The Journal of the American Medical Association

Published under the Auspices of the Board of Trustees

VOL. XLIX.

CHICAGO, ILLINOIS, NOVEMBER 30, 1907.

No. 22.

Original Articles

FURTHER OBSERVATIONS ON OPSONINS IN NORMAL AND PATHOLOGIC SERA.*

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The following observations represent a summary of most of the work which has been done under my direction since June, 1906. The more definitely planned portion, carried on in Professor Hiss' laboratory at the College of Physicians and Surgeons (Columbia) from Dec. 1, 1906, to April 30, 1907, was made possible by a grant from the Commission for Investigating Respiratory Diseases of the New York Department of Health, to whom I wish here to acknowledge my sincere thanks. The remainder comes from the Lederle Laboratories and from the laboratory of the Private Hospital Association. I have also included some of the results of Dr. Krumwiede's and my observations at the French Hospital, a detailed report of which will be published elsewhere. Drs. Bradley, Hopkins, Avery and Young have performed the details of the technic, and for five months we have had the advantage of Dr. Chas. E. North's direction, advice and skilled assistance. I take pleasure in acknowledging very helpful suggestions and assistance from Professors Prudden and Hiss, from Dr. H. H. Mason, and my fellow-worker, Dr. N. E. Ditman.

The technic employed was essentially that of Wright. Its accuracy depends on several factors, all of which vary within rather wide limits.

VARIATIONS IN SERA.

Figure 1 illustrates the variations in the opsonic indices to staphylococci and to tubercle bacilli in three healthy adults whose sera furnished the laboratory normals at the Lederle Laboratories during February, March and April. Similar variations occurred in the opsonic indices of supposedly normal sera to these two germs throughout our studies and to colon bacilli, streptococci and to pneumococci. Of the two double curves for each sera the upper pictures the worker's indices estimated to the average of his own and two or more other sera, the lower that of the worker's indices figured on the other's sera alone. The lower curve naturally exhibits the more striking fluctuations. There is noticeably less variation in the curves of the tubercle bacillus than in those of the staphylococcus, as has been already noted by Wright and others.

We attempted to determine whether any variations in the counts of duplicate sera could be attributed to the

method of obtaining the samples of blood. We compared sera in triplicate obtained by squeezing the finger vigorously, with sera in triplicate obtained from a large, deep prick furnishing free drops of blood without any squeezing. There was quite as much variation in the phagocytic counts of the triplicate specimens as in the two groups. We, therefore, concluded that such manipulation is not a fruitful source of error and certainly can not be measured by the Wright method. Another experiment devised to determine whether any differences could be detected in specimens of blood taken from different parts of the body, ear, finger, toe, etc., furnished a similar result.

To determine differences dependent on transportation, we sent duplicate sera through the mail and had them returned to the laboratory. They were then compared with other duplicates which had been left in the laboratory at the room temperature and still others kept in the icebox. The last showed the highest phagocytic count; the sera sent farthest the next, those left at room temperature the lowest.

We compared many times 1 to 10 specimens of duplicate sera to staphylococci, streptococci, tubercle bacilli and other organisms in order to determine the percentage of variation in the phagocytic counts and corresponding indices. The variations were not less than 30 per cent., and the counts for colon and tubercle bacilli and for streptococci varied even more strikingly than for staphylococci. By making use of the relative percentage of phagocytizing and non-phagocytizing cells (following Simon) we were unable to narrow materially the variations. This percentage in general corresponded to the opsonic indices.

VARIATIONS IN CORPUSCLES.

On several occasions I have called attention to my belief that the source of the leucocytes which form the corpuscular cream was responsible for marked variations in the opsonic indices. We found that the number of corpuscles at different layers of the cream varied, as shown by the figures in Table 1 on page 1817.

Despite these variations in the numbers of polymorphonuclears at different layers of the cream, Table 2 and the chart in Figure 2 make it evident that such variations influence the phagocytic counts but little, provided that the leucocytes are obtained from the same source.

With tubercle bacilli a cream of half thickness phagocytes but 10 to 20 per cent. more than the usual cream. If, however, the leucocytes are obtained from different sources the variations are more striking.

In Figure 3 and Table 3 the leucocytes taken February 26 from J. G., a patient with pulmonary tuberculosis and chorioiditis, ingested from 40 to 75 per cent. less bacilli than those from a supposedly normal individual. This is graphically represented by the curve at the left (Fig. 3, Q). The curve at the right (Fig.

* Presented to the Association of American Physicians, at Washington, May 8, 1907.

Fig. 1.—Opsonic indices of three normal sera. Solid line represents variations to staphylococcus; dotted lines, variations to tubercle bacillus.

Fig. 2.—(O) Opsonic indices estimated. Solid line, usual leucocytic cream (21,800 polynuclears to 1 c.mm.); crossed line, usual cream diluted with equal volume of red corpuscular remains at bottom of centrifuge tube (9,900 polynuclears to 1 c.mm.). (P) Ratio in per cent. of phagocytosis by normal leucocytes: (a) usual cream; (b) diluted cream.

Fig. 3.—Crossed line, patient's leucocytes (J. G.), tuberculosis of lungs and chorioiditis. Solid line, normal leucocytes (H. M.). (Q) Ratio in per cent. of patient's leucocytes as compared with normal leucocytes. (R) Tuberculo-opsonic indices obtained with two sets of leucocytes.

Fig. 4.—Crossed line, patient's leucocytes (J. G.), tuberculosis of lungs and chorioiditis. Solid line, normal leucocytes (H. M.). (X) Ratio in per cent. of patient's leucocytes as compared with normal leucocytes. (Y) Tuberculo-opsonic indices obtained with two sets of leucocytes.

TABLE 1.—FOUR LEUCOCYTIC CREAM COUNTS.

Date.	Before Titration.			In the Middle of Titration.			Directly After Titration.		
	Total Leuc. in 1 c.mm.	Per cent. of Polys.	Total Polys. in 1 c.mm.	Total Leuc. in 1 c.mm.	Per cent. of Polys.	Total Polys. in 1 c.mm.	Total Leuc. in 1 c.mm.	Per cent. of Polys.	Total Polys. in 1 c.mm.
Mar. 22.	30,000	...	...	20,000	...	...	...	...	...
Mar. 23.	30,000	74.4	22,320	32,000	87.5	28,000	24,975	65.0	16,233
Mar. 25.	31,000	...	...	26,520	...	...	...	...	...
Apr. 26.	35,000	...	...	30,200	...	...	31,000	...	...

TABLE 2.

Serum.	Date.	Phagocytic Index.		Ratio in percentage	Opsonic Index.	
		Whole Cream, 21,800.	Diluted Cream, 9,300.		Whole Cream.	Diluted Cream.
N.—Peritoneal Tb. . . .	Apr. 24.	129	160	1.23	0.79	0.85
A.—Normal	Apr. 25.	162	189	1.16	1.15	1.00
J. G.—Tb. of lungs and chorioid.	Apr. 23.	155	182	1.17	0.95	0.96
C. A.—Tb. chorioid and glands.	Apr. 25.	121	138	1.14	0.74	0.71

TABLE 3.

Patient Whose Leucocytes Were Used. Diagnosis. Condition.	Date.	Phagocytic Count; 200 Cells.		Ratio in percentage.	Opsonic Index.		Serum.	No. of Leucocytes in 1 c.mm. of Leucocytic Cream.		Inverse ratio in percentage.	Organism.	White Count.
		Normal Leuco-cytes.	Patient's Leuco-cytes.		Normal Leuco-cytes.	Patient's Leuco-cytes.		Normal Leuco-cytes.	Patient's Leuco-cytes.			
		H. H. M.	J. G.		H. H. M.	J. G.		H. H. M.	J. G.			
J. G.—Tb. of lungs and chorioiditis.	Feb. 26.	406	174	0.43	1.32	1.45	J. G.—Tb. of lungs and chorioiditis. C. O.—Tb. Chorioid. C. A.—Tb. chorioid and glands. M. D.—Tb. hip and sinus. F. F.—Tb. hip and sinus. Normal: H. H. M	52,000	85,000	0.61	Tubercle bacilli.	12,300
		325	173	0.52	1.06	1.45						
		227	138	0.60	0.74	1.15						
		310	136	0.43	1.00	1.10						
		541	127	0.24	1.75	1.06						
		307	120	0.39	1.00	1.00						
												4,600

TABLE 4.

Name of Patient Whose Leucocytes Were Used. Diagnosis. Condition.	Date.	Phagocytic Count; 100 Cells.		Ratio in percentage.	Opsonic Index.		Serum.	No. of Polynuclears in 1 c.mm. of Leucocytic Cream.		Inverse ratio in percentage.	Organism.
		Normal Leuco-cytes.	Patient's Leuco-cytes.		Normal Leuco-cytes.	Patient's Leuco-cytes.		Normal Leuco-cytes.	Patient's Leuco-cytes.		
		H. H. M.	J. G.		H. H. M.	J. G.		H. H. M.	J. G.		
J. G.—Tb. of lungs and chorioiditis.	Apr. 18.	151	90	0.59	1.26	1.25	J. G.—Tb. of lungs and chorioiditis. C. O.—Tb. chorioiditis. C. A.—Tb. Chorioiditis and glands. F. R.—Tb. lungs. M. D.—Tb. hip and sinus. F. F.—Tb. hip and sinus. L. N.—Tb. hip and sinus. M. L.—Sinus. H. H. M.—Normal. Normals: A. N. H. Average normals.	25,280	30,855	0.81	Tubercle bacilli.
		97	57	0.58	0.81	0.79					
		105	71	0.67	0.88	0.98					
		66	55	0.83	0.55	0.76					
		152	73	0.48	1.27	1.01					
		142	80	0.56	1.19	1.11					
		186	101	0.54	1.56	1.40					
		88	47	0.53	0.73	0.65					
		132	84	0.63	1.10	1.16					
		112	75	0.66	0.94	1.04					
		139	75	0.53	1.17	1.04					
		106	68	0.64	0.89	0.94					
		119	72	0.60	1.00	1.00					

TABLE 5.

Patient Whose Leucocytes Were Used. Diagnosis. Condition.	Date.	Phagocytic Count; 50 Cells.		Ratio in percentage.	Opsonic Index.		Serum.
		Normal Leucocytes.	Patient's Leucocytes.		Normal Leucocytes.	Patient's Leucocytes.	
		N. D.	M.		N. D.	M.	
M.—Chronic acne staph. Treated with x-ray.	Jan. 25.	175	119	0.68	1.43	1.00	M.—Chronic acne staph W.—Normal.
		122	117	0.95	1.00	1.00	
M.—Chronic acne staph. Treated with x-ray.	Jan. 25.	N.	M.		N.	M.	M.—Chronic acne staph. W.—Normal.
		169	119	0.70	1.43	1.00	
N. D.—Normal	Jan. 25.	118	117	0.99	1.00	1.00	M.—Chronic acne staph. W.—Normal.
		N. D.	N.		N. D.	N.	
N.—Normal	Jan. 25.	175	169	0.96	1.43	1.43	M.—Chronic acne staph. W.—Normal.
		122	118	0.96	1.00	1.00	

3, R) exhibits quite striking variations in the tuberculo-opsonic index depending on which leucocytes were employed.

In Figure 4 and Table 4 the experiment was repeated nearly two months later, during which time the patient had decidedly improved under inoculations of tuberculin. There was still between 18 to 52 per cent. less phagocytic power of the patient's leucocytes. The opsonic indices (Fig. 4, Y), though not identical, varied but little.

treatment. In the chart in Figure 6 the same patient's leucocytes are compared three weeks later with leucocytes from a case of impetigo and with leucocytes from a supposedly normal individual. In the chart in Figure 7 they are compared with leucocytes from the same normal two weeks later. Figure 8 represents the same conditions as Figure 6, but nearly two months later.

Dr. Krumwiede and I, while studying streptococcus and pneumococcus infections at the French Hospital, noted similar variations. Although the number of our

Fig. 5.—Solid lines, normal (N. D.) leucocytes; crossed lines, normal (N.) leucocytes; dotted lines, patient's (M.) leucocytes. (E) Ratio in per cent. of patient's leucocytes as compared with normal leucocytes. (F) Staphylo-opsonic indices obtained from two sets of leucocytes. (G) Ratio in per cent. of patient's leucocytes as compared with normal leucocytes. (H) Staphylo-opsonic indices obtained from two sets of leucocytes. (I) Ratio in per cent. of leucocytes from one normal individual as compared with leucocytes from another normal. (J) Staphylo-opsonic indices obtained from two sets of leucocytes.

Fig. 6.—Solid lines, normal (N.) leucocytes; dotted lines, patient's (M.) leucocytes; crossed lines, patient's (H. P.) leucocytes, thirty days after inoculation. (A) Dotted line, ratio in per cent. of patient's leucocytes as compared with normal leucocytes. Patient with chronic acne. Crossed line, ratio in per cent. of patient's leucocytes as compared with normal leucocytes. Patient with chronic acne, after inoculation. (B) Staphylo-opsonic indices obtained with two sets of leucocytes. (C) Ratio in per cent. of two patients' leucocytes as compared with normal leucocytes. (D) Staphylo-opsonic indices obtained with two sets of leucocytes.

Fig. 7.—Dotted lines, patient's (M.) leucocytes much improved; solid lines, normal (N.) leucocytes. (A) Ratio in per cent. of patient's leucocytes as compared with normal leucocytes. (B) Staphylo-opsonic indices obtained with two sets of leucocytes.

A similar result is shown by the next four charts and tables. In the chart in Figure 5 two sets of supposedly normal leucocytes are compared with the leucocytes from a patient with chronic acne who had just begun x-ray

observations was very limited, we found in general that during the height of the infection the phagocytic power of the patient's corpuscles, as compared with that of corpuscles from supposedly normal individuals, was diminished and more noticeably so than the opsonic index of the serum, that during recovery this phagocytic power rose well above the normal and again distanced the opsonic index in the serum, and that during convalescence the phagocytic power of the leucocytes and the opsonic index gradually fell to normal or just below.¹

These tests, though suggestive, do not, of course, merit positive conclusions. The method is not sufficiently accurate, the observations are too few, the leucocytes were not washed carefully enough and the creams were not accurately balanced. It is, however, fair to state that the opsonic indices of sera vary with the source of the leucocytes and sometimes even when the sources are two or more apparently normal individuals and that the leucocytes from patients the subjects of bacterial in-

TABLE 6.

Patient Whose Leucocytes Were Used. Diagnosis. Condition.	Date.	Phagocytic Count; 50 Cells.			Ratio in percentage.		Opsonic Index.			Serum.	Organism.
		Normal Leucocytes.	Patient's Leucocytes.	Patient's Leucocytes.	Patient's Leucocytes.	Patient's Leucocytes.	Normal Leucocytes.	Patient's Leucocytes.	Patient's Leucocytes.		
		N.	M.	H. P.	M.	H. P.	N.	M.	H. P.		
M.—Chronic acne staph. Treated with x-ray.	Feb. 15.	154	112	177	0.72	1.15	1.06	0.85	1.24	M.—Chronic acne staph	Staph. aureus. (P.)
		113	89	131	0.78	1.16	0.78	0.67	0.92	H. P —Impetigo with paronychia of toes and fingers; staph. aureus.	
		162	108	129	0.67	0.79	1.12	0.82	0.91	Normals:	
		138	112	146	0.81	1.06	0.95	0.85	1.03	W.	
		135	177	150	1.31	1.11	0.93	1.34	1.06	A.	
		145	132	142	0.92	0.97	1.00	1.00	1.00	N.	
Average normals.											

TABLE 7.

Patient Whose Leucocytes Were Used. Diagnosis. Condition.	Date.	Phagocytic Count; 100 Cells.		Ratio in percentage.	Opsonic Index.		Serum.	Organism.
		Normal Leucocytes.	Patient's Leucocytes.		Normal Leucocytes.	Patient's Leucocytes.		
		N.	M.		N.	M.		
M.—Chronic acne staph. Treated with x-ray. Much improved.	Mar. 1.	241	378	1.56	0.79	0.95	M.—Chronic acne staph.	Staph. M.
		329	420	1.27	1.08	1.05	Normals:	
		292	414	1.41	0.96	1.03	A.	
		290	367	1.26	0.95	0.92	N.	
							H.	
		303	400	1.32	1.00	1.00	Average normals.	

TABLE 8.

Patient Whose Leucocytes Were Used. Diagnosis. Condition.	Date.	Phagocytic Count: 50 Cells.			Ratio in percentage		Opsonic Index.			Serum.	No. of Polynuclears in 1 c.mm of Leuco- cytic Cream.			Inverse Ratio in percentage.		Organism.			
		Normal Leucocytes.	Patient's Leucocytes.	Patient's Leucocytes.	Patient's Leucocytes.	Patient's Leucocytes.	Normal Leucocytes	Patient's Leucocytes.	Patient's Leucocytes.		Normal Leucocytes.	Patient's Leucocytes.	Patient's Leucocytes.	Normal Leucocytes.	Patient's Leucocytes.		Patient's Leucocytes.	M.	H. P.
N.	M.	H. P.	N.	H. P.	N	M.	H. P.	N.	M.	H. P.	M.	H. P.							
M.—Chronic acne staph. Treated with x-rays.	Apr. 22.	199	165	207	0.82	1.04	1.28	1.11	1.25	M.—Chr. acne staph.	16,940	17,160	35,600	0.98	0.47	Staph. aureus (P.)			
		142	148	237	1.04	1.66	0.90	1.00	1.43	M. S.—Chr. acne and comedones. H. P.—Impetigo with paronychia of toes and fingers. Staph. aureus.									
		185	159	270	0.85	1.45	1.19	1.07	1.63										
		161	160	140	0.99	0.86	1.03	1.08	0.84		Normals:								
		162	131	171	0.80	1.05	1.04	0.88	1.03	W.									
		143	153	186	1.06	1.30	0.91	1.03	1.12	A.									
										N.									
		155	148	165	0.94	1.06	1.00	1.00	1.00	Average normals.

Fig. 8.—Dotted lines, patient's (M.) leucocytes, cured; crossed lines, patient's (H. P.) leucocytes, acne; solid lines, normal (N.) leucocytes. (A) Ratio in per cent. of patient's leucocytes as compared with normal leucocytes. Patient cured (M.). Patient, chronic acne, (H. P.) seven days after inoculation. (B) Staphylo-opsonic indices obtained with two sets of leucocytes. (C) Ratio in per cent. of two patients' leucocytes as compared with normal leucocytes. (D) Staphylo-opsonic indices obtained with two sets of leucocytes.

eral of the toes on both feet showed a suppurative inflammation with scanty purulent discharge from beneath the wall of the nail, with redness, swelling and soreness. Fairly uniform improvement under local (chiefly antiseptic) treatment. At one time the lesions on the face had all disappeared and the toes seemed almost in normal condition, though there was still some redness and some remaining infiltration of the nail-wall in several places. Evidently the morbid tendency had not been overcome." The patient was referred to me October 2 for investigation and treatment. Patient's home duties were so urgent and her home so distant from the city that it was impossible for her to be seen at any regular intervals. Her opsonic curve is shown in Figure 10. I was unable to produce much more than a transitory improvement in the condition of her face; the slight improvement was not sufficient to outweigh the effect of such inimical factors as fatigue, or cold weather, and for the toes much walking and the wearing of rubbers. The intervals of inoculation were not frequent enough either to retain the improvement, to keep up the opsonic index, or to prevent the marked drop of the latter and the corresponding aggravation of the lesions during menstruation.

One case of furunculosis in a young woman with a high opsonic index was cured by general tonic treatment and catharsis and without inoculation. With especial attention to her skin and improved hygienic conditions she has remained well for several months.

cilli were above normal, that to one staphylococcus below normal. The other staphylococcus would not phagocyte when activated with normal serum, even after several attempts on Dr. North's part to modify its virulence by cultivation. During the progress of these investigations Dr. W. T. Bull adopted my suggestion of employing fresh horse serum to dress a part of the wound. It unquestionably stimulated some improvement, but was too painful and annoying to the patient. Shortly before the patient died a dose of 300 millions staphylococci were administered without effect.

Reports on four striking streptococcus infections which we have studied follow:

CASE 3.—*History*.—J. B. M., male, aged 30, entered the New York Hospital, on the service of Dr. S. W. Lambert, Oct. 22, 1906. He had septicemia, ulcerative endocarditis and double pleurisy with effusion. Blood cultures were made twice and the *Streptococcus tenuis* found. Leucocytes varied from ten to twelve thousand. Septic temperature, 99 to 103 F. Opsonic index to streptococcus from blood October 31 was 0.46. Died November 2 before vaccine was completed. Not inoculated.

CASE 4.—*History*.—M. V., female, aged 23, was seen with Dr. W. S. Bryant, April 10, 1907, at the French Hospital. She gave a history of cold for seven days, earache for three days. A right mastoid operation was performed April 5.

Fig. 10.—Case 2, Miss H. P. L., impetigo of face, paronychia of toes and fingers, showing opsonic determinations, etc.

Another case of furunculosis in a young adult male was cured by the internal administration of yeast, general tonics and a trip to the woods. He remained well for several months. Two small boils appeared recently, but he improved promptly on yeast and tonics so that he required no inoculation. His staphylococcus-opsonic index was below and rose above normal after the administration of yeast.

A carbuncle (*Staphylococcus aureus*) which developed on the back of my neck April 26 was treated surgically. As it seemed to resolve very slowly, I took 200 millions *Staphylococcus aureus* (stock vaccine) May 1 and 300 millions *Staphylococcus aureus* (from the lesion itself) May 3. Dr. J. B. Walker, who incised and treated the carbuncle, tells me that the progress after the inoculations was strikingly rapid. My opsonic index ranged between 0.80 and 0.90 and was not raised by inoculation.

A very extensive sloughing necrotic ulcer covering more than one-half of patient's trunk furnished four organisms, a colon bacillus, a short unknown bacillus and two staphylococci. The opsonic indices to both ba-

lood culture showed streptococcus (Dr. Krumwiede). There was extensive otitis; very little pus. On April 6 the wound sloughed. April 7 and 8 it was dressed with horse serum and the sloughing stopped. April 10 she was inoculated with 30,000,000 streptococci (from patient A. R. in Case 5). April 11 second operation, with excision of right internal jugular, curettage of lateral sinus. April 15 she was inoculated with 60,000,000 streptococci from the same source. Patient became delirious. Metastases developed in the left shoulder and right wrist. Died April 16 from septicemia. Autopsy on April 17 showed a meningitis. Inoculation gave no appreciable effect on clinical condition nor on opsonic index, which remained normal (Fig. 11).

CASE 5.—*History*.—A. R., male, aged 20, entered my service in the French Hospital Feb. 15, 1907. No antecedent sore throat, venereal or other illness. For four or five days before admission had had pain in left shoulder, indigestion, vomiting and diarrhea. Three days before had pain in right knee and fever. Two days before had a slight nose bleed and chilly feelings.

Examination.—Patient was cyanotic, with flushed cheeks and eyes bright. Conjunctivæ were injected, the lips dry and thickly-coated tongue. There was swelling with edema above and to the inside of the left shoulder joint and over lower part

of neck. Left arm was held immobile. Attempt at motion was apparently very painful and was resisted by patient. The right knee was enlarged and tender and there was fluid in joint. Abdomen was tympanitic, spleen palpable just below costal margin and soft. Liver was slightly enlarged, edge palpable. There was nothing abnormal in rectum. No discharge from urethra. Calomel, 1/10 gr., was given every ten minutes for ten doses.

Fig. 11.—Case 4, M. V., streptococcus septicemia, meningitis; inoculated with streptococcus from Case 5 (A. R.); showing temperature chart and opsonic index.

but restless sleep. Liquids were given. Aspirin was substituted for salicylate of soda.

February 19: Faint, soft systolic murmur was heard at base and apex. Induration was increased beneath left sternocleidomastoid. Right femoral and inguinal glands were enlarged and rather soft. Femoral glands were tender. Urine was amber, slightly cloudy, with trace of albumin, no sugar, few epithelial cells and leucocytes.

February 20: Patient showed a slight conjunctival icterus. The edema about shoulder had extended slightly and was more brawny. Tongue was cleaner. Patient was rather somnolent and was catheterized.

February 21: Patient was less somnolent and his pulse bounding. Urine was dark amber, slightly cloudy, specific gravity 1020, acid, faint trace of albumin and sediment as above. He was given Epsom salts daily and ½ oz. whisky every four hours. Blood culture showed *Streptococcus pyogenes* (Dr. Krumwiede).

February 22: He had slight nosebleed, but had slept better than any night. Was much less restless.

February 23: Aspirin was omitted. February 24 an attempt was made to determine patient's opsonic index to the streptococcus isolated from his blood. No phagocytosis occurred. February 25 patient in profuse perspiration. Vomited yellow curds. February 26 there was softening and localization behind sternocleidomastoid. Abscess was opened under cocaine by Dr. Peck. Few drams of yellow pus were drained. Culture showed *Streptococcus pyogenes*. February 27 several wheals were seen on trunk. February 28 second attempt to determine patient's opsonic index was successful (Fig. 12).

March 1: Patient had free perspiration at night. Urine was dark amber, with few granular casts. The next day the abscess about shoulder was opened. Culture showed *Streptococcus pyogenes*. March 3 patient's general condition continued the same. There was involuntary micturition. Patient was put on soft diet.

March 5: Vaccine was prepared, but its use was delayed because patient's general condition had slightly improved. The urine on the following day was dark amber, sp. gr. 1014, with no casts. March 9 wheals had gradually disappeared.

this patient would have been inoculated and his subsequent recovery doubtless have been attributed to its use.

CASE 6.—History.—A. H., female, aged 58, was seen with Dr. A. J. Bristow and Dr. W. H. B. Pratt, Brooklyn, Feb. 25, 1907. Patient had rigors, fever, general muscular pains and intense headache. On March 1 she was well. March 4 patient had a repetition of previous attack, with more severe headache. On March 10 she had recovered. March 11 there was tenderness over left side of neck. Had a temperature of from 100 to 103 F. March 17 there was moderately circumscribed swelling of left submaxillary triangle; no fluctuation. Leucocytes numbered 15,000; polynuclears, 78 per cent. March 18 the swelling was less painful and less tender. Leucocytes numbered 12,000; polynuclears, 78 per cent.

March 20: Swelling was more diffuse and painful. March 21 leucocytes numbered 10,000; polynuclears, 75 per cent. March 23 swelling had extended to clavicle and was more tender. Leucocytes numbered 11,000; polynuclears, 83 per cent.

Operation.—Dr. Bristow, on March 23, made a long incision parallel with the anterior border of sternocleidomastoid; the tissues were much thickened and infiltrated. Deep in the submaxillary fossa a small abscess cavity was opened, the pus evacuated and drainage instituted. Culture showed *Streptococcus longus* and a bacillus.

March 24: Edge of wound was glazed and there was very little discharge. Urine was normal; daily total quantity, from 60 to 90 oz., sp. gr., from 1016 to 1020. March 26 patient had an intermittent pulse, was given caffeine. March 27 had severe pain in left leg and some tenderness over internal condyle. March 28 infiltration of neck was slowly disappearing. March 30 patient had two slight convulsions limited to the face and upper extremities; eyes deflected to right; face livid. Was given sodium bromid and salicylate of strontium. There was a blowing murmur over mitral area. March 31 patient had pain, swelling, redness and tenderness in right knee and left forefinger and wrist.

April 1: Was seen by Dr. Potter. Opsonic index to streptococcus (from Case 5), 0.74. April 2 blood culture (Dr. N. E. Ditman) sterile. Patient inoculated with 25,000,000 streptococci from Case 5. April 4 wound was diminished in size one-half; joints had improved. Was reinoculated with 50,000,000 streptococci from same vaccine. April 11 wound was practically healed and convalescence uninterrupted.

The striking features of this case are the improvement of the wound and joint symptoms within forty-eight hours after the first and the sudden drop in the temperature and rapid improvement following within forty-eight hours after the second inoculation and closely corresponding to the rise in the opsonic index, as plainly shown in Chart 13. The vaccine was derived from Case 5.

We have studied a few cases of pulmonary tuberculosis and have inoculated some of the patients with tuberculin. Owing to patients' disappearance and to lack of time, our observations are incomplete. We have studied a large number of cases of joint tuberculosis, chiefly among the children in the wards at the Hospital for Ruptured and Crippled Children. We have investigated frequently, over a period of six months, a number of cases of obstinate sinuses. The tuberculo-opsonic indices have been nearly persistently high and, if we follow the principles advanced by Wright, the patients require no tuberculin.

Delay in the preparation of the vaccines and an outbreak of scarlet fever prevent judgment from being passed as yet on our attempts at the inoculation of the germs obtained from the discharging sinuses. It is interesting to note that from one sinus a colon bacillus, from another a pneumococcus and from a third a diphtheria bacillus were cultivated by Dr. North.

GLANDULAR AND OCULAR TUBERCULOSIS.

We have studied three cases of glandular tuberculosis. One patient, a boy operated on for a recurrent involvement of the right cervical glands. An extensive dissection of the left side had been made a year previous. His tuberculo-opsonic index before and after the operation was well above normal. As yet he has not been inoculated. Another, an adult male with an involvement of the left cervical glands following a tonsillar infection and an acute pleuropulmonary involvement, exhibited a persistently high tuberculo-opsonic index. After absolute rest in the open air and extra feeding, his index approached normal, and he was inoculated with minute doses of tuberculin. An intercurrent pneumonia (pneumococcus) interrupted treatment. He is now progressing satisfactorily, the dosage of tuberculin is being very guardedly increased and his index is always well above normal. The third, an adult male with a very chronic process in the neck, has been away for the winter and we have not yet begun his tuberculin inoculations. His index has been normal or just below.

Fig. 13.—Case 6, Mrs. A. H., streptococcus abscess in neck, with multiple arthritis; inoculated with streptococcus from Case 5 (A. R.), showing temperature curve and opsonic index.

We have followed three cases of probable ocular tuberculosis.² In one of these were suggestive signs of an old bacillary process at one apex, and in another there was definite evidence of active pulmonary tuberculosis. Tuberculin has been employed in all three in such dosage and at such intervals as seemed most likely to avoid a marked local ocular reaction. The tuberculo-opsonic indices have been estimated as frequently as possible in the hope of gaining some information as to the value of opsonic determinations for guidance in inoculation. The curves (Fig. 14) indicate the doses employed and the tuberculo-opsonic indices. As far as the observations have extended, the determination of the opsonic indices has been of very little assistance in regulating the dosage or the intervals of inoculation.

2. Reported in full by Drs. Coleman W. Cutler and Alexander Duane at the American Ophthalmological Association at Washington, May 10, 1907.