Treatment of Septic Meningitis by Intra-Carotid Serum Therapy*†

Report of Two Cases of Pneumococcus Meningitis and One of Meningococcus Meningitis

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IN THE treatment of any form of meningitis it is of utmost importance to bring our medication in as great a concentration and as close proximity as possible to the greatest area of disease. Intra-spinous was the first improvement over intravenous therapy in this direction and combined with the latter is often successful in the treatment of meningococcus meningitis. The next step was intra-cisternal injections[1], then intra-ventricular, and finally intra-arachnoid injections together with various combinations of these methods. All of these procedures often fail when plastic exudates have caused sub-arachnoid blocks.

Hirsch, Myerson and Halloran[2] first used intra-carotid injections of arsenicals in the treatment of general paresis. Kolmer[3], et al, following this lead, injected pneumococcus serum and numoquin-base into the carotid arteries of dogs in which they had induced pneumococcus meningitis. They attained 66% cures in these dogs after disappointing results in curing control animals of experimental pneumococcus Type I meningitis by combined intra-carotid, intra-cisternal and intra-spinal injections of anti-pneumococcus serum and numoquin-base.

It is most important to deliver our antibodies to the cerebral and basal meninges in as great concentration as possible. Lumbar intra-thecal India ink injections in cadavers have been found by Ayers[1] to diffuse higher than the cervical region only to a very limited extent. Intra-cisternal injections enable the India ink to reach the basal and cerebral cortical meninges. However, Kolmer[4] found that many of his failures to cure experimental septic meningitis by cerebral sub-arachnoid injections were due to remaining foci of plastic meningitis over the cerebral meninges. Therefore, even sub-arachnoid injections often fail to eradicate the disease here because of plastic exudates blocking the diffusion of antibody solutions over the surface of the cerebral hemispheres. Intra-carotid injections allow the serum to be brought to the cerebral meninges directly with a minimum of dilution and

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sub-arachnoid blocks can have no effect in inhibiting its diffusion. Kolmer[3] states that precipitin tests after intra-carotid injections of antibody serum into normal animals have proved the presence of antibodies in the spinal fluid. Some of the serum is certainly lost through the external carotid artery, but this being the smaller branch, the loss is comparatively unimportant.

As suggested by Kolmer, we have tried the combined intra-carotid, intra-cisternal and intra-spinous injections of Huntoon's antibody solution plus ethylhydrocuprein base together with cisternal and spinal drainage in two cases of pneumococcus meningitis with failure. The first of these two cases, a girl of eighteen, had a stiff neck and vomiting for two days before entering the hospital. Fifteen cubic centimeters of turbid spinal fluid under great pressure containing 1,250 pus cells per cubic millimeter were replaced by ten cubic centimeters of anti-meningococcus serum. A smear stained immediately by Gram's method showed Gram positive encapsulated pneumococci, confirmed by culture. The next morning, the third of her illness, both carotid arteries were exposed under light ethylene anesthesia and twenty cubic centimeters of a mixture of Huntoon's pneumococcus antibody solution and five cubic centimeters of 1% numoquin-base were injected into each artery through a small guage hypodermic needle. Immediately after, a cisterna magna puncture was made, eight cubic centimeters of bloody spinal fluid were withdrawn, and replaced by ten cubic centimeters of the same mixture as above. There was no untoward reaction but five hours later the patient died very suddenly from what seemed clinically a cerebral embolism.

The second fatal case of pneumococcus meningitis was secondary to a long debilitating illness with measles, otitis media and mastoiditis in a girl of seven. The only meningeal symptom was gradually increasing stupor, but no clinical signs of meningitis developed before treatment for meningitis was instituted. Meningitis was first suspected on the forty-second day of illness when lumbar puncture yielded six cubic centimeters of cloudy spinal fluid under increased pressure containing 260 lymphocytes and 1,000 pus cells. The smear stained by Gram's method showed Gram positive diplococci present. In the next four days six intravenous injections of forty to fifty cubic centimeters of Huntoon's pneumococcus antibody solution were administered. Five spinal drainages and five simultaneous intra-spinal injections of four to ten cubic centimeters of Huntoon's solution plus 1% numoquin-base were given in the same four days. During these days the temperature had dropped from a daily height of 104° to 102° and the pulse from 150 to 90. On the sixth day the spinal fluid still being cloudy and definite meningeal signs having now developed desperate measures were considered justified. Under ethylene anesthesia both carotid arteries were exposed and eleven cubic centimeters of Huntoon's pneumococcus antibody solution plus five cubic centimeters of 1% numoquin-base were injected into each carotid artery. The cisterna magna was immediately drained of ten cubic centimeters of cloudy fluid and six cubic centimeters of the antibody solution plus one cubic centimeter of 1% numoquin-base injected. The patient never recovered consciousness and died seven hours later. The culture showed a mixed streptococcus viridans infection.

Following these two failures an apparently fulminating case of meningococcus meningitis presented itself in which coma had developed within twelve hours of the first signs of meningitis. It seemed advisable to us to try to reach the cerebral and basal meninges with antiserum in such a case as thoroughly as possible.

Case Report: A farmer of forty-two was admitted to the hospital February 19, 1930, unconscious. Three days before he had caught cold. On the morning of the third day he had a terrific headache and the same evening became unconscious. On admission the temperature was 102°, pulse 88, respiration 20, and white blood count 24,250. The pupils were regular, equal and reacted to light. There was haziness of both optic discs, a purulent discharge from both nostrils, congested pharynx and herpes about the mouth. The neck was very rigid. The knee jerks were exaggerated bilaterally, ankle clonus was present on both sides with bilateral positive Babinski together with positive confirmatory Oppenheim and Gordon signs. Kernig's sign was elicited bilaterally. Spinal fluid on entrance was cloudy with a cell count of 12,000, about 80% of which were pus cells. Gram positive diplococci were seen in the smear. The culture was reported positive for meningococci. Fifteen cubic centimeters of antimeningococcus serum were given intraspinally at the same tap. For the next three days a daily intra-carotid injection of antimeningococcus serum was given, combined with cisterna puncture and serum injections. Both arteries were exposed in the neck, no anesthesia being required the first day, and under light gas anesthesia on the second and third days. Five cubic centimeters of antimeningococcus serum were in-

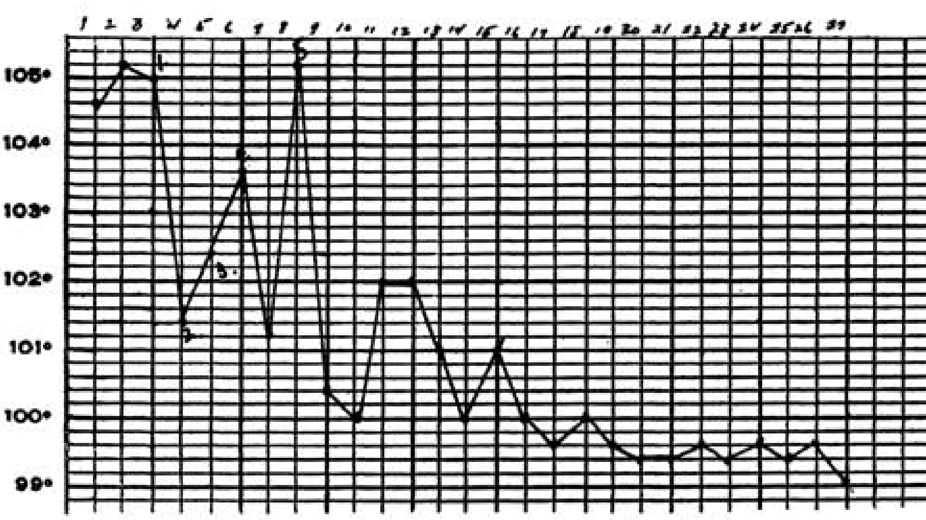

CHART I. Condensed temperature chart giving highest temperature each day. Points 1, 2, and 3 indicate intra-carotid and cisterna magna medication. Point 5 indicates highest temperature reached during serum sickness.

Antimeningococcus serum was given intraspinally daily the first seven days in the hospital, then every other day for the next ten days, then every third day for the next nine days. Last injection after lapse of one week.

In all, 350 cc. of antimeningococcus serum were given by various routes.

jected slowly into each common carotid artery with a small hypodermic needle. There was no bleeding following withdrawal of the needle though on one occasion a small hematoma formed in the wall of the vessel. Ten cubic centimeters of turbid spinal fluid were withdrawn from, and ten cubic centimeters of antimeningococcus serum were injected into, the cisterna magna at each cisternal puncture. The first two days he also received serum intravenously and intraspinously.

The evening following the first intra-carotid and intra-cisterna magna treatment the patient recovered consciousness. He received ten to twenty cubic centimeters of antimeningococcus serum intraspinally daily for the first two weeks in the hospital. Convalescence continued uneventfully except for a serum reaction on the eighth day when the temperature rose to 103.8°. The chart and table appended show the detailed progress of the case. The smear became negative for organisms in one week but the culture was not reported negative until the twenty-third day. We discharged him on the twenty-eighth day apparently recovered. When last heard from seven months later the patient was well. His home doctor reported that he started work one month after discharge from the hospital and that for four months he was quite deaf.

Table 1. Cerebral Spinal Fluid Examination of a Case of Meningococcic Meningitis—(Lumbar Puncture)

Date	Pressure	Character	Cells	Globulin	Colloidal Gold Curve	Wass.	Culture	Smear
2-18-30	Increased	Cloudy	12,000	Positive	0000112321	Neg.	Positive	Positive
2-20-30	Increased	Cloudy	8,000	Positive			Positive	Positive
2-22-30	Normal	Translucent	2,750	Positive	0000012332	Neg.	Positive	Positive
2-25-30	Normal	Translucent	5,280	Positive		Neg.	Positive	Negative
2-27-30	Normal	Translucent	2,120	Positive				
3- 1-30	Normal	Transparent	1,620		0000012332	Neg.	Positive	Negative
3- 6-30	Normal	Fairly clear	340					
3-13-30	Normal	Clear	130	Positive	0000012332	Neg.	Negative	Negative

*A clear jelly-like clot formed on standing fifteen minutes.

Conclusions

1. On theoretical and experimental grounds intra-carotid combined with intra-cisternal serum therapy would seem the most efficacious method in treating an infectious process in the cerebral meninges.

2. Two cases of pneumococcus meningitis were treated unsuccessfully by this method.

3. A very fulminating case of meningococcus meningitis was treated successfully, the patient regaining consciousness eight hours after the first treatment.

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