activities favor blood-flow. The oncometer shows conclusively that the moderate rise of pressure which is observed in anesthetized animals is, in most cases, exclusively cardiac.

The method adopted for studying the effects of caffeine was the same as that used for studying the effects of strychnin in the acute infectious and hypotensive cases. Caffein sodio-salicylate was invariably employed.

Data: There were three cases of severe pneumonia, one of general peritonitis, one of fatal tuberculous enteritis, two of traumatic shock and one fatal septico-pyemia.

Results: 1. Eight out of nine times there was no effect on the systolic pressure. Once it fell 35 mm. during the period of treatment. There was not a single rise in systolic pressure as a result of administering caffeine.

2. Five out of six times there was no effect on the diastolic pressure. Once it fell 10 mm. during the period of treatment.

3. Nine out of ten times there was no effect on the rate of the pulse. Once it rose 10 beats per minute during the period of administration.

4. In no instance was there a measurable change in respiration.

It could not be demonstrated, with the method used, that either strychnin sulphate or caffein sodio-salicylate has any beneficial effect on the cardiovascular disturbances of the infectious diseases.

SUMMARY

1. Since the blood-pressure is not low either in persons showing grave symptoms of pneumonia or in those dying of that disease, and since it has been proved that the vasomotor arcs are normal in animals near death from pneumonia, it is logical to conclude that the vasomotor mechanism is not impaired in pneumonia.

2. Strychnin does not improve or augment the work of the heart in persons suffering from broken cardiac compensation.

3. It could not be shown that either strychnin or caffeine stimulated the cardiovascular apparatus in any of the conditions studied.

329 Beacon Street.

ABSTRACT OF DISCUSSION

DR. LAWRENCE LITCHFIELD, Pittsburgh: Dr. Newburgh gave the impression that blood-pressure increases in pneumonia and that many patients die therefrom. I think the blood-pressure varies in pneumonia as it does in persons without pneumonia and, therefore, this should be taken into account. So far as my observation goes, most of the pneumonia patients that I lose are either those who have a low blood-pressure or those in whom the pressure falls in spite of treatment. I do not think that pneumonia in the beginning affects the blood-pressure specifically. Pressure varies in pneumonia as it does in health and there are very wide variations in healthy people.

DR. BERNARD FANTUS, Chicago: The critical study of the action of drugs on diseased human beings is something that we are very much in need of; and Dr. Newburgh's paper is an excellent example of the kind of work of which we should have a large amount. On the other hand, using drugs in a routine manner does not enable us to formulate any judgment concerning the value or lack of value of that particular form of treatment. As far as my own observations are concerned I must take issue with the statement made by the previous speaker that strychnin is of value in pneumonia. I had occasion to make some observations on the death-rate of pneumonia patients some years ago, in services at the Cook

County Hospital in Chicago, in which strychnin was used and in other services in which it was not used, and my impressions were such as would confirm the belief that the patients had a better chance for life in the services in which strychnin was not used in a routine manner.

DR. L. P. HAMBURGER, Baltimore: What is the history of the clinical use of strychnin in this country? In Germany it is not viewed at the "life-preserver" which we here deem it!

DR. C. S. WILLIAMSON, Chicago: One important point is that the variations in the systolic blood-pressure alone are by no means a reliable criterion of improvement, or the reverse. Sahli, some years ago, made a study of cases associated with high blood-pressure, and concluded that the blood-pressure was kept up by the cyanosis and venous congestion of the medullary centers, a condition to which he gave the name *Hochdruck-Stauung*—high pressure stasis. Now every clinician of much experience sees these cases occasionally. The blood-pressure is very high, despite outspoken signs of broken compensation, and after the use of some of the digitalis bodies intravenously or otherwise, the systolic pressure drops as much as 20 or 25 mm., with a simultaneous great improvement in the condition. One must therefore bear in mind this group of cases, or otherwise run a great risk of misinterpreting the results. Might not the high pressure in some of Dr. Newburgh's cases be due to medullary stasis, as in the cardiac group just referred to?

DR. L. H. NEWBURGH, Boston: It is a fact that we find high blood-pressure in cases of pneumonia. Because a drug does not raise or does not affect the pressure does not permit us to decide whether or not it is a good drug. Caffein probably is a good drug, as has been shown, but its effect is not primarily on the blood-pressure, though it does augment the circulation without increasing the blood-pressure appreciably. Incidentally it has no effect on the pulse. I merely stated that there was no measurable effect.

A COMPARISON OF CHOLESTERINIZED AND NON-CHOLESTERINIZED ARTI- FICIAL ANTIGENS IN THE WAS- SERMANN REACTION *

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Since the introduction of cholesterinized antigen by Sachs¹ from Ehrlich's laboratory, reports concerning its specificity have been conflicting, varying from the assertion that an artificial antigen had been found possessing the requirements of an ideal "standard antigen,"² to an assertion that it was unreliable and hence a menace to the clinician.³

In view of such diversity of opinion, it appeared desirable to investigate its merits in our own hands before relying on it, and to report the result of that investigation extending over a series of four hundred reactions. In these cases, as accurate knowledge of the clinical condition of the patient was obtained as a mixture of hospital and dispensary practice and referred cases would permit. Inadequacy of clinical records and personal histories have alone been influential in excluding about two hundred more reactions in a straight series of approximately six hundred cases. Study of the clinical data led me to adopt the five divisions of clinical diagnosis with reference to syphilis as follows: (1) positive, (2) probable, (3) for diagnosis (this division [six reactions] was omitted in

* From the Department of Clinical Pathology and Experimental Medicine of the College of Physicians and Surgeons, Baltimore.

1. Sachs, H.: *Berl. klin. Wchnschr.*, 1911, lxxviii, 2066.

2. McIntosh, J., and Fildes, P.: *Syphilis*, London, 1911, p. 220; *Ztschr. f. Chemotherapie.*, 1912, i, 79.

3. Thomas, B. A., and Ivy, I. H.: *Use of Cholesterinized Antigens in the Wassermann Reaction*, *THE JOURNAL A. M. A.*, Jan. 31, 1913, p. 363.

a consideration of those cases in which there was a diversity of results with the antigens used), (4) doubtful, and (5) negative.

Approximately half of the reactions included in this study were performed at the laboratory of Dr. Charles E. Simon and the remainder by myself. The moderate discrepancy of parallelism between these two portions of the series is adequately explained on the ground that, in one instance, tests are made on all the male public patients of the Mercy Hospital by one of us as routine, while at least a suspicion of lues is entertained when specimens are referred to the other.

The comparison in the reactions of this series was confined to the analysis of the same serum or spinal fluid tested in duplicate with two antigens, one, the acetone-insoluble lipoid extract of beef-heart of Noguchi (designated in the accompanying tables as N. A.), and the other, cholesterinized alcoholic extract of beef-heart prepared after the method of Sachs (designated as S. C. A.). Repeated titration of anti-

fluids (27.7 per cent. and 33 per cent., respectively), gave in varying degree a more marked deviation of complement with standard cholesterinized antigen than with Noguchi antigen. But 5 serums (1.25 per cent.) and no spinal fluids gave more complete fixation of complement with Noguchi antigen than with standard cholesterinized antigen.

CASES IN WHICH RESULTS WERE IDENTICAL

1. As shown in Table 1 there were 116 positive reactions. Of these, 2 were clinically doubtful and 1 clinically negative. These three were all in negroes, and though not showing signs of syphilis, one cannot escape the lingering suspicion that their faulty observation, not to question their veracity, might account for the discrepancy in past history. The remaining 113 positive reactions were not at variance with the clinical findings or histories.

2. There were 16 inconclusive reactions. Of these, 4 were negative, the same number for diagnosis, 1 was probably luetic and 7 were definitely so. Of the last, 2 were general paretics and 2 were active cases, all 4 undergoing vigorous antiluetic treatment, leaving 3 positive cases which were not detected by either antigen.

3. There were 137 negative reactions. Of this number, 25 had positive histories, 24 of which had been under long-continued antiluetic treatment. The remaining case was diagnosed as brain syphilis (Case 1, Table 2 and Case 1, Table 4) the cerebrospinal fluid giving complete complement fixation with both antigens.

In this group there were two cases in which lues was clinically probable. One was tentatively diagnosed as congenital syphilis—parenthetically, congenital lues is the evil genius of the Wassermann reaction—and the other a chancre. In the latter case the appearance of a secondary rash four weeks later substantiated the clinical diagnosis, at which time a second blood Wassermann gave a +++ reaction with both antigens.

Twenty-nine out of a total of 42 cases which were clinically for diagnosis yielded a negative reaction, and 26 out of 28 cases which were clinically doubtful were likewise negative.

4. A separate consideration of the so-called parasymphilitic diseases is of interest. This includes 14 general paretics. All except 4 had had vigorous treatment, including in most cases intraspinal injections of salvarsanized blood-serum. Of the 4 untreated cases, 1 gave a negative and 1 an inconclusive reaction, while 2 were strongly positive. Of the 10 treated cases, 1 persisted with complete complement fixation, the remaining 9 being modified to a greater or less extent by treatment (or otherwise). One case of tabes dorsalis yielded complete complement fixation.

Fourteen spinal fluids were examined in which identical results were obtained with both antigens (Table 2).

Six of these were clinically positive cases and gave complete complement fixation in all dilutions. One was tentatively diagnosed as brain syphilis and gave a ++ reaction in the stronger dilutions only. The remaining seven cases were Wassermann-negative even in the strong concentrations. The clinical diagnoses in these cases were as follows: multiple sclerosis, 1 case; sciatica, 1; neurasthenia, 2 (one of which had active lues and a positive blood-serum Wassermann); chorea, 1 (congenital lues was considered but not

TABLE 1.—CASES IN WHICH BLOOD-SERUM RESULTS WERE IDENTICAL WITH THE TWO ANTIGENS

Reaction *	Total No. of Cases	Clinically and Historically					Positive Cases Include
		Positive	Probable	For Diagnosis	Doubtful	Negative	
+++	95	73	13	7	2	0	One case of tabes and 3 of general paresis.
++	21	18	0	2	0	1	Two of long-standing lues with active treatment; 1 of general paresis.
+	10	6	1	3	0	0	One of long-standing lues with active treatment; 1 general paresis.
±	6	1	0	1	0	4	One of long-standing lues with active treatment; 1 general paresis.
±	22	3	2†	5	4	8	Three of long-standing lues with active treatment.
—	115	22	0	24	22	47	Eight of general paresis; 21 of long-standing lues with active treatment, and 1 of cerebrospinal lues.
Total	269	123‡	16	42	28	60	

* In this and the following tables +++ and ++ indicate, respectively, strongly positive and positive; + and ± inconclusive, and — and —, negative.

† One case in the primary stage and one also of congenital lues.

‡ Included in the 32 doubtful and negative reactions were long-standing with active treatment, 26; cerebrospinal lues, 1; general paresis, 10, 9 of which were of long standing with active treatment.

complementary and antigenic power of these two antigens during the course of the series gave a constant titer of one in ten parts of 0.9 per cent. salt solution. They hence exhibited complete parallelism and splendid keeping power.

The antigen of Noguchi was selected for the comparison, not only because it was one which we had previously been using, but also because it is considered the most efficient⁴ of uncholesterinized artificial luetic antigens.

This series includes 379 serums and 21 spinal fluids. The tests on the latter were usually made in more than one dilution, each dilution being made in duplicate with either antigen. Two hundred and sixty-nine serums, or 71 per cent., and 14 spinal fluids, or 66 per cent. of the total number of each, gave reactions which were identical with both antigens; 105 serums and 7 spinal

4. Kolmer, J. A.; Lanbaugh, E. E.; Casselman, A. J., and Williams, W. W.: Practical Studies on the So-Called Syphilis "Antigens," with Special Reference to Cholesterinized Extracts, Arch. Int. Med., December, 1913, p. 660.

established); paralysis of third right nerve, 1; for diagnosis, 1 case.

CASES IN WHICH RESULTS WERE NOT IDENTICAL

Most important, of course, are the 110 serums (29 per cent.) and the 7 spinal fluids (33.33 per cent.), in which there was not agreement in the results obtained

cholesterinized antigen than with Noguchi antigen are recorded in Table 4. All of these cases were undoubtedly luetic. Before treatment two of them (Cases 1 and 4) had shown the same degree of inhibition with the two antigens (compare Cases 1 and 4 of Table 2). Two others were before and after treatment in the same persons. These two exhibit one of the most

TABLE 2.—CASES IN WHICH CEREBROSPINAL FLUIDS YIELDED RESULTS IDENTICAL WITH THE TWO ANTIGENS

Case No.	Diagnosis	N. A.*							S. C. A.*						
		1-1	1-2	2-5	1-3	1-5	1-8	1-10	1-1	1-2	2-5	1-3	1-5	1-8	1-10
1	Brain syphilis	+++	..	+++	..	..	..	..	+++	..	+++	..	..	..	..
2	General paresis	..	..	+++	..	..	..	..	..	..	+++	..	..	..	..
3	Multiple sclerosis	..	..	..	..	..	..	..	..	..	..	..	..	..	..
4	Tabes	+++	..	+++	..	..	..	..	+++	..	+++	..	..	..	..
5	Brain syphilis	..	..	..	..	+++	..	..	..	..	..	..	+++	..	..
6	Tabes	..	..	..	..	+++	..	..	..	..	..	..	+++	..	..
7	Tabes	..	..	..	..	+++	..	..	..	..	..	..	+++	..	..
8	Brain syphilis ?	..	++	..	++	..	..	..	..	++	..	++	..	..	..
9	For diagnosis	..	..	..	..	..	..	..	..	..	..	..	..	..	..
10	Sciatica	..	..	..	..	..	..	..	..	..	..	..	..	..	..
11	Neurasthenia	..	..	..	..	..	..	..	..	..	..	..	..	..	..
12	Lues; neurasthenia ?	..	..	..	..	..	..	..	..	..	..	..	..	..	..
13	Chorea; congenital lues	..	..	..	..	..	..	..	..	..	..	..	..	..	..
14	Third nerve paralysis	..	..	..	..	..	..	..	..	..	..	..	..	..	..

* The figures heading the columns below (1-1, 1-2, 2-5, etc.) indicate dilutions. Thus 1-1 indicates undiluted spinal fluid; 1-2, 1 part spinal fluid and 1 part 0.9 per cent. saline; 2-5, 2 parts spinal fluid and 5 parts saline; 1-3, 1 part spinal fluid and 3 parts saline; 1-5, 1 part spinal fluid and 5 parts saline; 1-8, 1 part spinal fluid and 8 parts saline; 1-10, 1 part spinal fluid and 10 parts saline, of each of which 0.5 c.c. was used.

with the two antigens. For purposes of accuracy in clinical control it seemed advisable to disregard in this connection six additional cases which would, if not omitted, be listed "for diagnosis."

We considered these cases with reference to the degree of complement fixation exhibited by the more inhibitive antigen irrespective of the reaction of the weaker one. On this basis the same interpretation applies to the results here obtained as when the reactions were identical, namely, +++ and +++ being considered positive, + and ± as inconclusive, and ± as negative (obviously with our method of indicating complement fixation there could be no disagreement of results for degrees of inhibition less than ±).

Those cases in which the blood-serums yielded a greater degree of complement fixation with standard cholesterinized antigen than with Noguchi antigen are recorded in Table 3. This division yielded 68 (64.7 per cent.) positive Wassermann reactions, 29 (27.6 per cent.) inconclusive Wassermann reactions and but 8 (7.7 per cent.) negative reactions.

Of the 68 patients with positive reactions, all save 4 of the persons were or had been definitely infected with syphilis. Of the 4 who denied such infection, 3 admitted a history of chancroid, which is certainly suggestive of the possibility of a specific lesion, thus leaving only 1 case to be explained either on the ground of a non-specific reaction or false history. Which of these alternatives is correct remains an open question.

Of the 29 patients with inconclusive reactions, 9 gave no evidence whatsoever of lues. Seven were doubtful, considered clinically (1 gave a history of chancroid), 1 was a congenital luetic and the remaining 12 were undoubted cases of lues under the influence of vigorous treatment.

Of the 8 cases yielding negative reactions, 3 were clinically negative, 3 were doubtful and in 2 the reactions had changed from positive to negative in the course of vigorous antiluetic therapy.

Those cases in which the cerebrospinal fluids yielded a greater degree of complement fixation with standard

TABLE 3.—CASES IN WHICH BLOOD-SERUM COMPLEMENT FIXATION WAS GREATER WITH CHOLESTERINIZED THAN WITH NOGUCHI ANTIGEN

Reaction		Total No. of Cases	Clinically and Historically				Positive Cases Include
N. A.	S. C. A.		Probable	Doubtful	Negative	Positive	
++	+++	16	2	0	0	14	One case of general paresis; 1 of long standing with active treatment.
++	+++	8	3	0	0	5	
±	+++	2	0	0	0	2	One case of general paresis; 1 gave a +++ N. A. reaction before treatment.
±	+++	5	2	1*	0	2	
—	+++	19	3	1*	0	15	One gave a +++ N. A. reaction before treatment; 1 gave a + luetic reaction; 2 of long standing with active treatment; 5 general paresis and 1 of tabes.
+	++	5	1	0	1	3	
±	++	0	0	0	0	0	One gave a +++ N. A. reaction before treatment.
±	++	7	1	1*	0	5	
—	++	6	2	0	0	4	One of general paresis; 1 of long standing with active treatment.
±	+	1	0	0	1	0	
±	+	6	0	0	2	4	Four of long standing with active treatment; 1 of general paresis.
—	+	4	1†	2	0	1	
±	±	5	0	1	2	2	One of long standing with active treatment.
—	±	13	0	4*	4	5	
—	±	8	0	3	3	2	Two gave a +++ N. A. reaction before treatment. Two gave a +++ N. A. reaction before treatment; 5 of long standing with active treatment; 1 with brain syphilis.
—	±	8	0	3	3	2	
—	—	105	15	13	13	64†	Two of long standing with active treatment.

* One case with history of chancroid.

† Totals: a +++ N. A. reaction before treatment, 8; a + luetic reaction, 1; history of "chancroid," 4; long standing with active treatment, 19; congenital lues, 1; persistent — N. A. for one year, 1; general paresis, 8; tabes, 1; brain syphilis, 1.

‡ One case congenital lues.

notable features of the entire series, namely, the more resistant nature of standard cholesterinized antigen complement fixation during the course of treatment. After the collection of data for this paper was concluded, it is interesting in this connection to note that a third test in this same case gave negative results in all dilutions with both antigens, indicating that the reaction with standard cholesterinized antigen is amenable to complete change, provided that treatment is sufficiently extensive and intensive.

There remain for consideration only those cases in which Noguchi antigen gave a greater degree of com-

2. Standard cholesterinized antigen detects many luetic cases which do not yield positive results with Noguchi antigen.

3. Standard cholesterinized antigen, though amenable to the influence of treatment, is less susceptible to extinction by therapeutic measures.

4. Standard cholesterinized antigen possesses splendid keeping properties, is always available and is easy of preparation.

5. Standard cholesterinized antigen is an ideal artificial antigen.

Plymouth Hall.

TABLE 4.—CASES IN WHICH THE CEREBROSPINAL FLUID WAS MORE STRONGLY POSITIVE WITH CHOLESTERINIZED ANTIGEN THAN WITH NOGUCHI ANTIGEN

Case No.	Diagnosis	N. A.							S. C. A.						
		1-1	1-2	2-5	1-3	1-5	1-8	1-10	1-1	1-2	2-5	1-3	1-5	1-8	1-10
1	Brain syphilis	—	..	—	..	..	..	..	+++	..	+++	..	..	..	..
2	Tabes	..	+	..	+	..	..	..	..	+++	..	+++	..	..	..
3	Tabes	..	+	..	+	..	..	..	..	+	..	+	..	..	..
4	Tabes	..	+	..	+	..	..	..	..	+	..	+	..	..	..
5	Brain syphilis	..	+	..	+	..	..	..	..	+	..	+	..	..	..
6	Tabes	..	+++	..	+++	+++	..	..	..	+++	..	+++	+++	+++	+++
7	Brain syphilis	..	..	..	..	+	..	..	..	..	..	..	+++	..	..

See explanation under Table 2.

plement fixation than standard cholesterinized antigen. There were but five such cases (1.25 per cent. of the entire series) all occurring in blood-serums (see Table 5). One case probably luetic gave a positive reaction with Noguchi antigen and an inconclusive one with standard cholesterinized antigen. Three of the remaining four cases were definitely non-luetic or doubtfully so. The last case was definitely luetic, but, under vigorous treatment, the reaction was becoming negative.

TABLE 5.—CASES IN WHICH BLOOD-SERUM COMPLEMENT FIXATION WAS GREATER WITH NOGUCHI THAN WITH CHOLESTERINIZED ANTIGEN

Reaction		Total No.	Clinically and Historically—			
N. A.	S. C. A.		Positive	Probable	Doubtful	Negative
+++	+	1	..	1	..	..
±	—	4	1*	..	1	2
Total		5	1	1	1	2

Under active treatment.

SUMMARY

1. In a series of 379 serums and 21 spinal fluids, 269, or 71 per cent., of serums and 14, or 66.66 per cent., of spinal fluids gave identical results with standard cholesterinized antigen and Noguchi antigen.

2. In 110, or 29.05 per cent., of serums and 7, or 33.33 per cent., of spinal fluids, there was to a greater or less extent a lack of agreement between these two antigens. Of the 110 serums showing differences in complement fixation, 105, or 95.4 per cent., showed greater complement fixation with standard cholesterinized antigen than with Noguchi antigen, while 5, or 4.6 per cent., showed greater inhibition of hemolysis with Noguchi antigen than with standard cholesterinized antigen. No spinal fluid exhibited the latter phenomenon.

CONCLUSIONS

1. Standard cholesterinized antigen does not yield an appreciable number of non-specific reactions.

THE ADRENALS AND THE PULSE-RATE

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The adrenal glands seem to be an important factor in integrating the body for unusual muscular activity. Circulating epinephrin causes a depression of the digestive activities, a shifting of the blood from the splanchnic to the somatic structures, increased blood-pressure, dilated bronchioles and mobilization of dextrose. It is an efficient aid in abolishing fatigue.¹

During muscular exertion acceleration of the pulse occurs. It would seem that the acceleration might be due in part to a discharge of epinephrin, which is a well-known cardiac stimulant. But the general supposition is that in a normal animal the drug causes slowing of the heart, the depression being a reflex effect resulting from high blood-pressure. Such is the common text-book statement of the case. On this ground, Gasser and Meek² have recently concluded that epinephrin discharge is not to be considered a factor in the accelerated pulse which accompanies muscular exercise. On the face of the matter this would seem an anomaly. Why should adrenal secretion cause a number of other effects which favor muscular activity but oppose the acceleration of the pulse, which, as a matter of fact, occurs despite any such opposition?

The statement that epinephrin slows the pulse seems to be based on Oliver and Schaefer's³ and Szymonowicz's⁴ original reports on the effects of injecting adrenal extracts. Their observation, that the sudden injection of massive doses slows the pulse, has often been confirmed. But it is to be noted that such experi-

1. For a review of the literature see Cannon: *Am. Jour. Physiol.*, 1914, xxxiii, 357.

2. Gasser and Meek: *Am. Jour. Physiol.*, 1914, xxxiv, 69.

3. Oliver and Schaefer: *Jour. Physiol.*, 1895, xviii, 230.

4. Szymonowicz: *Arch. f. d. ges. Physiol.*, 1896, lxvi, 131.