CASES OF MENINGO-ENCEPHALITIS DUE TO THE COXSACKIE A-LIKE ECHO 9 VIRUS

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During the widespread and prolonged epidemic of poliomyelitis which occurred in South Africa in 1955-56-57, a number of cases of meningo-encephalitis were investigated. Most of these cases were admitted to hospital with a provisional diagnosis of non-paralytic poliomyelitis. From many such cases poliovirus was isolated, thus confirming the correctness of the diagnosis. In many others, poliovirus was not demonstrated. From several cases of the latter group viruses, resembling Coxsackie Group A viruses in their pathogenicity to baby mice, were isolated. Of these viruses 8 were found to be serologically similar to (but not to belong to any of) the recognized serological types of Coxsackie A virus, and were therefore regarded as new types. Subsequent studies have shown that these viruses are serologically similar to Echo type-9 virus. As this virus has been responsible for widespread epidemics of infection in Europe and in Northern America, and clearly is an important cause of the aseptic meningitis syndrome, it will be of interest to note the clinical and laboratory findings in these 8 cases and to review briefly the features of the outbreaks which have occurred elsewhere.

Case 1

R.C.H., a boy aged 5 years and 11 months, was admitted to the Fever Hospital under the care of Dr. Arnold Jackson on 28 February 1956, complaining of severe headache of 4 days duration. He developed severe headache on Sunday 24 February, and asked his mother for an aspirin to relieve it. On Monday 25 February, he insisted on going to school, but did not play with his friends because of his headache. On coming home he went to bed and the family doctor was called. He suspected that the child had poliomyelitis and arranged for his admission to hospital.

On examination his temperature was 100·4°F, pulse 108/minute and his blood pressure 110/60 mm. Hg. His pupils were equal and reacted normally to light and accommodation. No abnormalities were detected in the pharynx, chest or abdomen. No neck rigidity was apparent and Kernig's sign was doubtful. Slight spasm of the hamstring muscles was evident. The cranial nerves were intact, motor power good and no sensory changes detected. The knee tendon reflexes were increased, the right ankle reflex absent, the others were present and equal. A provisional diagnosis of non-paralytic poliomyelitis was made.

The following day both knee jerks were absent. On the third day after admission the tightness of the hamstring muscles still persisted and there appeared to be slight weakness of the right quadriceps muscle.

A blood count on the day of admission showed 14·8 g. haemoglobin, 4,870,000 red cells, 6,900 white cells, of which 69·0% were neutrophil leucocytes, 3% monocytes, and 28% lymphocytes. The red cells and platelets appeared normal.

The Widal, Weil-Felix and Brucella agglutination tests, the Paul-Bunnell test, the rickettsial complement-fixation tests, and the viral complement-fixation tests for herpes, lymphocytic choriomeningitis and mumps virus infections all gave negative results.

The cerebrospinal fluid showed a cell count of 56 polymorphonuclear leucocytes and 85 lymphocytes per c.mm., a total protein of 20 mg., chlorides 677 mg. and sugar 70 mg. per 100 ml.

Specimens prepared from rectal and throat swabs were inoculated each into tissue cultures of monkey kidney cells, and a litter of baby mice. No virus was established in the baby mice, but a virus was isolated in tissue culture. This virus was not neutralized by any of the 3 type-specific poliovirus antisera and so proved not to be poliovirus. The tissue-culture fluid was then injected into another litter of baby mice, which developed paralysis, and on histological examination showed lesions resembling those produced by Coxsackie A virus.

Case 2

O.J.N., a boy aged 7, was admitted to the Johannesburg Fever Hospital under the care of Dr. Arnold Jackson on 4 July 1956 complaining of severe headache and fever which had begun the previous day.

On examination his temperature was 102°F, pulse rate 120/minute, and his blood pressure 112/78 mm. Hg. He had a flushed face with circumoral pallor. His conjunctivae were suffused. The pupils were equal and reacted equally to light and accommodation. His tongue was coated but moist, tonsils small and pharynx healthy, ears normal, and there was no enlargement of the cervical glands. No abnormality was detected in his chest and abdomen.

His cranial nerves were normal. Motor power and sensation were unimpaired. There was no neck or back stiffness, but slight tightness of the hamstring muscles. His reflexes were all present and equal.

A blood count showed 17·7 g. haemoglobin, 5,600,000 red cells, 8,700 white cells, of which 83% were neutrophil leucocytes, 2% monocytes and 15% lymphocytes. The red cells and platelets were normal in appearance.

The Widal, Weil Felix and Brucella agglutination tests, and the viral complement fixation tests for herpes, lymphocytic choriomeningitis and mumps virus, and the Paul-Bunnell test all yielded negative results.

Cerebrospinal fluid taken on the day of admission showed 129 polymorphonuclear leucocytes, 5 lymphocytes and 9 red cells per c.mm., with 40 mg. protein, 60 mg. sugar and 673 mg. chloride per 100 ml.

A virus, producing lesions in baby mice similar to those of Coxsackie Group A infections, was isolated directly from a specimen of faeces by the inoculation of a litter of baby mice.

Cases 3 *and* 4

The next 2 patients were brothers, D.H., aged 4½, and C.H., aged 2, both of whom had had 2 inoculations of poliomyelitis vaccine the previous year and had completed their course in 1956 about 2 months before the onset of their illness.

D.H. became ill on the morning of 16 October 1956 with severe headache, vomiting and fever. He was found to have slight neck stiffness and tightness of the hamstring muscles. He had no diarrhoea and no rash was noted. On the third day of illness all symptoms disappeared and he appeared quite well again.

His brother, C.H., became ill on 20 October 1956 with severe headache and vomiting, but no diarrhoea and fever. He was found to have stiffness of the neck and tightness of the hamstring muscles. His temperature continued high for 5 days, when it subsided with general improvement, though some pain in the hamstring and calf muscles of the right side still persisted. On the seventh day he was completely normal.

Both these patients were suspected of having poliomyelitis and specimens of faeces from each were sent for virus investigations. Suitably prepared suspensions were then inoculated into litters of baby mice and tissue cultures of monkey kidney cells. The mice remained healthy; a virus was isolated in the tissue cultures from each case. Baby mice inoculated with infected tissue-culture fluid became paralysed and histological examination showed a diffuse myositis similar to that produced by Coxsackie A virus.

Cases 5 *and* 6

These patients were sisters living in Durban. They were admitted to hospital as cases of non-paralytic poliomyelitis. The cerebrospinal fluid showed a pleocytosis, and from the cerebrospinal fluid of each patient a virus was isolated in tissue culture of monkey kidney cells, but not in baby mice from the original specimen. However, baby mice inoculated with infected tissue-culture fluid became paralysed and showed muscle lesions similar to those of Coxsakie A virus infections.

These viruses were isolated in the virus laboratory of the Union Health Department (under the supervision of Dr. Schapera) by Miss Westwood and Miss Hodge. The viruses were not neutralized by poliovirus antisera and therefore were sent to the laboratories of the Poliomyelitis Research Foundation for identification.

Baby mice inoculated with suspensions from the original specimens remained healthy, but a virus causing marked cytopathogenic changes was isolated in tissue culture. Infected tissue-culture fluid, inoculated into baby mice, produced paralysis and on histological examination a marked diffuse myositis, similar to that associated with Coxsackie Group A infections, was seen.

Case 7

A.P., a boy aged 8, was admitted to the Elizabeth Donkin Hospital, Port Elizabeth, under the care of Dr. Connacher, on 26 December 1956. He first became ill the day before admission complaining of headache, stiffness of the neck and back and feeling feverish. He was seen by the family medical practitioner, who suspected that he had poliomyelitis and arranged for his admission to hospital.

In the past the patient had had measles, whooping cough and chickenpox, but not scarlet fever, diphtheria or enteric fever. He had been given his first inoculation of poliomyelitis vaccine in October 1956.

On examination he was found to have a temperature of 101·2°F, pulse rate 138 and respiration rate 24/minute. No rash was seen. His throat and cervical glands were normal and no abnormalities were detected in his heart and lungs. There was marked tenderness in the right iliac fossa, but the abdomen was soft and the spleen was not palpable. The pupils were equal, there was no rigidity and Kernig's and Brudzinski's signs were negative and the reflexes were present and equal. There was no paralysis.

On lumbar puncture, the cerebrospinal fluid was under normal pressure and was clear, and was found to have 3 polymorphonuclear leucocytes per c.mm. and 10 mg. protein, 680 mg. chloride and 48 mg. sugar per 100 c.c. The Wassermann reaction was negative and no bacteria were detected either directly or in culture. The blood count showed 14·1 g. haemoglobin, 4,800,000 red cells, 11,800 white cells, of which 57% were neutrophils, 5% monocytes, 32% lymphocytes and 6% eosinophils. It was noted that there was a slight eosinophilia, but no parasites or parasitic ova were detected in an examination of a specimen of faeces.

Another specimen of faeces was sent to the laboratories of the Poliomyelitis Research Foundation for virus studies. From this specimen a virus was isolated in tissue culture, which was shown by neutralization tests not to be poliovirus. On passage to baby mice it was found to produce lesions similar to those produced by Coxsackie A virus.

Case 8

F.J.S., aged 1 year and 4 months, was admitted to the Johannesburg Fever Hospital on 24 February 1956. Six days before admission the patient began to vomit. The following day she was feverish. Three days before admission it was noted that she was unable to stand although she had walked well before the onset of her illness. She had 2 siblings both of whom were well.

On examination it was noted that she was unable to walk or stand. Her temperature was normal (98·4°F) and her pulse rate was 106. No abnormalities were found in the ears, nose or throat, or in the chest and abdomen. No rash was noted.

There was mild back stiffness and both legs were weak. The reflexes were present and equal. Two days after admission the knee and ankle reflexes of the left leg were found absent. The other reflexes were present and equal on both sides. The weakness of the left leg persisted and was still apparent on the day of discharge from hospital, 3 weeks later.

The specimen of cerebrospinal fluid which was taken on the day of admission showed the presence of 13 polymorphonuclear leucocytes and 3 lymphocytes; the total protein was 40 mg., chloride 721 mg. and sugar 56 mg.%. Bacteria were not detected on direct or cultural examination and the Wassermann reaction was negative. This fluid was inoculated into a litter of baby mice, which remained apparently healthy. Suspensions prepared respectively from a throat swab and 2 rectal swabs were also inoculated each into a litter of baby mice, but none developed

signs of illness. However, tissue-culture tubes inoculated with the rectal swab suspension showed cytopathogenic changes. In tissue-culture protection tests it was noted that this effect was not neutralized by any of the 3 types of poliovirus antiserum. Baby mice then inoculated with infected tissue-culture fluid developed paralysis. Histological sections showed lesions of the voluntary muscles resembling those produced by Coxsackie Group A virus infection.

These 8 cases presented signs and symptoms of meningo-encephalitis, including severe headache, vomiting, stiffness of the neck and tightness of the hamstring muscles and were all suspected of having poliomyelitis. The cerebrospinal fluid of the 6 cases in which this was examined, showed a pleocytosis compatible with this diagnosis. However, in none of them was poliovirus isolated.

From the cerebrospinal fluid of 2 patients, and from the faeces of the other 6, a virus was isolated. In 1 case the isolation was made directly in baby mice. In the other 7 the isolation was made in tissue culture but not in baby mice. The identity of these viruses was established in detailed laboratory studies.

LABORATORY STUDIES

Isolation of virus. Specimens of blood, cerebrospinal fluid, throat swabs and faeces were submitted from these cases for virus studies. Suspensions were prepared from the throat swabs and faeces in Hank's solution containing antibiotics. Each was then inoculated into a litter of 7 one-day-old mice and into 2 or 3 tissue-culture tubes prepared from trypsinized suspensions of monkey kidney cells.

One of the 7 baby mice of the first litter, inoculated with a suspension prepared from the faeces of case 2, developed paralysis. This one was sacrificed and a suspension prepared from its carcase and inoculated into another litter. On passage the infection gained virulence and produced evident disease in most of the baby mice (Table I). Histological sections of the tissues and organs of the mice with paralysis showed an extensive acute diffuse myositis similar to that produced by Coxsackie Group A virus infections.

TABLE I. CASE 2. LABORATORY PROTOCOL

	Baby mice	Days after Inoculation 1	2	3	4	5	6	7	8	9	10	11	12
Faeces	1	—		—	—	—	—	—	—		P*		
	2	—		—	—	—	—	—	—		—	—	—
0·1..	3	—		—	—	—	—	—	—		—	—	—
	4	—		—	—	—	—	—	—		—	—	—
13 July 1956 ..	5	—		—	—	—	—	—	—		—	—	—
	6	—		—	—	—	—	—	—		—	—	—
	7	—		—	—	—	—	—	—		—	—	—

* Kept for pathological investigation and passage, 23 July 1956.
Path. no. 5715—Limb—diffuse myositis=Coxsackie A.

		1	2	3	4	5	6	7	8
	1	—	—	—	—	W		P*	
Faeces	2	—	—	—	—	W		P	P
	3	—	—	—	—	W		P	P
Passage 1 ..	4	—	—	—	—	W		P	P
	5	—	—	—	—	W		W	P
23 July 1956 ..	6	—	—	—	—	W		W	W
.. ..	7	—	—	—	—	W		W	W

* Kept for passage.

		1	2	3	4	5	6	7	8	9
	1	—	—	W	W	W*				
Faeces	2	—	—	W	W	W		W	W	P
	3	—	—	W	W	—		W	W	W
Passage 2	4	—	—	W	W	—		W	W	W
	5	—	—	W	W	—		W	W	W
30 July 1956 ..	6	—	—	W	W	—		W	W	W
	7	—	—	W	W	—		W	W	W

* Kept for passage.

		1	2	3	4	5	6	7
	1	—	—	—	—	P*		
Faeces	2	—	—	—	—	—		P
	3	—	—	—	—	—		P
Passage 3	4	—	—	—	—	—		P
	5	—	—	—	—	—		P
6 August 1956 ..	6	—	—	—	—	—		—
	7	—	—	—	—	—		—

* Kept for passage.

		1	2	3	4
	1	—	—	W	D
Faeces	2	—	—	W	D
	3	—	—	W	D
Passage 4 ..	4	—	—	—	D
	5	—	—	—	P
13 August 1956	6	—	—	—	P } Kept 17 August 1956.
	7	—	—	—	P

P=paralysed. D=dead. W=weak.

The virus so isolated was not neutralized by Coxsackie Group A antisera A1-12 and 14-19 (A 13 was not tested) but was fully neutralized by Echo 9 antiserum.

The litters of baby mice inoculated with suspensions prepared from the faeces of the 5 other cases showed no apparent signs of infection. Histological sections were not prepared from these mice; so it is not known whether any developed lesions of the muscles suggestive of Coxsackie A virus infections. The tissue-culture tubes inoculated with these suspensions showed cytopathogenic changes similar to those produced by poliovirus, but evolving more slowly and less completely.

The tissue-culture tubes inoculated with cerebrospinal fluid of the 2 Durban cases showed similar changes, and in passage the cytopathogenic effect was maintained.

Each of these 7 viruses in a challenge dose of about 100 TCD_{50} was then tested against each of the 3 types of poliovirus antiserum. None of the viruses were neutralized and it was concluded that none were poliovirus (Table II).

TABLE II. TISSUE CULTURE NEUTRALIZATION TEST USING POLIOVIRUS TYPES 1, 2 AND 3 SPECIFIC ANTISERA

Virus	Virus only	Antiserum Type 1		Type 2		Type 3		Interpretation
C.C.H. ..	+	+	+	+	+	+	+	Not poliovirus
D.H. ..	+	+	+	+	+	+	+	" "
B.H. ..	+	+	+	+	+	+	+	" "
A.R. ..	+	+	+	+	+	+	+	" "
J.R. ..	+	+	+	+	+	+	+	" "
A.P. ..	+	+	+	+	+	+	+	" "
O.J.N. ..	+	+	+	+	+	+	+	" "

Suspensions of each virus derived from tissue cultures were then inoculated into a litter of 1-day-old baby mice. In each case a proportion of the litter developed paralysis. Histological sections showed lesions of the voluntary muscles resembling those produced by Coxsackie Group A virus.

In a series of baby-mouse protection tests, 5 of these viruses

TABLE III. BABY MOUSE NEUTRALIZATION TESTS USING A1-A19 COXSACKIE AND ECHO 9 SPECIFIC ANTISERA

Antiserum	Virus F.S.	B.H.	O.J.N.	J.R.	A.P.
Coxsackie:					
A 1	—	—	—	—	—
2	—	—	—	—	—
3	—	—	—	—	—
4	—	—	—	—	—
5	—	—	—	—	—
6	—	—	—	—	—
7	—	—	—	—	—
8	—	—	—	—	—
9	—	—	—	—	—
10	—	—	—	—	—
11	—	—	—	—	—
12	—	—	—	—	—
13	—	0	0	—	0
14	—	—	—	—	—
15	—	—	—	—	—
16	—	—	—	—	—
17	—	—	—	—	—
18	—	—	—	—	—
19	—	—	—	—	—
Echo 9 (Dalldorf) ..	+	0	+	+	+

0=not tested. +=protective. —=non-protective.

were tested against specific antiserum prepared against Dalldorf's classical Coxsackie A 1-12 and A 14-19 strains. Two were also tested against Coxsackie A 13 antiserum. None of the viruses were neutralized in these tests (Table III).

An antiserum was then prepared in mice against strain F.S., isolated from case 8 of this series. This serum protected against the homologous virus and against each of the viruses isolated from these patients, but not against the Coxsackie Group A 1-19 viruses (Table IV). It was concluded that these

TABLE IV. BABY MOUSE NEUTRALIZATION TESTS USING F.S. SPECIFIC ANTISERUM

Antiserum	*Virus*								
	Coxsackie A1-A19	*C.C.H.*	*D.H.*	*B.H.*	*A.R.*	*J.R.*	*A.P.*	*O.J.N.*	*Echo 9*
F.S.	—	+	+	+	+	+	+	+	+

—=non protective. +=protective.

viruses were immunologically similar and that they were representative of a new type of Coxsackie Group A virus.

When the characteristics of the Echo type-9 virus, responsible for widespread epidemics of aseptic meningitis in Europe and North America, became known, antiserum protective against this strain was received first from Dr. G. Dalldorf and then from Dr. A. Sabin and Dr. J. L. Melnick. This antiserum was tested against 4 of the 8 viruses and it was found to be fully protective (Table III). Antiserum prepared against the F.S. strain was conversely found to protect against Echo 9 virus (Table IV).

The results of this series of protection tests have revealed that the viruses from these 8 cases are immunologically similar to one another and also serologically similar to the Echo type-9 virus.

DISCUSSION

In 2 of these cases the virus was isolated from the cerebrospinal fluid and thus their role in causing the patients' illness is clear. In the remaining 6 cases the isolations were made from the faeces; thus their role was not proved. However, as the clinical pictures of the cases were similar and other viruses were not detected, there is good reason for suspecting them also as the cause of the patients' illness.

Echo virus type 9 has recently been incriminated in Europe and North America as the cause of epidemics of illness often associated with a rash, and in many cases with the aseptic meningitis syndrome.

One of the first of such outbreaks was described by Archetti and his co-workers[1] as Marche meningo-neuraxitis in Italy in 1955. From several cases a virus was isolated which produced lesions in baby mice similar to those caused by Coxsackie Group A virus infections. Subsequent studies have shown that this virus is immunologically related to, if not identical with Echo virus type 9.

Another similar outbreak, described by Garnett *et al.*,[2] occurred in Suffolk, England, in September 1955. The prominent signs and symptoms were fever, headache, nausea and vomiting, pain in the neck and shoulders, flushed face, photophobia and, in about 25% of cases, mostly children, a maculo-papular rash somewhat resembling that of measles. The cerebrospinal fluid (when examined) showed a pleocytosis. Recovery was usually rapid and complete and without paralysis or residual effect. A virus related to Echo virus type 9 was isolated from the cerebrospinal fluid of representative cases.

The following year, 1956, Rotem[3] noted that from July to November 100 patients suffering from aseptic meningitis, were admitted to the Leicester Isolation Hospital. These cases had an acute onset, headache, pyrexia, vomiting, neck and back rigidity and occasionally a rubelliform rash. Pleocytosis, predominately lymphocytic, was found in the cerebrospinal fluid of most patients. All patients recovered without specific treatment and without serious sequelae. A virus related to Echo virus type 9 was isolated from faeces, cerebrospinal fluid, and throat swabs from several cases.

A similar outbreak of aseptic meningitis with exanthem occurred in Coventry in 1956 and has recently been described by Galpine and his associates.[4] Fifty-one cases were admitted to hospital. In some of the patients the history suggested a pre-meningeal phase followed by a remission before the onset of meningeal symptoms. In most there appeared to be an early onset of meningeal symptoms. The patients presented with headache (often severe), irritability, unimpaired consciousness and pyrexia. Neck and back stiffness was noted in over a half of the cases, but in 20 of the 51 these signs were slight or absent.

A rash was seen in 19 of these cases. It was first noted from the first to sixth day of illness. In 17 cases it was erythematous, in 1 mixed erythematous and petechial, and in 1 petechial. The rash consisted of small pink discrete macules or maculopapules and always involved the face. In some cases it spread to involve the neck, shoulders and trunk, and in one infant, 15 months old, became generalized.

The cerebrospinal fluid showed a pleocytosis of usually less than 500 cells per c.mm. although in 2 cases it was over 2,000. The proportion of polymorphonuclear leucocytes and lymphocytes was approximately equal. The blood count showed a normal total or a leucopenia due to a neutropenia.

From 19 of 27 patients examined, a virus related to Echo virus type 9 was isolated. In addition, 18 of the patients showed a fourfold or greater rise in antibody titre against this virus during the course of their illness.

Boissard *et al.*[5] recovered viruses from the cerebrospinal fluid, throat washings and faeces of patients in a number of outbreaks of aseptic meningitis. They noted further that a number of these strains were found to cause lesions resembling those of Coxsackie Group A infections in newborn mice.

Maclean and Melnick,[6] who also studied strains of virus isolated in England in 1955 and 1956, noted that these strains produced myositis and paralysis in infant mice indistinguishable from that produced by Coxsackie Group A viruses. Also in 1956 a widespread epidemic of this condition involved most of Western Europe and the findings in various countries have been reported. Thus von Magnus[7] in Denmark isolated 21 viruses from a total of 147 specimens of cerebrospinal fluid tested. These viruses were neutralized by Echo antiserum type 9. The first tissue culture passage of 10 strains produced paralysis in newborn mice. The remaining 11 were non-pathogenic even after 5 passages in tissue culture. In a study of acute and convalescent sera from 14 patients, an increase in the neutralizing antibody titre was noted to occur in 13 instances.

Outbreaks of similar illness in which Echo virus type 9 was incriminated as the cause, have been described in Belgium,[8] Holland[9] and Germany,[10], and also in Canada[11] and the USA.[12] This virus has thus been responsible for one of the most extensive epidemics of aseptic meningitis so far recorded.

The present study has shown that the same infection was widespread in South Africa during 1956, as cases occurred as far apart as Johannesburg, Durban and Port Elizabeth. However these cases were sporadic and during this period no epidemic of this infection was recognized. More widespread epidemics may occur in the future. For this reason the clinical findings have been described in detail and the features of the extensive epidemics which have occurred in Europe and North America have been noted.

Whether Echo virus type 9 is a Coxsackie A virus or not is an undecided question. It has all the properties which entitle it to be placed in this group. However, the primary isolation of nearly all strains has been made in tissue culture and not in baby mice. Only after passage through tissue culture have these produced obvious illness in the baby mice. It is, therefore, of interest to note that one of the South African strains was immediately pathogenic to baby mice. This suggests that there may be some variation in virulence, or in dose, determining their pathogenicity to baby mice, a variation which would not merit a distinction from other Coxsackie A viruses.

These findings emphasize that Echo and Coxsackie viruses are closely related and it has been suggested that they and the polio viruses should be grouped together as Enteroviruses.[13]

When first discovered the pathogenicity of the Echo viruses was not known. Many of them were isolated from the faeces of cases diagnosed as non-paralytic poliomyelitis or as aseptic meningitis. There was, therefore, a suspicion that they might be concerned in the aetiology of some of these cases. From the findings of the investigations reviewed in this paper it is clear that Echo virus type 9 has caused a widespread epidemic, almost a pandemic, of an illness often associated with a morbilliform rash and many cases of which developed meningo-encephalitis.

Other investigations have incriminated Echo viruses type 4 and type 6 as the cause of outbreaks of aseptic meningitis in Europe,[14] North America[15] and South Africa.[16]

Echo viruses types 2, 3, 7, 14 and 16 have also been isolated from individual cases of aseptic meningitis.[13] There is thus a suspicion that some of these types may also have a role in the aetiology of this syndrome.

It is clear that this newly discovered group of viruses includes important pathogens of man and includes some of the commonest causes of the aseptic meningitis syndrome, which has to be distinguished from non-paralytic poliomyelitis.

SUMMARY

During the epidemics of poliomyelitis which occurred in South Africa in 1955-56-57 a number of cases diagnosed as non-paralytic poliomyelitis were investigated and were found not to be due to poliovirus. Eight such cases are described. These had fever, severe headache, vomiting, often a stiff neck and occasionally a stiff back and tightness of the hamstring muscles and some alteration, usually loss, of some tendon reflexes. In none was a rash noted. The cerebrospinal fluid of 6 cases in which this was examined, showed a pleocytosis.

From the cerebrospinal fluid of 2 patients and from the faeces of the other 6 a virus was isolated. In one case the isolation was made directly in baby mice. In the other 7 the isolation was made in tissue culture, but not in baby mice. These viruses produced lesions in baby mice similar to those of Coxsackie A virus infections. They were shown to be serologically similar, but were found not to belong to any of the recognized serotypes of Coxsackie A virus and were therefore regarded as representatives of a new serotype. Subsequent study revealed that they were similar to Echo virus type 9.

As this group of cases included patients in Johannesburg, Durban and Port Elizabeth, it is apparent that this infection was widespread in South Africa at the time, but no epidemic was recognized.

Following epidemics in Italy and England in 1955, almost a pandemic of this infection occurred in the northern hemisphere in 1956 and outbreaks occurred in most countries of Europe, in Canada and in the USA. The clinical features of the illness in these epidemics are noted. The cases were characterized by fever, headache, vomiting, and in about 25% of cases by a rubelliform rash consisting of small pink macules involving the face and in some cases spreading to the neck, shoulders and trunk. Many cases developed the signs and symptoms of aseptic meningitis and a pleocytosis was found in the cerebrospinal fluid. The course of the illness was benign and the patients recovered fully.

Other investigations have incriminated Echo viruses types 4 and 6 as causing aseptic meningitis, and other types are also suspected. It is clear that the Echo viruses are important pathogens of man and amongst the most frequent causes of the aseptic meningitis syndrome.

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