

On the whole, it may be said that a milk-poor, restricted diet with addition of cereal, the exclusion of eggs and meat broths, as a rule, yields good results in a short period of time. Older infants should also be given fruits and vegetables.

Langstein reports a case in which the Finklestein treatment failed absolutely. The patient finally recovered after the internal administration of large quantities of salt. Czerny emphasizes the necessity of treating any underlying hereditary factor which may have been operative in the production of the disease. The administration of thyroid extract has done well in some cases.

100 State Street.

ABSTRACT OF DISCUSSION

DR. D. E. ENGLISH, Summit, N. J.: In making ointments I use unhydrated lanolin and soften it with lard oil, and in that way use only the animal fats.

THE SERUM TREATMENT OF EPIDEMIC MENINGITIS*

FRANK SPOONER CHURCHILL, M.D.
Assistant Professor of Pediatrics, Rush Medical College
CHICAGO

The bacteriology of meningitis is most varied and the cases may be divided into two groups, the tuberculous and the non-tuberculous. The tuberculous cases are due to invasion of the meninges by the bacillus of tuberculosis, the non-tuberculous to invasion by a great variety of organisms. The great majority of the latter group consist of those cases due to the *Diplococcus intracellularis* of Weichselbaum, 80 per cent. of non-tuberculous cases being due to this organism. It is familiarly known as epidemic meningitis. For the treatment of this particular form of meningitis we have now had for about two years a specific serum evolved by Simon Flexner. It is with this type of meningitis, and this alone, that this paper deals. It is with this type of meningitis, and this alone, that the Flexner serum is effective. It is useless in all other forms. This statement seems necessary in view of the requests which have been made of me to use the serum in tuberculous meningitis, in non-tuberculous meningitis due to the pneumococcus, to the streptococcus, in head injuries, and in meningitis occurring in the course of the various infectious diseases and secondary to intestinal infections. The specific nature of the serum must be borne distinctly in mind. It will do no more good in a pneumococcal or streptococcal meningitis than will diphtheria antitoxin in a pneumococcal or streptococcal tonsillitis.

The development of the serum is interesting. Flexner, studying the New York epidemic of meningitis in 1894, sought to influence favorably the course of the disease produced experimentally in animals by antisera prepared in several kinds of animals from *Diplococcus intracellularis*. His first reports showed that the course of the disease in guinea-pigs and monkeys could be modified favorably and animals saved from the fatal effects of the diplococcus.

Subsequently Flexner and Jobling developed a diplococcus antiserum, prepared from the horse, which has now been used for about two years in the treatment of epidemic meningitis in man. They have collected up

to date reports of about 600 cases, and the results in these cases justify the opinion expressed by them in an earlier publication: "It is our belief that the analyses of histories of cases of epidemic meningitis which have been presented furnish convincing proof that the anti-meningitic serum, when used by the subdural method of injection in suitable doses and at proper intervals, is capable of reducing the period of illness; of preventing, in a large measure, the chronic lesions and types of the infection; of bringing about complete restoration to health in all but a small number of cases, the recovered, thus lessening the serious, deforming and permanent consequences of meningitis, and of greatly diminishing the fatalities of the disease." Their cases, taken as a whole, show a mortality of 25 per cent; in a few serious cases, in which treatment was begun within the first three or four days, the mortality was 11 per cent. Furthermore, among the 75 per cent. of recoveries, there were few of the serious sequelæ generally noticed after this infection. Hitherto the mortality in epidemic meningitis has ranged from 75 per cent. to 80 per cent., and among the patients who survived the persistence of serious sequelæ has been so great that their survival has been considered unfortunate. In other words, treatment of this infection by the Flexner serum has reversed the proportion of deaths and recoveries.

I have had the opportunity of watching the effect of the serum in 41 cases of meningitis, 29 of which have been proved to be of the meningococcal type. In these 29 proved cases, 16 patients have recovered and 13 have died, a mortality of 44 per cent. Closer analysis of the series shows that of 16 patients receiving the serum within the first week, 6, or 37 per cent., died. Of these 6 cases, 3 were fulminating and the patients died within the first two days; the fourth was a bartender aged 43 and the other 2 were not closely followed up, but each received only one dose of the serum.

This series of cases represents only one of many series, reports from all of which are sent to Flexner, for analysis by him, from time to time. His figures therefore are a better average test of the serum than are my smaller ones. It will be noted that the average mortality in my series is much higher than in the grand total of all series. I attribute this higher mortality in my series to the fact that many of the patients were treated in their own homes, at widely separated points in three different states; hence the difficulty of following them closely and giving repeated doses of the serum. On the other hand, those patients treated directly under the eye, in hospital, as a rule have done better than those treated at home. It is the latter group which have raised the mortality rate. I have therefore come to the conclusion that it is extremely desirable to send meningitis patients to the hospital; they can be watched more closely, the serum can be given more persistently and thoroughly; furthermore, more exhaustive and extensive laboratory investigations, as to blood, spinal fluid, etc., can be carried out in hospitals; the advisability of these investigations is especially great in those early days of the serum, when more accurate knowledge as to its exact action is desired.

Cases studied in detail show several interesting phenomena which have to do with the mortality rate, the method of termination, the general course of the disease and the effect of the serum on the spinal fluid.

The most striking thing, of course, is the high percentage of perfect recoveries, i.e., recoveries without serious sequelæ, and an especially low rate of mortality

* Read in the Section on Diseases of Children of the American Medical Association, at the Sixtieth Annual Session, held at Atlantic City, June, 1909.

among those patients treated early in the disease, this mortality rate being as low as 10 per cent. in some series of patients treated within the first three or four days. Then the abrupt termination of the disease by crisis, in certain cases, has been most striking. Thus in 273 cases of recovery, Flexner and Jobling report 25 per cent. as terminating in this way.

EFFECT ON THE COURSE OF THE DISEASE

The course of the disease is materially shortened by the serum and a turn for the better is often noticed soon after the first injection; the mentality is clearer, there is less headache and general pain, the temperature is lower and the general condition of the patient seems improved. The rigidities, however, are apt to persist, e. g., the stiffness of the neck, Kernig's sign, etc. It is a remarkable sight to see in the children's ward, for instance, a patient twelve to eighteen hours after an injection, lying with head thrown back, perfectly comfortable and rational, or perhaps even playing with his toys—the same patient who previous to his injection was tossing about in delirium, with headache, high temperature and all the signs of a severe infection.

EFFECT ON THE SPINAL FLUID

Effect of the serum on the spinal fluid is most interesting and is perhaps more demonstrable in this direction than in any other. The first puncture usually shows a fluid turbid in varying degree; smears from this fluid stained by the Gram method show a variable number of leucocytes, chiefly of the polymorphonuclear variety, and numerous Gram-negative diplococci, some intracellular, but more extracellular. Cultures on different media show an active growth, examination of which confirms the observation of the smears, i. e., a Gram-negative diplococcus. The first injection of serum is now given. Eighteen or twenty-four hours later the second puncture shows a fluid still turbid, more or less so than the first according to the progress of the case and *pari passu* an increased or diminished number of leucocytes, still of the polymorphonuclear variety. But bacteriologically we already see a change: there are more of the diplococci within the cells and fewer without than there were at the first puncture, i. e., phagocytosis has been going on to a considerable extent; at this time the number of cocci extracellular may exceed those intracellular, but with the progress of the case, whether favorable or unfavorable, the extracellular organisms gradually disappear entirely, the number within the cells at first increasing and later diminishing until they too disappear. The more rapid the progress of the case toward recovery, the more rapid the phagocytosis and the total disappearance of the organisms from the spinal fluid. The more protracted the case, the more persistent are the organisms; especially is this so in cases coming late under treatment.

The cultural character of the organisms changes with the progress of the disease; at first profuse, abundant growths are noticed on the media; gradually, however, they grow more slowly, less abundantly, less characteristically, and finally cease to grow. After they cease to grow on cultures, however, they may still be detected in smears; they are present, but apparently dying and too weak to take root and grow: in a short time they disappear from the smears also, of course.

THE CELLULAR ELEMENTS

The behavior of the cellular elements of the spinal fluid is also interesting. At the first puncture the

leucocytes are numerous, remarkably so in some cases, and invariably of the polymorphonuclear type, 90 to 95 per cent. usually. If the case progress favorably the total number diminishes; they lose their characteristic morphology and staining qualities; the proportion of mononuclears is very apt to increase; indeed, in a few long-drawn-out cases the mononuclears have formed a large percentage of the cells.

TECHNIC

The method of giving the serum is important and I now describe it in detail.

All the active workers with the Flexner serum are of the opinion that, in order to get the best results, the serum must be brought closely in contact with the pathologic seat of the disease and that this can be done only by a lumbar puncture. It is useless to give it subcutaneously. After study of my own cases and those of other observers I have come to the following conclusions as to the method of using the serum:

In all cases which clinically resemble meningitis we must do a lumbar puncture; for this purpose we may use the needle of either a large antitoxin syringe or of a large aspirator, holding at least 30 c.c., the minimum dose to be given. Both patient and apparatus, of course, are to be surgically clean. The serum should be ready for injection. The puncture is to be made according to the usual rules laid down in text-books, i. e., in the third or fourth lumbar space, close to the spine, this point being determined by the imaginary line running from crest to crest of the ilia. The needle once in the spinal canal, the fluid begins to flow out; rarely is there any obstruction from clogging of the needle; if so it should be cleared with the obturator. The pressure of the fluid should be noted if possible with the sphygmomanometer or roughly by counting the number of drops per minute; its turbidity and color should also be noted.

Collect a few drops of the fluid on clean glass slides for immediate staining and microscopic examination. Also inoculate several test-tubes of culture media by allowing the fluid to trickle directly over the media; finally collect the remaining fluid in a sterile test-tube for counting the contained leucocytes and centrifuging for further examination. Evacuate in all 30 to 45 c.c., if possible. If it be the least bit cloudy or turbid inject the serum at once, without waiting to learn the result of even the smears, injecting as follows: To the needle still in the spinal canal attach the syringe previously filled with the serum (warmed to about the body temperature). Inject slowly, using only gentle pressure in forcing down the piston, give 30 to 45 c.c., except in small babies in whom a smaller amount may be used. Thirty c.c. may be given even if the amount of spinal fluid removed is less than this. It is desirable, though not necessary, to remove spinal fluid equal in amount to the serum to be given.

EXAMINATION OF THE SPINAL FLUID

The spinal fluid should be examined immediately. The glass smears are stained by the Gram method and examined for both cellular elements and organisms; care should be taken to note the relative number of diplococci within and without the leucocytes. Fortunately the smears are fully as reliable as the cultures; hence we do not have to wait long for an exact diagnosis. The cultures should, of course, be incubated and examined later. The total number of leucocytes in the spinal fluid should be counted by the Thoma-Zeiss apparatus as soon after evacuation as possible.

REPETITION OF THE SERUM

If the bacteriologic examination show the presence of the diplococcus subsequent injections of the serum should be given. In the earlier days of the serum it was customary to wait, if improvement followed the first injection, until unfavorable symptoms developed, e. g., increased temperature, great restlessness, pain, headache, etc., and then give the second dose. Subsequent observations, however, especially by Dunn, have shown that better results are attained by giving the serum daily for three or four successive days, regardless of the clinical and bacteriologic progress of the case. The serum can do no harm, and this concentrated method of giving it is undoubtedly better than waiting

mediate relief to the pain and apparent permanent improvement. Cushing has reported a similar case.

The following brief histories illustrate some of the points mentioned in this paper.

CASE 1.—This illustrates the disadvantage of coming late under treatment and the futility of giving small doses, scattered and in part subcutaneously. The patient, a nine-year-old boy, left the hospital apparently well, on the thirty-eighth day, but returned in three weeks with meningeal symptoms, from which he finally died five weeks later, the spinal fluid during this second stay in the hospital being sterile.

Chart 1 shows the temperature curve and method of dosage. It is a good illustration of how *not* to give the serum.

CASE 2.—George D., aged 3, entered my service at Cook County Hospital, April 13, 1909, on the fifth day of illness.

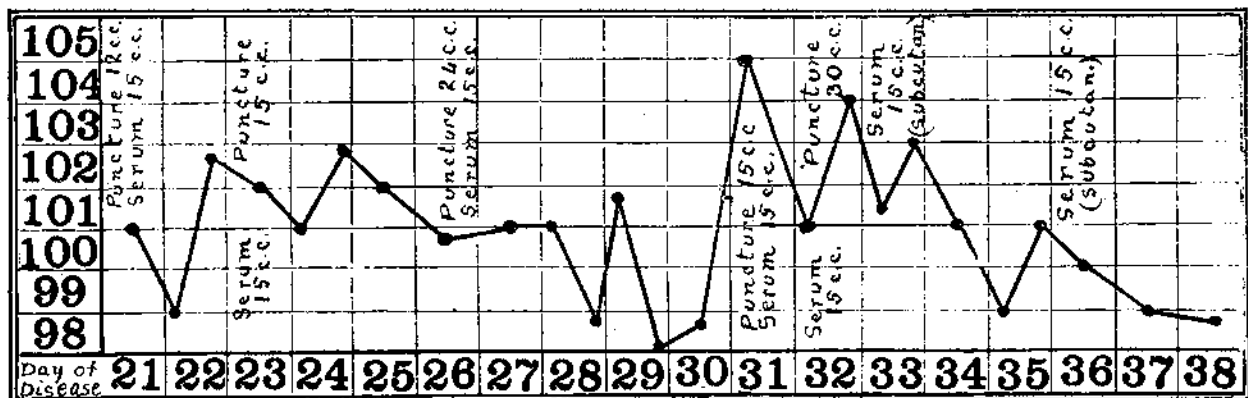


Chart 1.—Temperature curve in Case 1.

for symptoms to arise and then hitting them. In severe and fulminating cases the second dose should be given in from twelve to eighteen hours after the first, and 45 c.c. should be given. In several instances I have used this amount of serum without bad results, even though less than this amount of fluid had been removed.

Having thus given our first series of three or four doses on successive days, we may pause and note results; as a rule, improvement will be seen both clinically and bacteriologically, and no further injections will be necessary, at least in patients coming early under treatment. But if after an interval of a day or two untoward symptoms still persist another series of doses should be given daily, perhaps for two days, perhaps for four days, then another pause be observed. This process of alternate giving and withholding of injections may be continued until meningeal symptoms have ceased or bacteria have entirely disappeared from the spinal fluid, or the chronic stage has been established. As a rule, it will be found that the diplococci disappear comparatively early, and that we may then cease our injections. If the serum is to be effective it will be so early in the disease after a few doses. If, however, the organisms persist in the spinal fluid for a long time occasional doses should be given. In all cases, whether those of complete recovery or those running on into the chronic stage, lumbar puncture should be done from time to time until no organisms are found either in smears or cultures. We must leave our patient with a sterile spinal fluid.

Relapses should be treated as fresh cases. Certain complications, if due directly to the meningococcus, may be an indication for the local use of the serum. Thus in one of my series a severe arthritis of the knee, proved by bacteriologic examination of the aspirated fluid to be due to the meningococcus, received three doses of 15 c.c. each, given directly into the joint, with im-

mediate relief to the pain and apparent permanent improvement. He was given 30 c.c. of serum on each of the two following days, then through a mistake, none on the next two days, with consequent increase of symptoms, was then given 30 c.c. on each of the following four days, the last on the thirteenth day of the disease, with satisfactory results. The spinal fluid was sterile at the last puncture. The case illustrates the danger of ceasing injections too early and the value of sufficiently prolonged daily doses.

CASE 3.—A seven-year-old girl received her first injection on the second day. The case terminated by crisis after only two doses of the serum. Chart 3 tells the story graphically.

CASE 4.—In the case of Nately C., aged 15, the serum was not used persistently enough, and consequently we see a long-drawn-out case, though the patient finally recovered after in-

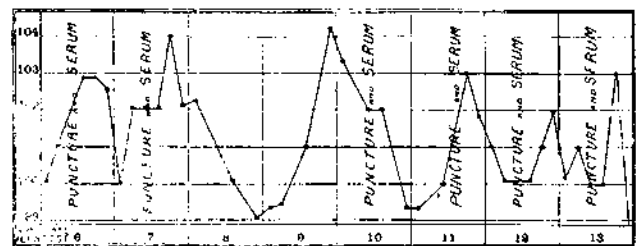


Chart 2.—Temperature curve in Case 2.

dividual, isolated doses at long intervals. The serum was given on the ninth, tenth, fourteenth, seventeenth, twenty-fourth, twenty-sixth and thirty-sixth days, respectively, the spinal fluid on the last date being sterile. The case also illustrates the value of perseverance in the use of the serum, even late into the disease. The patient was discharged from the hospital on the forty-third day.

CASE 5.—This case, from the service of Drs. Poorman and Ellis Kerr, at the Oak Park Hospital, was a severe fulminating case. The patient, Amelia D., was given her first injection twenty-three hours after the onset, with marked improvement in the general condition, temperature and spinal fluid. The injection was repeated on the second day, omitted on the third with increase in symptoms, given on the fourth and fifth days.

with diminution of the meningeal symptoms, but continued high temperature due to arthritis of the right knee joint. Fluid aspirated from this joint showed the meningococcus; serum, 15 c.c., was therefore injected directly into the joint on the ninth, tenth and eleventh days respectively, with much relief to the pain. Serum, 30 c.c., was also injected into the spinal canal on the seventh and ninth days, respectively, the fluid from the last puncture being sterile. A further complication, apparently an osteomyelitis of the right femur, prolonged the convalescence,

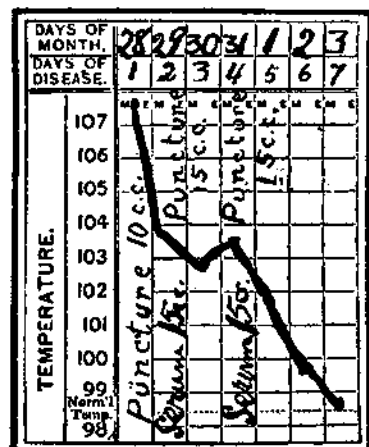


Chart 3.—Temperature curve in Case 3.

escence, but this also eventually disappeared and the patient has now, June 9, had a normal temperature for two weeks and is steadily improving.

The actual disease itself, the meningitis, in this case, was evidently checked by the first two doses of the serum, as was demonstrated, not only by the diminution in the meningeal symptoms, but also by improvement in the character of the spinal fluid. The termination of the disease itself was by crisis; indeed, it might almost be said that it aborted, so sudden and remarkable was the drop in the temperature. The prolonged character of

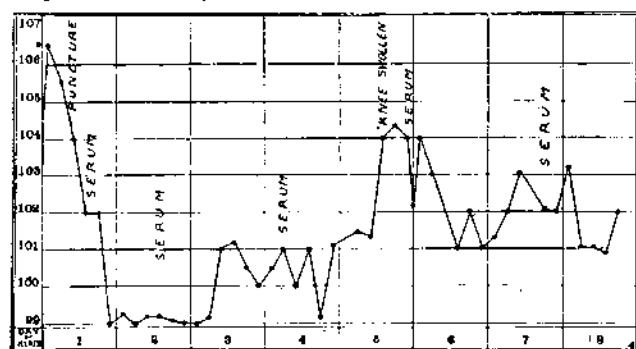


Chart 4.—Temperature curve in Case 3.

the case was due to the complications, over which the serum had no apparent control, aside from the relief of joint pain when locally applied.

SUMMARY

The main points in this paper may be briefly summarized as follows:

1. In all cases clinically suggesting meningitis, do a lumbar puncture as early as possible.
2. If the fluid thus obtained be turbid, immediately inject at least 30 c.c. of Flexner serum directly into the spinal canal without waiting to hear the bacteriologic report of the fluid.
3. Examine the spinal fluid bacteriologically. Smears are more important than cultures. If the *Diplococcus intracellularis* be found, repeat the injections daily for

the three or four following days; in severe cases give the second dose twelve hours after the first.

4. After the first series of doses, wait two or three days, and if necessary, repeat the series.

5. The serum is a specific and of value in meningococcal meningitis only.

6. It is useless to give the serum subcutaneously.

439 North State Street.

ABSTRACT OF DISCUSSION

DR. CHARLES HUNTER DUNN, Boston: The mortality of this disease at the Children's Hospital in Boston for the past ten years may be interesting. The average number treated was twenty, i.e., cases in which lumbar puncture confirmed the diagnosis of infection with the diplococcus intracellularis. Up to 1902 there was no particular treatment. In 1903-04-05 the condition was treated by repeated lumbar puncture. In 1906 we gave the diphtheria serum a trial, and in 1907 used a vaccine prepared from the diplococcus intracellularis. It was from November, 1907, to November, 1908, that the Flexner serum was first used. During the preceding nine years the mortality had varied from 60 to 80 per cent.—in fact, the mortality was not affected by the treatment. During the last year the mortality dropped to 19 per cent. Dr. Churchill was right in saying that I gave 45 c.c. of serum without getting any spinal fluid. Twice I have seen serious symptoms of collapse in babies from a large dose of the serum without withdrawal of a sufficient amount of fluid.

There are three classes of these fatal cases; first, the fulminating cases, in which the babies die before the serum has time to get in its work; second, the late cases in which so much damage had been done before the serum was given that the patient dies from the injury already inflicted on the nervous system. The third are the resistant cases. There is a type of case in which the organism disappears entirely yet there is no abatement of the symptoms. It has been thought by Flexner that this is due to a complete closure of the canal, as in some of these cases at autopsy there was found within the ventricles an enormous number of organisms. But there are cases in which the serum has practically no effect on the fluid or the symptoms. Recently we had two cases in which no effect at all appeared. I think possibly one explanation of that type of case is that it may be due to a variety of the *Diplococcus intracellularis* that is particularly resistant. Dr. Flexner wants any one who comes across such a case to send him a strain of the organism that he may inject his horses with it and get an effective serum for treatment.

DR. ALFRED HAND, Philadelphia: In the Children's Hospital in Philadelphia we have had but one case of the epidemic form treated with the serum, and this case worked very well. The first day we obtained 45 c.c. of fluid and got the *Diplococcus intracellularis*. On the second day I withdrew 45 c.c. of fluid and injected 30 c.c. of the serum. On the third day I did the same. On the fourth day I could get but 15 c.c. of the fluid and the child was greatly improved. I thought that I was justified in putting in 30 c.c. again and I did so with very little pressure. A couple of hours afterward the child was seized with a violent headache and was screaming with pain, but morphin relieved it, and in five days the child was perfectly well. I have seen cases run on for eleven, twelve, or thirteen months and then the child would die, one occasionally getting well. This case just mentioned was the first case in which we felt that the treatment had had some effect in curing the patient. I felt that there was no harm done by injecting a larger amount of serum.

DR. FRANK ALLEN, Chicago: I have had several cases of cerebrospinal meningitis treated with Flexner's serum. My experience has been much like that of Dr. Churchill. Often lumbar puncture alone would cause the temperature to drop, but without the injection of the serum it would rise again. With the injection of three or four doses of serum the temperature would drop and remain down. In one case in which I could not find the organism the patient died before I could make an injection. Another patient had all the symptoms of pneumonia. On the third day this patient developed cere-

bral symptoms, puncture showed the diplococcus; the serum was used with almost immediate improvement. In this case we had difficulty in getting out enough fluid. We used 15 c.c., and at one time 30 c.c., without any trouble. The spinal fluid cleared up and no diplococci could be found, but the pneumonia continued and the patient was in the hospital for three weeks with pneumonia, without recurrence of spinal symptoms. In most of the cases the temperature rapidly dropped after treatment.

Dr. WILLIAM M. WELCH, Philadelphia: I have seen Flexner's serum used in a large number of cases of cerebrospinal meningitis in our Municipal Hospital and I regret very much that I have no exact data at hand to show the results. The members of the hospital staff feel sure that the death rate has been considerably reduced by the serum treatment. We have found that it is more useful in the true form of the disease, in which the *Diplococcus intracellularis* is present. But I rise more particularly to speak of an unfortunate result in one instance. The patient was a negro, who was admitted to the hospital with well-marked symptoms of cerebrospinal meningitis. Lumbar puncture was done, but no fluid flowed out. The direction of the needle was changed once or twice, but still no fluid was obtained. It was determined, however, to inject the serum. The patient was sitting in the upright position with his arms and chest resting on the foot of the bed; 15 c.c. were injected without any symptoms, but before the entire contents of the second bottle of 15 c.c. had been used the man complained of severe pain in his head; his head dropped forward and he became unconscious. The respirations were very slow, not more than eight or ten a minute. The breathing was stertorous. The patient never regained consciousness, and died within fifteen or twenty minutes. I should conclude from this experience that it is dangerous to introduce into the spinal canal any considerable amount of the serum without first withdrawing a similar amount of the spinal fluid.

Dr. GEORGE D. SCOTT, New York: It is important to lay particular stress on the fact that the *Diplococcus intracellularis* should be found before the employment of the serum. In the epidemic in New York City some time ago I saw a number of cases in the hospital and in private practice and it was a question often of an absolute diagnosis from lumbar puncture alone. In many cases a wrong diagnosis had been made, sometimes due to the fact that the bacteriologist was not so well informed as he might have been. I find that it is better to inject a small amount of serum more often and not to allow too much of the spinal fluid to escape at each injection. Bearing those points in mind, we can get more benefit from the serum as Dr. Flexner has stated.

Dr. F. S. CHURCHILL: I have had the same experience of injecting more serum than we have removed fluid. I would emphasize what Dr. Scott says that it is of the utmost importance to remember that the serum is a specific. I think I must have been misunderstood by one of the gentlemen. I did not say that the serum was of more value in the epidemic form. It is of no value whatever in any other form of the disease. It is a specific for epidemic cerebrospinal meningitis and that fact must be borne in mind. In regard to the unfortunate termination of the case reported from Philadelphia I do not know whether the fact that the patient was sitting up had anything to do with it, but I never have given it to a patient sitting up. In one case of a baby, two years old, where I had employed two successive doses, I used an anesthetic at the third injection. It was a mild case and the baby was pretty thoroughly conscious. I removed the fluid, injected the serum, withdrew my needle and the child seemed all right. But suddenly the breathing stopped and, though we worked with her nearly an hour, she died. In that case the fluid was almost sterile at the last examination. I think I should use gas another time instead of any other anesthetic. We must remember that the serum must be given as early as possible, it must be given in the spinal canal and it must be repeated until the organisms are not found in the spinal fluid.

Practice of Medicine.—The everyday internist can and must be able to practice medicine scientifically. The most important aid to this end is a clinical laboratory properly equipped.—O. I. Halbert, in *Texas State Journal of Medicine*.

HEMOLYSIS OF HUMAN AND RABBIT ERYTHROCYTES BY CROTALUS VENOM *

JOSEPH McFARLAND, M.D., AND PAUL G. WESTON, M.D.
PHILADELPHIA

The first studies of the hemolytic action of serpents' venoms seem to have been made by Stevens and Myers,¹ who found that when cobra venom was added to shed blood, *in vitro*, destruction of the corpuscles (hemolysis) and retardation of coagulation took place. They also found the hemolytic power of the venom inhibited by antivenomous serum.

Myers² later studied the hemolytic substance—"cobralysine"—of the venom and found it destroyed by heat. During these studies he found that the susceptibility of the erythrocytes to cobralysine *in vitro* bore no relation to the susceptibility of the animal to subcutaneous intoxication by venom.

Stephens³ found that the hemolytic constituents of different venoms were not identical.

Myers⁴ made further studies of venom hemolysins and serum antihemolysins.

Mitchell and Flexner⁵ and Flexner and Noguchi⁶ have further studied the phenomena of agglutination, hemolysis, leucolysis, and the germicidal activity of the blood serum. They found that the phenomena of agglutination appeared rapidly in favorable solutions, while in weak solutions a delay of some minutes up to an hour might be noted. Active agglutination took place in 0.2 per cent. solutions, while weaker ones either produce no change at all or show imperfect fusion. They studied corpuscles of the dog, rabbit, guinea-pig, sheep, ox, pig, necturus and frog. The phenomena of hemolysis were found to be complicated. Solutions of 0.2 per cent. were found most favorable for bringing out the hemolytic property, though the different venoms differed considerably, cobra venom being most active, water moccasin, copperhead and rattlesnake venoms less so in the order named. They also found that the corpuscles of different animals differed in their susceptibility to the action of the venom, those of the dog's blood being most easily affected, those of ox blood least so. The intermediate animals in order of susceptibility were sheep, guinea-pig, pig and rabbit. Solutions of 5 per cent. were needed to hemolyze the corpuscles of the ox. Heating to from 75 to 80 degrees C. for 30 minutes does not diminish the hemolytic action of any venom; heating to from 90 to 96 degrees diminishes the activity of rattlesnake venom; heating to 100 degrees C. for fifteen minutes diminishes the hemolytic activity of cobra, moccasin and copperhead venom a little. They believe that venoms contain various intermediate bodies, not all of these being absorbed by any one kind of corpuscles. Venom leucolysis was carefully studied and it was found that venoms contain principles that are agglutinating and dissolving for the white corpuscles of which the agglutinating principle may be identical with those for the erythrocytes. The leucolytic principle is distinct from the hemolytic principle. The several varieties of white cells show different susceptibilities to the action of the venom.

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Sixtieth Annual Session, held at Atlantic City, June, 1909.

1. Brit. Med. Jour., Mar. 5, 1898, p. 621.
2. Jour. of Path. and Bact., 1899-1900, p. 415.
3. Jour. of Path. and Bact., 1899-1900, p. 273.
4. Trans. of the Path. Soc., London, Feb. 6, 1900.
5. National Academy of Sciences, 1901.
6. Jour. Exper. Med., March, 1902, vi, 3, p. 277.