REFRACTORY OR SO-CALLED "FAST" CASES OF MENINGOCOCCUS MENINGITIS *

HENRY HEIMAN, M.D.

NEW YORK

It is well known that since the introduction of the antimeningitis serum by Flexner in 1906, the mortality of meningococcus meningitis has decreased from 75 or 80 per cent. to 25 per cent. or less. Despite this fact, it is obvious that in a small percentage of cases the treatment of this disease has not yet reached perfection. That this small number of cases does not respond to the serum, in spite of its accurate and prolonged use, gives us food for thought and compels us to inquire into the causes of the occasional failure with this method of treatment.

CAUSES OF OCCASIONAL FAILURE

These causes may be grouped as follows:

1. *Fulminating Cases.*—The endotoxins of the meningococcus may be so virulent as to make neutralization by the antimeningitis serum impossible. The action of the serum is dependent on the presence of a number of immune substances, bacteriolysins or antibacterial substances, bacteriotropins (opsonins) and antiendotoxins. When those substances are not present in sufficient quantity or are not of sufficient potency to overcome the endotoxins of the invading organism, we have the fulminating cases which practically always end in death, despite early diagnosis and prompt treatment. It is questionable whether a serum of sufficient concentration or strength can be obtained to combat successfully this rapidly fatal type.

2. *Incomplete, Insufficient or Unskilled Use of the Antimeningitis Serum.*—It is needless to dwell on this cause of the failure of the serum to cure, for it is a matter of common knowledge that, in general, the mortality statistics are the lowest when based on the experiences of the most competent observers and workers in this field.

3. *Unstable Nervous System.*—In infants, lack of success is often due to the existence of an unstable and delicate nervous system and to the early development of acute hydrocephalus.

4. *Intercurrent Diseases.*—Complications having no direct connection with the disease, as tuberculosis or pneumonia, may produce a fatal result, in spite of the beneficial action of the serum.

* Read before the Section on Diseases of Children at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

5. *Refractory Cases.*—Though few, these cases do occur and must be considered as constituting a distinct type. Although the meningococcus is found in the spinal fluid of these patients, the cases are little or not at all influenced by the injection of the serum. On that account they run a prolonged course of weeks or months, usually with high, septic temperature and occasional remissions in symptoms, until they finally result either in death or in a gradual protracted recovery. They are the “fast” cases, so called by Flexner, because they are supposed to be due to the existence of strains of meningococci which are fast to the serum employed.

It is only in recent years that fundamental biologic distinctions have been made between the various strains of the meningococcus. One strain is more resistant to solution by immune serum; another is more easily digested by the intraleukocytic enzyme; another more virulent when injected into animals—differences formerly never recognized. When this is taken into consideration, it is readily seen why certain cases do not respond favorably to the ordinary antimeningitis serum—they are produced by a strain of the organism which is refractory or fast to the serum used. They must not be confused with the type of cases described by Dopter, in which the clinical course is the same, but in which the infecting organism is not the meningococcus, but the closely allied parameningococcus, which possesses specific agglutinins and precipitins, does not react to the ordinary antimeningitis serum, but does respond beneficially to the serum prepared from its own cultures.

The following are reports of two refractory cases of meningococcus meningitis:

CASE 1.—M. S., aged 6. There had been no previous illness. Two days before admission there had been headache, vomiting and apathy, these symptoms having increased in severity to the date of patient's entrance to the hospital. The physical examination on admission revealed typical signs of meningitis, apathy alternating with irritability, rigidity of the neck, scattered petechiae, Macewen, Kernig and Brudzinski signs, a tache cérébrale and a moderate temperature. Lumbar puncture revealed cloudy fluid which was under considerably increased pressure and which showed the meningococcus in smears and cultures. Flexner's serum promptly introduced into the spinal canal failed to result beneficially, and instead of a rapid recovery, as was expected, the symptoms continued unabated for about a month in spite of repeated injections, given almost daily for the first week, then somewhat less frequently. The temperature remained septic in type; the restlessness, headache and signs of spinal irritability continued as on admission, and the spinal fluid at each puncture showed the meningococcus. At the end of four weeks the child's condition began to improve and kept steadily becoming better until the patient was finally discharged well, fifty-eight days after admission. The last culture of the spinal fluid, taken twenty-six days before discharge, still contained meningococci.

CASE 2.—J. H., aged 7½. The onset of this case was sudden, four days before admission, the child having complained of very severe headache and

pains in the neck and back. The patient had vomited several times and had had high fever. Physical examination showed the usual manifestations of meningitis—irritability, tache, Kernig, Babinski and Brudzinski signs and a petechial rash. On lumbar puncture 35 c.c. of cloudy fluid was withdrawn and found to contain the meningococcus. The fluid withdrawn at the third puncture, that is, after two injections of the Flexner serum, showed no meningococci in smears and in culture mediums. The symptoms, however, continued for five weeks. Repeated lumbar punctures were made, and although the fluid was always reported sterile after the second injection, the antimeningitis serum was injected on several occasions. The patient recovered after a protracted illness of nearly sixteen weeks.

It is interesting to note that these two refractory cases of meningococcus meningitis came from the same neighborhood, were infected at about the same period of time and failed to react to repeated injections of the antimeningitis serum.

To combat effectively these refractory cases illustrated by the above abstracts, it might be wise to culture the various strains of meningococci and to establish a "fast" antimeningitis serum to be used only in this type of infection, just as Dopter has prepared and used his antiparameningococcus serum; so that by this means we may eventually hope for a still greater diminution in the mortality of meningococcus meningitis.

30 West Eighty-Eighth Street.