CUTANEOUS REACTIONS TO THE POLYSACCHARIDES AND PROTEINS OF PNEUMOCOCCUS IN LOBAR PNEUMONIA

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PLATE 32

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Clough, 1915, (1) employing a solution of alcohol precipitable protein derived from pneumococci, tested patients suffering from pneumonia by intradermal injections. There resulted in some instances a slightly elevated discrete papule surrounded by an indefinite zone of hyperemia; all of the reactions faded in 24 hours. Little or no difference was noted between the reactivity of patients with pneumonia and normal individuals, nor was the reaction affected by the stage of the disease in which the test was made. Weil, 1916, (2) prepared material from cultures of Type I pneumococcus. He allowed the organisms to autolyze at 37°C. for 2 hours, followed by heating at 60°C. for 1 hour. 0.1 cc. to 0.2 cc. of the supernatant fluid of this solution was used for skin tests. He obtained no reaction in patients tested during the acute phase of the disease. However, 1 to 21 days after crisis, injections produced a circumscribed erythema with slight infiltration at the point of puncture. A few cases did not react at any time; normal persons and patients suffering from other diseases gave no uniform response. In 1917, Steinfeld and Kolmer (3) carried out a series of skin tests, employing heat killed Type I, II, and III pneumococci. The reactions were read 48 hours after the injection; when positive the local lesion lasted 4 to 5 days. Six of 19 pneumonia patients gave positive reactions with one or another of the test organisms. No relation was noted between the type of pneumococcus eliciting the skin response and the causative organism of the disease. All of the positive reactions were obtained in patients tested after the crisis. Tests on control individuals were recorded as being negative. Weiss and Kolmer, 1918, (4) employed in a study of the cutaneous reaction of pneumonia patients, so-called pneumotoxin prepared by dissolving washed pneumococci in 2 per cent sodium choleate. This material was freshly made and standardized in terms of minimal lethal doses for guinea pigs. The reactions were read 48 hours after the injection. In adults positive reactions were obtained in 100 per cent of 31 acute cases. The period of reactivity ranged from the fifth day (2 days before crisis) to the thirteenth day (6 days after crisis) of disease. In children, tests were positive during the acute phase of illness and negative after recovery. No correlation was noted between a

positive test and the type of pneumococcus derived from the sputum. Bigelow, 1922, (5) prepared several varieties of test materials; they consisted of heat killed pneumococci, autolysates, and solutions. In some instances the material was derived from pooled cultures of Types I, II, III, and Group IV pneumococci; other preparations were prepared from organisms of a single type. In tests on 104 patients, he described two types of reaction. One of these was designated as type specific. It was described as an indurated papule surrounded by an areola, which reached its height 28 to 32 hours after inoculation. This form of response was best obtained with autolysates. It was considered by the author to be type specific since in 8 of 11 cases the material eliciting a positive reaction corresponded in type to that of the pneumococcus recovered from the patient. In 3 patients this correlation did not occur. The second or "common" reaction was obtained with most of the preparations. Lesions of this character reached their height in 18 hours and faded in 24 to 36 hours. It was obtained in 42.3 per cent of those tested and, in most instances, was elicited after crisis had taken place. Forty-five per cent of control individuals also gave this reaction. The author concludes that positive tests occur most commonly at the time during which antibodies would be present in greatest concentration. Herrold and Traut, 1927, (6) employed filtrates derived from a 5 day culture of an avirulent Type I pneumococcus. Reactions, when positive, appeared in about 12 hours and reached the maximum after 18 hours. Readings were made at the end of 24 hours. Of 38 patients acutely ill with pneumonia, 73 per cent failed to react, while only 15 per cent of normal persons, gave negative tests. Eight patients were repeatedly tested; one of these, negative at first, later became positive; another, originally positive, subsequently became negative; 2 were positive and 4 negative throughout the period of observation. They state that they found no relation between the material used for positive tests and the type of pneumococcus causing the infection.

From this review of the literature it will be seen that uniform results have not been obtained in pneumonia patients tested intracutaneously with pneumococcus products. It will be further noted that, with the exception of Clough (1) who used pneumococcus protein, the tests have been made with autolysates, heat killed organisms, solutions of pneumococci, and culture filtrates. Materials of this character are known to contain a variety of bacterial products, such as protein, carbohydrate, pneumotoxin, hemolysin, and the purpura producing substance, as well as other derivatives of enzyme action, in varying concentrations. Attention is directed to this point since the results reported in this paper demonstrate that the composition of the material used for injection influences the character of the reaction.

In the experiments presented in the present communication measured quantities of two distinct constituents of the pneumococcus cell

were separately employed for intradermal injection into patients acutely ill with and convalescent from lobar pneumonia. The material used for testing consisted of: 1. The purified, protein-free, carbohydrates of Types I, II, and III pneumococci,—the so-called soluble specific substances; 2. The somatic proteins of Pneumococcus. This material, the acetic acid precipitable fraction, consists largely of nucleo-protein. A description of both carbohydrate and protein is given further on. It has been shown by Avery and Heidelberger (7) that the pneumococcus carbohydrates are the type specific components; they react only in homologous type specific anti-sera, and, in purified form, are not antigenic. The protein fraction, on the other hand, is a common constituent of the pneumococcus species; antibodies elicited by immunization with it, react with protein derived from any strain of this organism.

In addition to the intradermal injection of the polysaccharides and protein, the experiments were supplemented by obtaining serum from the patients just prior to the skin test, and titrating for the presence or absence of antibodies reactive with the test solutions.

Material and Methods

Skin Testing Materials. 1. Soluble Specific Substances.—Type specific polysaccharides from each of three pneumococcus Types (I, II, and III) were employed. They were obtained in purified state according to the method employed in this laboratory by Heidelberger and Avery (8). As demonstrated by Heidelberger, Goebel, and Avery (9), these substances possess the chemical properties of complex sugars; they contain no phosphorous, no sulfur, and give none of the usual protein color tests. Type II and Type III substances are nitrogen-free. The Type I substance differs from the other two in containing nitrogen as an apparently essential component. The total nitrogen present in Type I is 5 per cent, half of which is present in the amino form. Despite the presence of nitrogen, the substance fails to give any of the protein color reactions. For skin tests, the polysaccharides were dissolved in *freshly* prepared physiological salt solution in such concentration that 0.1 cc. of solution contained 0.01 mgm. of specific polysaccharide. For purposes of sterility the solutions were heated at 100°C. for 10 minutes before being used.

2. Pneumococcus Protein.—The material was prepared according to the method described by Avery and Morgan (10). Cultures of an R strain of pneumococcus originally derived from Type II S organisms served as the source from which the protein was obtained. The preparations were filtered through Berkefeld filters and tested for sterility before being used for injection. The material was stand-

ardized by nitrogen determinations and diluted in fresh physiological salt solution so that 0.1 cc. of solution contained 0.01 mgm. of protein.

In each instance the material was injected in 0.1 cc. amounts into the skin on the flexor surface of the forearm.

Titration of Sera for Antibodies.—Blood, obtained from patients by venapuncture, was allowed to clot, centrifuged, and the clear serum pipetted off. Tests for precipitins reactive with carbohydrate and protein were separately carried out. 0.2 cc. serum diluted with 0.3 cc. physiological salt solution was mixed with 0.5 cc. of varying dilutions of the precipitinogens. Readings were made after the tubes had been allowed to incubate at 37°C. for 2 hours and then placed in the ice-box over night. It was found that type specific antibodies were more easily demonstrable by agglutination tests with the intact type specific cells. Consequently this test was more commonly used. 0.5 cc. of varying dilutions of serum was mixed with 0.5 cc. of heat killed organisms of each of Types I, II and III. The tubes were incubated at 37°C. for 2 hours and kept on ice over night. A positive reaction was detected by the presence of the characteristic disc formation.

On admission to the hospital patients were injected intradermally with Types I, II and III carbohydrate solutions, protein solution, and a control injection of fresh physiological salt solution. The tests were often repeated several times both during the acute phase of the illness and after crisis. Freshly prepared materials were always employed for injection. This precaution was considered to be of considerable importance since it was found that solutions which had been standing for several days often gave rise to immediate reactions which were deceptive. In addition to skin tests, serum obtained, in most instances at the time of intradermal injection, was titred for antibodies reactive with the carbohydrates and protein. Typing of the pneumococcus derived from the sputum of the tested patients was also carried out.

Cutaneous Reactions to Specific Polysaccharides

Observation on the skin reaction of nineteen individuals suffering from lobar pneumonia have been made following injection of 0.01 mgm. of each of the type specific polysaccharides. Classified on the basis of the pneumococcus type derived from the patient, the cases may be divided into: 11 cases of Type I infection; 3 of Type II; 2 of Atypical Type II; and 3 of Group IV. Unfortunately, no instances of Type III pneumococcus infection were available during the period of this investigation.*

* While this communication was in press a patient, convalescent from Type III pneumococcus pneumonia, has shown a positive reaction with the Type III polysaccharide. The patient's serum contained type-specific antibodies at the time of the positive test.

In the 11 cases of Type I infection, 10 reacted to Type I S carbohydrate and none to the Type II or III substances. Of the 3 Type II cases one reacted to Type II polysaccharide, whereas all three were negative to the sugars derived from Types I and III. The 2 atypical Type II and the 3 Group IV cases were entirely negative.

With regard to the time of appearance of a positive reaction, none of the cases before recovery reacted positively. Of the 11 cases in which a positive test was obtained, 10 reacted at the time of recovery. One patient, suffering from Type I pneumococcus pneumonia did not give a positive skin test until the twenty-sixth day after recovery from the acute phase of the illness. He had persistent fever, and evidence of pleurisy during this time and only after these signs of persistent infection began to subside did the skin test become positive.

A positive reaction, when obtained, was very striking and may be described as follows:

> Ten to twenty minutes after the intradermal inoculation, there appears at the site of injection a wheal-like swelling with intense white edema. Surrounding the wheal, a zone of erythema appears which becomes increasingly larger and more intense. The edges are irregular due to the "pseudopods" of erythema extending in different directions. The height of the reaction occurs between 30 and 60 minutes after the inoculation. (See Figs. 1 and 2.) Within another hour the acute phase has entirely faded; a gradual regression then takes place leaving a firm, pale, edematous area which may require 24 hours or longer to disappear completely. Reactions of this character have been found to be strictly type specific and to occur only with the polysaccharide corresponding to the serological type of the infecting organism. At the site of injection of the carbohydrates of heterologous types and of the salt solution, no reaction appeared. The "wheal and erythema" form of reaction, just described, differs strikingly from the delayed response elicited by the bacterial protein.

In testing the sera of patients, it was found that in all instances in which a positive skin reaction was elicited with the specific carbohydrates, agglutinins for the homologous type of pneumococcus and precipitins for the reacting polysaccharide were present. Furthermore, the time at which specific antibodies were demonstrable in the circulation has been coincident with the development of a positive skin reaction. However, the fact that individuals may possess circulating specific antibodies without responding to the intradermal injection of the homologous specific substance will be subsequently shown.

Ten of the 11 cases in which a definite skin response to the homolo-

gous specific polysaccharide was obtained, suffered from Type I pneumococcus infection. Eight of these cases were treated with Type I antipneumococcus horse serum in 100 cc. doses at six hour intervals until recovery. Regardless of the amount of serum administered the skin reaction did not become positive until the patient had clinically recovered. The investigations are not as yet sufficiently extensive to determine the exact relations between specific antibodies introduced therapeutically and the occurrence of a positive skin reaction. However, the results are suggestive that the production of a local response with the specific polysaccharide may, under certain conditions, be helpful in determining when sufficient serum treatment has been given. Studies are being continued in an attempt to determine this point.

The single instance of Type I infection, which failed to react to the Type I carbohydrate occurred in a patient who developed pneumococcus meningitis and died on the twentieth day of disease. This patient, after receiving 800 cc. of serum, possessed demonstrable circulating Type I antibodies, but gave only doubtful or negative skin test. Another individual, after recovering from the acute phase of the illness, continued to run a low grade fever and showed signs of pleurisy. He reacted positively to the Type I specific substance only after beginning cessation of infection. These two cases suggest that persistence of infection, even though specific antibodies are present, may inhibit the skin response.

In two patients suffering from Type I pneumococcus pneumonia, no serum was administered. In both instances a positive skin response was obtained after recovery, indicating that a positive test is not dependent upon the presence of therapeutic serum. Of three Type II cases included in this series one gave a typical positive reaction to the Type II specific polysaccharide. The reaction first appeared as the result of a test made the day after crisis; the patient's serum at this time contained Type II agglutinins and precipitins. The other two Type II patients failed to react even to 0.1 mgm. of specific substance. These failures occurred despite the fact that the blood serum, in each case, contained specific Type II antibodies and that all evidence of infection had completely subsided. As formerly noted the two atypical Type II and 3 Group IV cases of pneumococcus in-

fection gave no response at any time to the skin tests with the polysaccharides of Types I, II, or III.

In all patients, tests were repeated every few days during convalescence. Those patients in whom the reactions were positive on several occasions and subsequently became negative, ceased to react at the time of disappearance of specific antibodies from the circulation.

In Table I a protocol of five cases is given, which serves to show the time of appearance and duration of skin sensitivity in relation to both recovery of patient and occurrence of demonstrable specific antibodies in the circulation.

Cases Ka. and La. suffered from Type I pneumococcus infection and were treated with Type I antipneumococcus horse serum. Case Ka. is interesting in that skin sensitivity to Type I carbohydrate and circulating Type I antibodies have persisted for 127 days after recovery; observations on this patient are being continued. Case La. first reacted on the day after recovery; three days later his capacity to react had ceased coincident with the disappearance of specific agglutinins and precipitins. Patient Ca., the case of pneumococcus meningitis referred to above failed to give a definite positive reaction at any time. Cases St. and Mo. were instances of spontaneous recovery from Type I and Type II pneumococcus infections, respectively. They each gave typical responses after crisis and continued to do so, as long as demonstrable circulating antibodies were present. In the other patients, who gave a positive skin test, the same relations were found to hold as those presented in Table I.

The local reaction resulting from the intradermal injection of 0.01 mgm. of the type specific polysaccharides presented three distinctive characteristics; first, the carbohydrate eliciting a response was always homologous in type to that of the infecting organism; second, both the gross appearance of the lesion and the rapidity with which it developed and retrogressed were characteristic of the typical wheal and erythema type of reaction; third, the capacity to react, when evident, developed at the time of the patient's recovery, and was, in this group of cases, correlated with the presence of homologous type specific agglutinins and precipitins.

Cutaneous Reactions to Pneumococcus Protein

The local reaction resulting from the intradermal injection of 0.1 mgm. pneumococcus protein presented distinct differences from that

Skin Reactions with Pneumococcus Polysaccharides in Rel

Day of disease.....		1	2	3	4	5	6	7	8	9	10	11	12
Ka. Age 14	Agglutinins Precipitins						− −	+++ +					++ +
Type I	Skin Test.						neg.	pos. C					pos.
La. Age 34	Agglutinins Precipitins						− −	+ +			− −		
Type I	Skin Test.						neg.	pos. C	pos.		neg.		
Ca. Age 55	Agglutinins Precipitins				− −	++ +		+++ +					+++ +
Type I	Skin Test.				neg.	neg.	neg.	neg.					?
St. Age 33	Agglutinins Precipitins			− −									
Type I	Skin Test.			neg.				C				pos.	
Mo. Age 33	Agglutinins Precipitins				− −			++ +				+++ +	
Type II	Skin Test.				neg.			pos. C				pos.	

Agglutinin titre in terms of highest positive serum dilution. Agglutination characterized by disc formation.

− = Completely negative.
± = Doubtful agglutination in serum dilution of 1:2.
+ = Agglutination in serum dilution of 1:2.
++ = Agglutination in serum dilution of 1:10.
+++ = Agglutination in serum dilution of 1:20.
++++ = Agglutination in serum dilution of 1:40.

I

re of Circulating Specific Antibodies and Recovery of Patient

4	15	16	17	18	19	20	21	22	23	24	26	27	28	29	49	97	109	133
								++					+		+	+	+	+
								+					+		+	+	+	+
								pos.					pos.		pos.	pos.	pos.	pos.
									−									
									−									
									neg.									
						Death Meningitis												
			?															
+									+					±				
+									±					−				
ios.									pos.					?				
-++					++++										(47)			
+					+										−			
ios.					pos.										neg.			

Precipitin test = 0.3 cc. serum + 0.2 cc. salt solution + 0.5 cc. 1–40,000 dilution of polysaccharide.

Skin test:

pos. = positive reaction.

? = doubtful reaction.

neg. = negative reaction.

C = day of crisis.

TABLE II

Skin Reactions to Pneumococcus Proteins in Relation to Titre of Circulating Protein Precipitins and Recovery of Patient

Type I

Day of disease		Ka. age 15						Ga. age 17				*Co. age 26			
		6	7	12	22	29	36	3	4	6	13	4	16	23	36
Protein Precipitin Titre.	1–500	++	Crisis.	+	+++	+++	+++	+++	+++	Crisis.	+++	++	++±	++	+±
	1–1000	++		+±	++	++	++	++	+++		+++	+±	++	++	+±
	1–2000	+		+	++	++	+	+±	+++		+±	+	+	++	+
	1–4000	±		−	±	+	+	+	++		++	±	−	+	±
	1–8000	−		−	±	±	±	+	++		+	±	−	−	−
	1–16000	−		−	−	−	−	±	+		±	−	−	−	−
Skin test.		neg.		?	pos.	pos.	pos.	neg.	neg.		pos.	neg.	neg.	neg.	neg.

* Patient Co. had a prolonged illness followed by recovery.

Type II

Day of disease		Fl. age 33					Lo. age 24				
		4	8	10	20	27	2	5	*7	17	24
Protein Precipitin Titre.	1–500	0	Crisis.	+	+±	++	++	++	++	+++	+++
	1–1000	0		±	+	+	++	++	++	+++	+++
	1–2000	0		±	+	+	+++	+++	+±	+++	+++
	1–4000	0		±	±	±	+++	+++	+	++	++
	1–8000	0		−	−	−	+±	+	±	+	++
	1–16000	0		−	−	−	±	+	−	±	±
Skin test.		neg.		neg.	pos.	pos.	neg.	0	?	pos.	pos.

* Day of crisis.

Type Atypical II — Group IV

Day of disease		Wa. age 24				Ne. age 42				Ha. age 36	
		1	8	17	27	7	10	14	24	*4	12
Protein Precipitin Titre.	1-500	+±	Crisis.	+	+	++	Crisis.	++	+	+++	++
	1-1000	+		+	+	++		+±	+	+++	++
	1-2000	+		+	+	+±		+	±	++	+±
	1-4000	±		±	−	+		±	−	+	+
	1-8000	−		−	−	±		−	−	+	−
	1-16000	−		−		−		−	−	−	−
Skin test.		neg.		pos.	pos.	neg.		pos.	pos.	pos.	pos.

* Day of crisis.

Precipitin Tests:

+++ = precipitate at bottom of tube with faintly cloudy supernatant fluid.
++ = slight precipitate with cloudy supernatant fluid.
+ = cloudy fluid.
± = faintly cloudy fluid.
− = completely negative.
0 = not done.

Skin Tests:

pos. = Typical delayed reaction greater than 1 cm. in diameter.
? = Reaction 0.5 − 1.0 cm. in diameter.
neg. = No reaction.
0 = Not done.

obtained with the carbohydrates. Of twelve patients tested while acutely ill, all failed to react. In eight individuals repeated injections were made both before and after recovery. Seven of them gave positive tests after crisis, and also with each repetition of the test during convalescence. These patients have not been retested since discharge from the hospital.

A test, when positive, developed slowly as compared with the reaction elicited by the carbohydrates. In 6 to 8 hours there appeared a small, dark red, circumscribed lesion, about 0.5 cm. in diameter. It gradually increased in size until a maximum was reached in 18 to 24 hours. Readings were recorded at this time. (See Fig. 3.) Regression which began after 36 to 48 hours, usually proceded slowly, and 3 to 4 days often were required for complete disappearance. When at its height, the lesion varied from 1 to 5 cm. in diameter; it consisted of a small central papule, dark red in color, surrounded by a bright pink erythema; the edges faded gradually into normal skin; slight tenderness was some times present and the local temperature often seemed to be increased. The protein reactions were similar in many respects to the tuberculin response. That this type of reaction, in contrast to the response induced by polysaccharides, was unrelated to the type of pneumococcus causing infection is borne out by the fact that of the 7 patients, in whom positive tests were obtained, 2 had Type I pneumonia, 2 Type II, 2 Atypical Type II, and 1 Group IV.

In determining the presence of pneumococcus protein precipitins, it was found that the sera of all the patients possessed antibodies reactive with this test material. The titre ranged from 1:2,000 to 1:16,000 in the different cases. However, in a single individual, variations in amount of precipitins occurring coincident with the progress of the disease were not sufficiently striking nor constant to be considered of significance. In Table II, the results of the protein skin tests are given for those cases in which repeated injections were made.

Table II shows the relation of the development of skin sensitivity both to the time of recovery from infection and to the titre of anti-protein antibodies with serum. From the data it appears that the protein sensitiveness develops after crisis, but, as contrasted with the

reaction to the carbohydrate, is unrelated to the quantity of precipitins present in the circulation.

The presence of antibodies to pneumococcus protein in the serum of human beings, has not, as a search of the literature reveals, been the subject of previous investigation. The possible significance of their occurrence is a part of this, as yet uncompleted, study. In addition to the cases cited above, the sera of 13 other pneumonia patients have been tested at frequent intervals after admission to the hospital until discharge. They were all found to possess in their serum protein precipitins in concentrations comparable to those recorded in Table II. The study of the anti-protein antibodies is being continued and a more complete report will be made in a later communication.

DISCUSSION

Although the observations reported in this paper on a relatively small number of patients represent an investigation which is, as yet, incomplete, sufficiently definite results have been obtained to warrant presentation. It has been shown that pneumococcus polysaccharides, when injected intradermally into pneumonia patients after crisis, can bring about in some instances, a local reaction. The cutaneous response, when obtained, was always elicited by the carbohydrate homologous to the type of pneumococcus causing infection in the patient. A patient's capacity to react became manifest coincident with recovery from infection. Furthermore, skin sensitivity has been found to parallel closely the presence of circulating type specific antibodies. The two phenomena have been found to appear at about the same time, to persist for a similar period, and to disappear at about the same stage of convalescence. However, the mere presence of type specific antibodies in the circulation is not the only factor necessary for the excitation of a skin response. The fatal case complicated by pneumococcus meningitis possessed type specific agglutinins in high titre but at no time could a definite skin response be obtained. Further investigation on a larger number of cases is necessary before the underlying mechanism can be fully interpreted. However, undetermined as the problem at the present may be, it is an interesting fact that these bacterial sugars, *protein-free*, and belonging

to that group of immunologically specific substances known as haptens, are capable of producing a reaction in the skin of convalescents from pneumococcus pneumonia. The character of the skin response incited by the polysaccharides is unique in that it is urticarial-like in appearance and runs its course in 1 to 2 hours.

The reaction caused by pneumococcus protein, on the other hand, is similar both in appearance and evolution to that evoked by tuberculin. The protein reactions, when positive, reached the maximum intensity about 24 hours after injection and some times required 3 to 4 days to subside completely. Furthermore, a patient's capacity to react to protein has no relation to the type of pneumococcus causing the infection. Sufficient observations on the presence and quantitative variations of anti-protein antibodies have not yet been made to justify final conclusions. In the instances reported in this paper, antiprotein precipitins were found in all cases both before and after crisis. In any single individual the titre did not markedly vary during the course of disease, nor did it appear to influence skin sensitivity.

The data presented in this paper represents observations made in the course of lobar pneumonia. Similar tests on normal individuals and patients suffering from other diseases are being carried out and the results will be reported in a subsequent paper.

CONCLUSIONS

I. a. Pneumococcus polysaccharides, when injected intradermally into patients convalescent from pneumonia, are capable of eliciting a response. The polysaccharide inducing a cutaneous reaction was found always to be homologous in type to that of the pneumococcus causing the infection.

b. The character of the reaction incited by the protein-free bacterial sugars is of the immediate wheal and erythema type.

c. A patient's capacity to react was found to be intimately associated both with recovery from infection and with the presence of type specific antibodies in the circulating blood.

II. a. The so-called nucleo-protein of pneumococcus, when injected intradermally, also causes a local cutaneous reaction in patients during convalescence from lobar pneumonia.

b. The local lesion resulting from the injection of protein is tuberculin-like in character, and differs from that evoked by the type-specific polysaccharides in gross appearance, time of development, and duration.

c. Individuals, acutely ill with and convalescent from pneumococcus pneumonia, possess in their circulating blood, precipitins reactive with pneumococcus protein. In the observations recorded, the concentration of anti-protein antibodies in the blood serum did not seem to influence the patient's capacity to react to intradermal injection of the protein.

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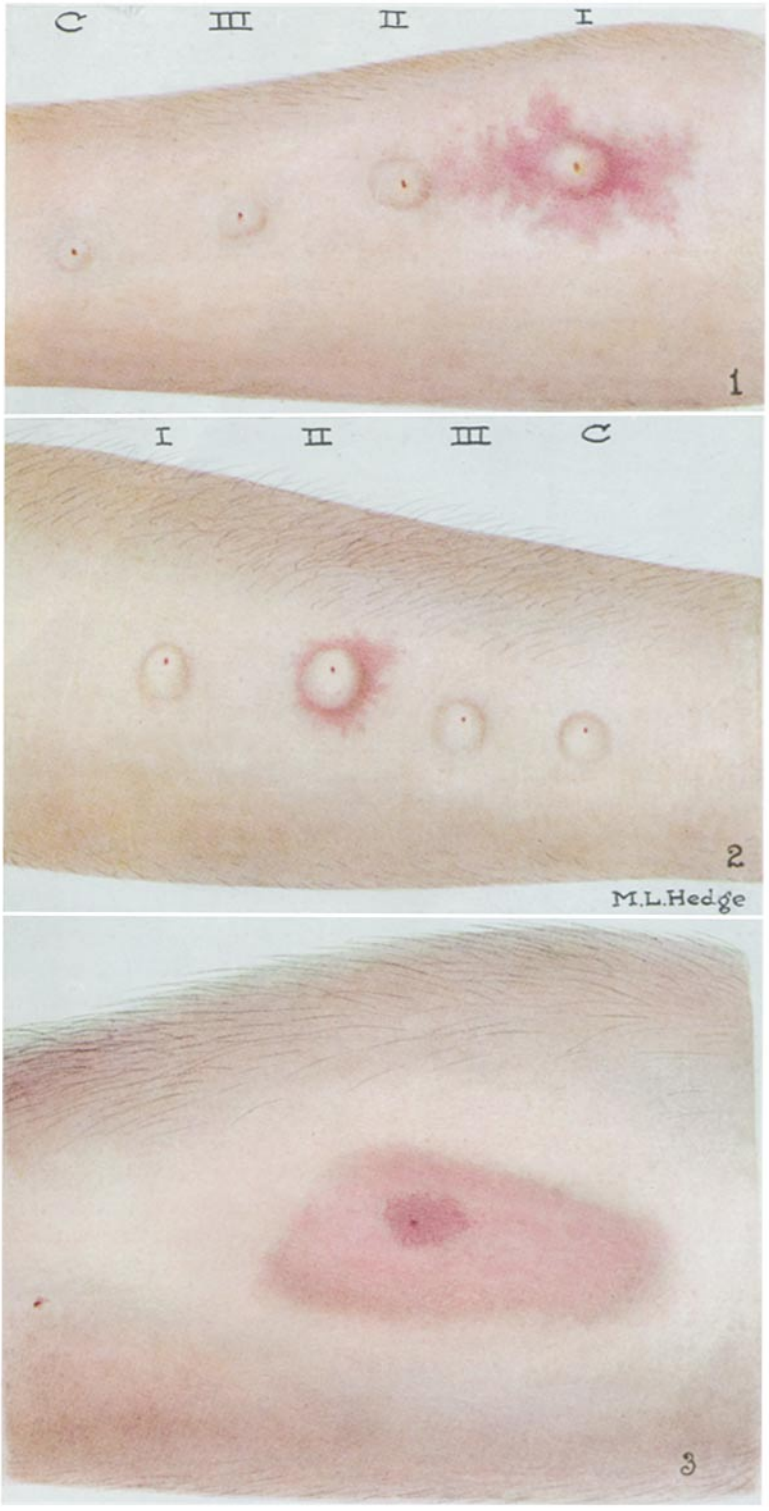
EXPLANATION OF PLATE 32

FIG. 1. Cutaneous reaction 30 minutes after the injection of 0.01 mgm. of Type I polysaccharide in a patient convalescent from Type I pneumococcus pneumonia. This illustrates the immediate wheal and erythema response to pneumococcus polysaccharide. Specific substances of Types II and III, and salt solution are negative. Roman numerals I, II, and III, designate the site of injection of Types I, II, and III carbohydrates; C represents the site of injection of salt solution. One-half natural size.

FIG. 2. Cutaneous reaction 30 minutes after the injection of 0.01 mgm. of Type II polysaccharide in a patient convalescent from Type II pneumococcus pneumonia. Specific substances of Types I and III, and salt solution are negative. Roman numerals and C serve the same purpose as in Fig. 1. One-half natural size.

FIG. 3. Cutaneous reaction 24 hours after injection produced by 0.01 mgm. of pneumococcus protein. This illustrates the delayed tuberculin-like response to pneumococcus protein. Four-fifths natural size.



(Tillett and Francis: Cutaneous reactions in lobar pneumonia)