At about this time she became euphoric and her depression departed; it was also noticed that her speech was becoming slurred. On October 11 slurring was more pronounced, and she volunteered the statement that she saw double on looking to the left. On examination her pupils reacted to light and accommodation, but the left pupil reaction was not sustained. There was no ptosis, and no abnormalities of the cranial nerves were detected except for weakness of both sixth nerves, especially the left. There was no weakness or altered sensation of the limbs, but all tendon reflexes were exaggerated; the plantar responses were equivocal. The fundi showed some blurring of the disk margins—about the same on both sides.

October 14.—Lumbar puncture was performed. The fluid was not under increased pressure; it was contaminated by blood, and so useless for further tests.

October 16.—The patient started vomiting, and did so several times daily for the next three days, the vomiting being unaccompanied by nausea.

October 19.—Speech was still slurred and there was marked euphoria. Slight facial weakness was observed on the left side only. The disks were still slightly blurred. There was intention tremor of both hands, more on the right; and dysdiadokokinesis of the right hand, with past-pointing to the right. The tendon reflexes were exaggerated; abdominal reflexes were absent on the left and weak on the right.

October 26.—The weakness of face and alteration of reflexes were much less marked. There was nystagmus, coarse and horizontal on looking to the left, finer and vertical on looking to the right. There had been very marked mental weakness, with delusions and hallucinations, during the preceding days, but this had slightly improved.

October 30.—Her speech had now become more articulate and lower in pitch, and her appearance was more that of a normal woman. Practically all physical signs had disappeared, except intention tremor on the right and some nystagmus on looking to that side.

November 17.—She was at this date discharged quite well, having been able to walk and to look after herself for over a week.

AFTER-HISTORY

November 26, 1937.—A little more than a year after her discharge the patient attended the follow-up department. She had been very well and fit in every way, both mentally and physically, and neither she nor her family had noticed any sequelae. On examination, reflexes, tone, power, and sensation were all normal, as were the fundi. There was slight intention tremor, more marked on the right hand. Dysdiadokokinesis was present on the right, and there was slight horizontal nystagmus on looking to that side. The position sense was normal.

Discussion

There would seem to be no doubt at all that this was a case of encephalitis beginning with multiple focal and diffuse lesions, and later concentrating on the cerebellar functions. Fortunately, the sequelae were minimal, affecting cerebellar function only and unaccompanied by mental defect or personality change.

The possible differential diagnosis of acute disseminated sclerosis would seem to be excluded on two counts: first, by the mental symptoms in the acute attack; and, secondly, by the absence of any further development in over a year.

Whether the illness followed an atypical attack of measles without the rash can be less certainly claimed. The existence of these *formes frustes* of measles is well recognized. Box (1937) states: "Some of the mildest attacks are aberrant, the rash failing to appear, and only Koplik's spots giving a clue to the disease." Blackfan (1933) says: ". . . the fever and catarrhal symptoms may follow the usual course with an eruption which is scanty or atypical. Koplik's spots are found even in the atypical cases." The same period of thirteen days existed between the illness of the first and the second child as between the second child and the mother, while the second child took longer than usual to develop the rash. In both their cases the measles was mild in type. The clinical development of the illness was such that there can be little doubt that it was measles. Koplik's spots were seen, and the chest symptoms and early photophobia were characteristic. Only the rash was lacking.

My thanks are due to Dr. C. H. Whittle for permission to publish the case.

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SULPHANILAMIDE THERAPY IN MENINGOCOCCAL MENINGITIS

REPORT ON THREE CASES

BY

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The following cases are considered worth reporting in view of the widespread interest in the treatment of meningococcal meningitis by drugs of the sulphanilamide group. Two of these cases were due to a Type I meningococcus; the second is included because, although bacteriological evidence was lacking, the case both clinically and epidemiologically was almost certainly of a similar type. The site of the disease in meningitis is accessible by spinal puncture, and the inflammatory exudate can be seen, estimated, and readily examined by cytological and bacteriological methods in a way that is rarely available in other acute infections.

Treatment

1. Prontosil soluble was given intravenously (20 c.cm. of a 2.5 per cent. solution), and this dose was repeated at eight-hour intervals for from two to three days. In addition $1\frac{1}{2}$ grammes of prontosil album were given in the twenty-four hours by mouth. The first two or three intravenous injections were followed almost immediately by vomiting, which was not repeated with subsequent injections; apart from this no ill effects were noticed.

2. All prontosil was stopped forty-eight hours after the cerebrospinal fluid became sterile and the cell count had dropped to a fairly low level. Contrary to L. J. Willien's experience this was not followed by a relapse; he continues the drug by the mouth for ten days after the symptoms and laboratory findings have returned to normal.

3. In addition anti-meningococcal serum was given intrathecally twice a day for three days. This is

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probably not necessary, as L. J. Willien has treated a series of six cases with sulphanilamide alone with excellent results. We feel, however, that until further experience has been gained in the treatment of this disease with sulphanilamide compounds it is not justifiable to withhold serum ; animal experiments also tend to show, according to Brown, that in mice infected with meningococci the administration of both agents simultaneously produced " a greater degree of protection than either of the agents by itself."

Case I

A recruit, aged 17, of excellent physique (weight 132 lb.) was admitted at night on February 15, 1938, in a comatose condition. It was afterwards ascertained that he had felt sick and had vomited the day before. He had remained on duty until lunch-time on the 16th, when he lay down on his bed and later on was found unconscious. On admission marked neck rigidity and Kernig's sign were present. The diagnosis was confirmed by lumbar puncture ; meningococci were seen in the direct smear, and a profuse growth of Type I meningococcus was

PROGRESS IN CASE I

Date	Total White Cell Count	C.S.F. Count	Temp.	Culture	Prontosil Soluble	Prontosil Album Orally	Serum Intrathecally	Serum Intramuscularly
15/2/38 ..	28,000 ; polymorphs, 90% eosinophils, 0	20,000 Meningococci+ in smear	101.0°	Positive Type I	20 c.cm.		15 c.cm.	10 c.cm.
16/2/38 A.M. .. P.M. ..		17,600 8,800	98.6°	Sterile	30 c.cm. 20 c.cm.	3 grammes	8 c.cm. 10 c.cm.	
17/2/38 A.M. ..	16,800 ; polymorphs, 72½% eosinophils, 0	2,100	98.4°	Sterile	10 c.cm.	1½ grammes	10 c.cm.	
P.M. ..		160; C.S.F. pressure, 150 mm.						
18/2/38 ..	12,100 ; polymorphs, 70% eosinophils, 0		98.2°			1½ grammes	Nil	
19/2/38 ..	5,600		98.4°			Nil	Nil	
20/2/38 ..	10,200 ; polymorphs, 65% ; eosinophils, 3½%		98.4°			Nil	Nil	

PROGRESS IN CASE II

Date	Total White Cell Count	C.S.F. Count	Temp.	Culture	Prontosil Soluble	Prontosil Album Orally	Serum Intrathecally	Serum Intramuscularly
22/3/38 P.M. ..	34,800 ; polymorphs, 87%	10,200 No orgs. seen	100°	Sterile	20 c.cm.		10 c.cm.	20 c.cm.
23/3/38 A.M. .. P.M. ..		6,400 16,600	102.4°	Sterile	20 c.cm. 10 c.cm.	1½ grammes	15 c.cm. 15 c.cm.	
24/3/38 A.M. .. P.M. ..		19,600 6,200	102°	Sterile	10 c.cm. 20 c.cm. 20 c.cm.	1½ grammes	15 c.cm.	
25/3/38 ..	16,800 ; polymorphs, 71% eosinophils, 1%	6,200	100°	Sterile	20 c.cm. 10 c.cm.	1½ grammes	30 c.cm.	
26/3/38 ..	10,400		97.6°		Nil		Nil	
27/3/38 ..	9,600 ; polymorphs, 68%		98.4°		Nil		Nil	
28/3/38 ..	7,600				Nil		Nil	

PROGRESS IN CASE III

Date	Total White Cell Count	C.S.F. Count	Temp.	Culture	Prontosil Soluble Intravenously	Prontosil Album	Serum Intrathecally	Serum
23/3/38 A.M. ..	24,000	28,000 Meningococci scanty	103.4°	Positive ; Group I	20 c.cm.		15 c.cm.	20 c.cm. I.V.
P.M. ..		14,600			20 c.cm.		15 c.cm.	5 c.cm. I.M.
24/3/38 A.M. .. P.M. ..		15,000 26,000	101°	Sterile	20 c.cm. 20 c.cm. 20 c.cm.	1½ grammes	10 c.cm. 15 c.cm.	
25/3/38 ..	11,400 ; polymorphs, 77%	8,400	101°	Sterile	20 c.cm. 20 c.cm.	1½ grammes	5 c.cm.	
26/3/38 ..	7,400 ; polymorphs, 67% eosinophils, 2%		99°		Nil	Nil	Nil	
27/3/38 ..	7,400		98°			Nil		

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obtained on culture. His temperature fell to normal in twenty-four hours and he made an uninterrupted recovery, apart from the usual serum rash.

Case II

A well-built youth, aged 15, weight 119 lb., was admitted on the night of March 22, 1938. His temperature was 100.6° on admission. He was completely deaf, but was able to answer written questions and appeared very anxious. There was marked neck rigidity and a positive Kernig sign was present. Auriscopic examination was completely negative, both tympani being intact and normal. An examination of his central nervous system, apart from the involvement of both eighth nerves and a definite papilloedema of the optic disks, was negative. Interrogation later revealed that he had reported sick with a headache on the day of admission and had been treated for nasopharyngitis, and towards evening he suddenly became stone deaf in both ears. He states that there was no tinnitus or vertigo, but as he was in bed the latter might not have been noticed. A turbid cerebrospinal fluid was obtained on lumbar puncture containing 10,200 cells per c.cm. (95 per cent. polymorphonuclears). No organisms were seen in direct smears and all cultures were sterile. The diagnosis of cerebrospinal meningitis with eighth nerve involvement was made on clinical grounds, and treatment was started. He made a complete recovery from his meningitis, but the deafness, which is of a nerve type, persists, although it has improved slightly. On March 30 examination showed a complete nerve deafness of the left side; on the right side a shouted voice could be heard at three feet.

Case III

A youth, aged 16, of average build (weight 124 lb.), was admitted at noon on March 23, 1938. His temperature was 103.4°. He complained of intense frontal headache, photophobia, and neck rigidity; an erythematous rash was present on the trunk and upper limbs, with a few scattered petechiae. The diagnosis was confirmed by lumbar puncture; scanty Gram-negative diplococci were present in the direct smear, and after forty-eight hours' incubation a Type I meningococcus was grown. Apart from a herpes labialis and a serum rash which appeared on the 28th he has made an uninterrupted recovery.

Comment

Three cases of meningococcal meningitis have been treated with prontosil and anti-meningococcal serum. We were greatly impressed with the rapidity in resolution of the pathological findings in the cerebrospinal fluid, together with the dramatic clinical improvement in the patients' condition, and on comparing these cases with others treated in the past with anti-meningococcal serum alone we feel that the results obtained were largely due to prontosil.

The object of pushing prontosil soluble during the first seventy-two hours is to sterilize the cerebrospinal fluid before morbid changes with their lasting sequelae have time to occur.

In the second case the eighth nerves were already involved when treatment commenced, and an unfavourable prognosis as regards hearing was inevitable.

In view of the American experience it is probably wise to give sodium bicarbonate grain for grain with sulphanilamide to combat acidosis.

In our opinion the giving of sulphanilamide intrathecally is unnecessary.

The use of prontosil album orally to combat the carrier problem opens a large field for experiment.

Our thanks are due to Group Captain E. W. Craig, *M.C.*, Officer Commanding Princess Mary's R.A.F. Hospital, for his kindness, help, and co-operation.

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Clinical Memoranda

Chronic Schizophrenia with Remission following a Spontaneous Epileptiform Seizure

Contrary to the experience of most workers, this case affords yet another example of a cardiazol remission occurring in an advanced case of schizophrenia of some eight years' standing.

The patient, Mrs. X., aged 34, was admitted to Warlingham Park Hospital on April 9, 1931, suffering from schizophrenia of the depressed type of some six months' duration. Prior to admission she had swallowed methylated spirits and said she hoped she would die. When admitted she was notably self-absorbed and evinced little interest in her surroundings, being also indifferent about her dress and personal appearance. Shortly after admission she was described as dull and resistive, having auditory hallucinations and requiring to be fed by tube. Her subsequent history was one of apparent progressive dementia, with faulty habits, complete self-neglect, and impulsive suicidal tendencies extending over years. She became mute, and from time to time exhibited katatonic stuporous tendencies, alternating with periodic excitement. Her physical condition, never robust, deteriorated, as will be seen from the following note dated March 11, 1938:

"She remains physically in poor condition, being emaciated and still losing weight, despite full extra diet. Her weight is now 5 st. 2 lb., indicating a loss of 10 lb. in the last two months, and this without evidence of organic disease; mentally she is restless, excitable, and impulsive, continually discarding her clothing, and is both wet and dirty. She will crouch naked in atavistic attitude, silent, morose, and indrawn, portraying little evidence of mind."

On April 12, 1938, at 2 p.m., she had a spontaneous epileptiform seizure, a phenomenon unprecedented in her case. The seizure lasted some three minutes, and, beyond transient confusion, produced no other mental change that day. During the next two days, however, she showed great mental improvement, becoming relatively accessible, talking rationally though hesitantly, and sitting up in bed, knitting. This sudden change in an apparently "lost" and demented patient was striking enough to call for considerable comment. The improvement was not maintained, and within the next few days the patient gradually lapsed into her former state.

On May 3 cardiazol treatment was begun despite her poor physical condition, in the hope of regaining remission by therapeutic convulsions. A dose of 4 c.cm. of a 10 per cent. solution of "pentamethylenetetrazol" was given intravenously, and produced a typical major epileptic fit. The procedure was repeated on May 9, and the patient showed almost immediate mental improvement, the same evening becoming partially accessible and conversing rationally, though with considerable retardation. Since then the treatment has been repeated every third day, the dose at no time having exceeded 5 c.cm. of the 10 per cent. solution. The patient has continued to show marked mental and physical improvement, being indeed scarcely recognizable as the same person. She spontaneously asks to be allowed to assist in the ward, converses brightly and rationally, and writes sensible letters to her relations. She shows every promise of making a good recovery, and her physical improvement is almost equally marked. All faultiness of habit has disappeared, and she now takes pride in her personal appearance. So far she has had nine therapeutic seizures, and treatment is still being continued.

An interesting side aspect of this case lies in the fact that her husband, regarding her as hopeless, contemplated divorce proceedings under the new Matrimonial Causes Act. Within the short period of one month the complexion of this case has totally altered, and it affords an instance of the need for extreme caution before finally

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