and 1 was " No pneumococci found "; in 2 a Type III was reported as a Type I,—1 on the result of a " suggestive " Krumwiede (such as were later disregarded) and 1 on the result of a tube of agglutination. Those reported as " Group IV " and " No pneumococci found " yielded, with 1 exception, mixed mouse exudates and were finally typed from mouse's heart blood cultures or from colonies fished from cultures. One yielded a practically pure culture of Type I, both from the mouse's exudate and heart's blood culture, and had failed to give a positive result either by the Sabin or the tube agglutination method.

NOTE: We are much indebted to Edith Beckler, Director, Massachusetts State Bacteriological Laboratory, for the great aid and encouragement given us in carrying out this work. Likewise, Georgia Cooper of the New York City Laboratories has been very helpful in rendering valuable assistance in many ways. We wish to take this opportunity to express our thanks to both Miss Beckler and Miss Cooper for their many kindnesses.

Much of the diagnostic sera used throughout this work was obtained from Miss Cooper in New York City.

CONCLUSIONS

1. Pneumococcus typing is being requested by increasing numbers of physicians in Massachusetts.

2. During the past winter all 32 (Cooper) types of pneumococci excepting Types XXV and XXXII were found.

3. There was no especial geographical distribution evident of any of the types found.

4. Multiple cases of lobar pneumonia occurring in the same family at approximately the same time were very uncommon.

5. The Krumwiede, Sabin and tube agglutination methods of typing were and still are largely used and were found to be over 99 per cent accurate when definitely positive.

6. The Sabin method of typing has given a greater number of accurate positive typings in a shorter period of time than any other method studied, and is a method readily learned by technicians inexperienced in this work.

7. Of 789 specimens typed at the State Bacteriological Laboratory during the 11 months, September 1, 1931, to July 31, 1932, the type of pneumococcus found was checked in 94.6 per cent of the cases by a second method of typing or from a culture of the organism.

8. The various sub-types (Types IV to XXXII) were found more frequently during the 6 winter and spring months, December to May, than during the warmer months.

9. In view of the results to date, and until conclusive proof to the contrary is

obtained, it is felt that every type determination done by the Krumwiede, Sabin, or tube agglutination method should be checked by some other method of typing. Typing the organism obtained from cultures of the mouse heart's blood affords the most valuable means of checking.

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The Private Practitioner and Preventive Medicine

NOTHING is more difficult than to determine the beginning or the end of great events. All we can say today is that we have been the witnesses of the greatest epoch of advance in the science and art of medicine of which there is any record in the history of mankind. Not the 5th century B.C. in Greece, nor the great 13th century in Europe, not the Renaissance itself, can show a similar acquisition of new knowledge and its application as occurred in the hundred years following 1832. We can say even more: in no previous age has there been such growth of the conception of preventive medicine. . . .

When we reflect upon modern preventive medicine we naturally think of the change and improvement which has occurred in our external environment. We think of the great pioneers and their work for the provision of public and wholesome water supplies, for the isolation of the sick, the removal of nuisances, the reform of housing, drainage, sewerage and sewage treatment, the inspection of food, the Factory Acts, and vital statistics. Looking back we see what they did, and are more grateful than their contemporaries to Chadwick and Simon and Farr, to Bentham and the Mills, to Lord Grey, to Owen and Cobbett, to Lord Shaftsbury, and to the statesmen who took occasion by the hand. When we reflect again, our minds turn to the masters of physiology who illuminated the 19th century—to Helmholtz, Claude Bernard, and Carl Ludwig; they were followed by the masters of pathology, Virchow, Pasteur, and Koch. Perhaps we remember even the great clinicians who created and led professional opinion, Bright, Addison, and Hodgkin—the Guy's trinity—Gull and Jenner, Osler, Allbutt, and Barlow; and we wonder whether, after all, it is not the work of these eminent men which laid the foundations of prevention. Lastly, we are learning to see that preventive medicine owes an irredeemable debt to Edward Jenner, to the anesthetists Morton and Simpson, to the antiseptic principles of Lister, to the discoverers of the causes of disease, such as Pasteur, Koch, and Manson, and to the "immunizators" who followed them. . . . —Sir George Newman, *Brit. M. J.*, July 30, 1932, p. 190.