COMPARATIVE EXPERIMENTS ON THE PRESENCE OF COMPLEMENT BINDING SUBSTANCES IN THE SERUM AND URINE OF SYPHILITICS.*

UDO J. WILE, M.D.
BERLIN, GERMANY.

In 1906, Wassermann, Neisser and Bruck¹ published a series of experiments demonstrating that when the inactivated serum of a syphilitic patient was brought together with an alcoholic extract of syphilitic tissue, for example, congenital syphilitic liver, and a small amount of normal complement (guinea-pig serum) was added, a reaction took place between these three substances, this reaction being indicated by the addition of a hemolytic system. This reaction has since been known as the Wassermann reaction.

In 1907 Bab² investigated the milk of syphilitic women and found that here also the complement-binding substances were demonstrable, and in June, 1908, Franz Blumenthal and I³ published a preliminary report on the presence of complement binding substances in the urine of syphilitics. We tested the serum of 50 patients, and simultaneously applied the same test to the urine, using the latter at first in three concentrations, 1 c.c., 0.5 c.c. and 0.2 c.c., later using only 1 c.c., as it was found that the reaction occurred most uniformly in this concentration.

It is the purpose of this paper to give the results of the investigation of 100 cases, in which both serum and urine were tested, to compare the relative value of each in the diagnosis of syphilis, and, if possible, to show the influence of treatment received, on the presence or absence of the reaction.

Of the 100 patients examined, 76 were, or had been syphilitic, 24 were control or normal cases. Among the 76 syphilitics we found a positive reaction in both serum and urine in 50; in 15 the reaction was negative in both serum and urine; in 8 it was positive in the serum and negative in the urine, and in 3 it was negative in the serum and positive in the urine. (Table 1).

A most interesting fact was noticed in certain of the cases in which the urine was positive, in that no hemolysis occurred in the control test tube, containing urine plus complement, plus hemolytic serum, and in our preliminary report we suggested that the urine might contain substances which in these cases acted in the same manner as the syphilitic extract.

In general, the results were more striking in the serum than in the urine, although in a few cases sent to us for diagnosis the reaction occurred much stronger in the urine than in the serum. In practically all of the cases studied it was noticed that hemolysis was retarded or to a slight degree prevented by the urine, and, keeping this fact in mind, we counted only those cases positive in which there could be no question as to the prevention of the hemolysis.

Of the 24 control cases, 22 were found uniformly negative in both serum and urine; in one case, in which scabies was present, a weak positive reaction was found in the urine, and in this case it may be noticed (see table) that the reaction in the serum was not entirely negative. In the other control case, in which we were dealing clinically with a soft chancre, the urine showed

a strong positive reaction, while the serum was negative. In this case no evidence of syphilis was present at the time and a previous infection could most probably be excluded.

TABLE 1.*

Case No.	Diagnosis.	Serum.	Urine.
1.	Lues II	+++	+
2.	Latent Lues	+++	+
3.	Lues II	++	++
4.	Normal case	—	—
5.	Lues II	+	+
6.	Lues II	+++	+
7.	Normal case	—	—
8.	Scabies	0	+
9.	Lues II	+++	+++
10.	Normal case	—	—
11.	Lues II	+++	+++
12.	Lues II	++	++
13.	Lues II	0	0
14.	Lues II	+	+
15.	Lues II	+	++
16.	Normal case	—	—
17.	Normal case	—	—
18.	Lues II	0	0
19.	Lues III	—	+
20.	Lues II	++	+
21.	Lues II	—	+
22.	Lues II	+++	+++
23.	Lues II	++	++
24.	Lues II	+++	+++
25.	Latent Lues	—	—
26.	Lues II	—	—
27.	Lues III	++	++
28.	Lues I and II	+++	++
29.	Lues II	—	—
30.	Lues I and II	+++	—
31.	Normal case	—	0
32.	Lues II	++	+++
33.	Lues III	+	++
34.	Lues II	++	0
35.	Lues	++	+
36.	Lues II	+++	++
37.	Lues II	+++	+
38.	Lues II	++	0
39.	Normal case	—	—
40.	Latent lues	+++	+++
41.	Lues I	++	+
42.	Lues III	++	+
43.	Lues II	+	+
44.	Lues II	+++	+
45.	Lues II	+++	+++
46.	Lues II	+++	+++
47.	Normal case	—	—
48.	Latent lues	+++	+++
49.	Lues III	+++	+++
50.	Lues III	+++	+++
51.	Lues II	+++	+++
52.	Lues II	+++	+++
53.	Ulcus molle	—	+++
54.	Lues II	++	++
55.	Lues II	++	++
56.	Lues II	+++	+++
57.	Lues II	+++	++
58.	Lues I and II	+++	+
59.	Normal case	—	—
60.	Lues II	—	—
61.	Lues III	+++	+
62.	Latent lues	++	+
63.	Latent lues	—	—
64.	Normal case	—	—
65.	Lues II	—	—
66.	Normal case	—	—
67.	Normal case	—	—
68.	Normal case	—	—
69.	Normal case	—	—
70.	Normal case	—	—
71.	Lues II	+++	+++
72.	Lues II	—	—
73.	Latent lues	+++	+++
74.	Latent lues	+++	+++
75.	Latent lues	—	—
76.	Tabes latent lues	++	+++
77.	Normal case	—	—
78.	Latent lues	0	0
79.	Normal case	—	—
80.	Lues III	+++	—
81.	Latent lues	—	—
82.	Lues III	+++	+++
83.	Latent lues	+++	++
84.	Latent lues	+++	++
85.	Lues III	+	+++
86.	Heredit. lues	+++	+
87.	Normal case	—	—
88.	Latent lues	—	++
89.	Lues II and III	+++	+++
90.	Normal case	—	—
91.	Normal case	—	—
92.	Lues II	+++	+++
93.	Latent lues	+	+++
94.	Lues II	—	—
95.	Lues II	+++	+++
96.	Normal case	—	—
97.	Lues III	++	+++
98.	Latent lues	+++	+++
99.	Latent lues	+++	+++
100.	Normal case	—	—

*Number of crosses notes strength of reaction; 0 = interpreted as negative reaction.

*From the Dermatologic Clinic of the University of Berlin.
Director: Geh. Med.-Fat. Prof. Dr. Lesser.

1. Deutsch. med. Wchnschr., 1906, No. 19.

2. Deutsch. med. Wchnschr., 1907, No. 30.

3. Berl. klin. Wchnschr., 1908, No. 22.

Of the 50 cases in which both serum and urine were positive this result was obtained as early as five weeks after the infection and as late as twelve years afterward. In the 15 cases of syphilis in which the serum and urine were both negative this result was found as early as five weeks after the infection and as late as 15 years afterward. Of the 13 negative cases, however, 9 patients had been infected two or more years previously, thus indicating that in general the reacting substances tend to disappear spontaneously in both serum and urine after a lapse of a few years.

Of the 8 patients in whom the serum was positive and the urine negative, 3 were infected less than two months before, and at the other extreme was one patient with an infection dating back thirty years. The first 3 cases agree entirely with the observation that the reaction appears later in urine than in serum.

In the three cases of syphilis in which the serum was negative and the urine positive, two patients had been infected about two years previously and the third patient's was a very early case (primary sore).

The effect of treatment on the presence or absence of the reaction was first studied by Citron,⁴ who showed that under vigorous treatment the reaction tended to disappear in the serum. Of our 75 patients a large proportion were in the early secondary stage of lues, and up to the time of their examination had received little or no treatment whatever. A majority of these gave positive reactions in both serum and urine. For accuracy of figures it would be better to select only the cases of latent and tertiary lues, and those sent for diagnosis which proved to be lues. Of these there were 31 cases, of which 20 were positive in both urine and serum; 9 of these 20 had received no treatment whatever, 10 had received inefficient treatment, consisting of a few injections or inunctions, and the remaining case alone had been through six courses of injections.

In 10 cases of latent lues in which both serum and urine were negative all but one had received vigorous antiluetic treatment, and finally, in the remaining one case which showed a negative result in the serum, and a positive one in the urine, there had been but four courses of twelve injections of mercury salicylate. (This last case does not seem to be of any significance as illustrating the effect of treatment on the reaction).

CONCLUSIONS.

The conclusions which may be drawn from these statistics are as follows:

1. The urine in a large percentage of cases of syphilis contains substances which behave in the same way as the antibodies in the serum of the same cases.

2. These substances seem to appear a little later in the urine than in the serum and at times are present in one and not in the other and vice versa.

3. The diagnostic value of the reaction in the urine must for the present be viewed with caution inasmuch as in 2 per cent. of our total number of cases a positive reaction was found in the urine while the serum in these cases was negative.

4. In both serum and urine these bodies tend to disappear under vigorous antisiphilitic treatment.

I take this opportunity of extending my sincere thanks to Dr. Franz Blumenthal, under whose direction this work was undertaken and to whom I am indebted for many valuable and kind suggestions.

THE ANEMIA OF HEPATIC CIRRHOSIS SIMULATING THE PERNICIOUS TYPE.

JAMES E. TALLEY, M.D.

PHILADELPHIA.

It appears pretty generally admitted that a secondary anemia may change to the primary pernicious type. The theory that progressive pernicious anemia is always cryptogenic was negatived when cases with the typical blood and marrow changes were demonstrated with bothriocephalus, syphilis, malaria, gastrointestinal mucosa atrophy and small pyloric cancer as precursors.

In ordinary secondary anemia the blood picture differs essentially from that of the primary type, but when in the secondary type the process reaches a point at which not only hemolysis, but deficient hematogenesis is present, the blood findings may approximate closely those of the pernicious disease. In such cases as these, in which a pathologic process sufficient to cause the anemia is problematic, but not actually demonstrated, it may take the autopsy to decide to which class the anemia actually belongs. Of course if the case is seen early enough the probability is that the change from the secondary to the pernicious type could be traced definitely in the blood findings. Such a change has been traced by Lazarus. Ordinarily, however, cases like those under consideration come under observation too late for such help in the diagnosis.

In hepatic cirrhosis there is usually a more or less marked anemia of the ordinary secondary type; Ewing states, however, that cases with hemorrhage may terminate in the pernicious type.

My research has not been exhaustive, but so far no reference has been found to cases of hepatic cirrhosis without hemorrhage so terminating. I shall cite two cases, one pretty conclusive, the other but suggestive, perhaps from the lack of opportunity for further study of the blood.

A man of 55, in Ebstein's enviable stage of obesity—he was of medium height and weighed 211 pounds—with evident anemia, yellow-tinted skin, clear sclerae and an alcoholic history, came under my care over a year ago. The diagnosis was reduced to hepatic cirrhosis or else primary pernicious anemia. The abdominal fat precluded the definite determination of the size of the liver and the other signs and symptoms of cirrhosis were lacking. Though the postmortem examination showed 2,500 c.c. of fluid in the abdomen, it appeared to be a terminal process, for it was only late that suspicions were aroused on this point. In any case, since the pelvis may hold over a liter before the fluid begins to accumulate in the abdomen proper, and since Oestreich and de la Camp state that a clearly demonstrable collection of fluid in the abdomen usually means several liters, doubts on this point in the examination of a fat man were perhaps excusable. On the one hand was the alcoholic history suggesting a possible cirrhosis, and on the other the blood and whole aspect of the patient, suggesting rather a pernicious anemia. The blood examinations are detailed in the accompanying table.

The study of the blood, though not as complete as we could wish, shows a majority of the characteristics of the blood of pernicious anemia: The average number of erythrocytes 1,260,000, leucocytes diminished, lymphocytosis except toward the end of life when with no complications the polymorphonuclears rose, a condition noted by Ewing, color index continually above one,

4. Deutsch. med. Wchnschr., 1907, No. 29.