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Benign Myalgic Encephalomyelitis (Iceland Disease) in Alaska

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After recalling that Brill's disease turned out to be a variant of a previously well-known entity and that alastrim was found to have a like relationship to another familiar scourge, one hesitates to postulate the appearance of a new disease. However, when there is concurrence by the editors of *Lancet* as reported in the *Journal of the American Medical Association*,[1] one may feel he can venture a little way out on that limb and state that there has appeared on the medical horizon in recent years a syndrome previously unrecognized as such and appearing to be a new and fairly distinct disease entity. It appears to be reasonable to designate it as benign myalgic encephalomyelitis on clinical grounds; autopsy studies are not available.

With the development of specific tests for poliomyelitis as well as specific vaccines, it becomes possible on the one hand, and rather necessary on the other, to distinguish cases of genuine poliomyelitis virus infection from various imitations. The disease under discussion in this paper is most difficult to distinguish from poliomyelitis in its primary phases,[2] but from all appearances it is not the genuine article. To make diagnosis even more difficult, it appears to occur simultaneously with clinically typical poliomyelitis in at least some of the reports.

The first report of this syndrome by Sigurdsson, et al,[3] came from the Akureyri district of Iceland, where the disease struck with characteristic explosive force in the winter of 1948-49. Within the next few years almost identical outbreaks were reported from upper New York State[4] and Australia[5,6] and more recently from Great Britain[7] and Germany.[8] Points which differentiated these outbreaks from typical poliomyelitis and linked them as similar to each other, and to an outbreak in Seward, Alaska, in 1954, are listed in table 1.

Table 1. Points Differentiating Encephalomyelitis from Poliomyelitis

1. Long drawn-out persistence and recurrence of muscular pain and stiffness
2. Infrequency of persistent paralysis and atrophy of muscle
3. High frequency of persistent neuropsychiatric symptoms
4. Paucity of spinal fluid changes
5. Appearance of paresthesias
6. High incidence among females between 15 and 45 years of age (fig. 1)
7. Frequency of multiple cases in a single household
8. Explosively high morbidity rates with very low mortality

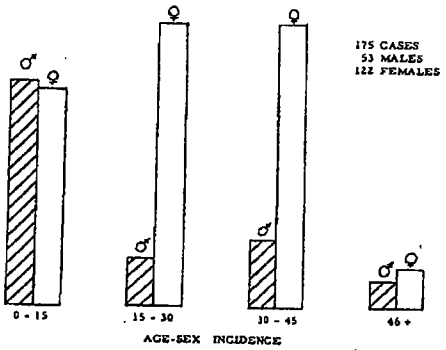

Fig. 1. Showing high incidence of encephalomyelitis among females between 15 and 45 years of age.

The Seward Outbreak

On July 4, 1954, Seward, Alaska, might have been considered a virgin community from the standpoint of poliomyelitis. There had not been any cases closer than Moose Pass, 30 miles away, two years before. On July 5, 1954, the first case of poliomyelitis was diagnosed in the community. It appeared typical in onset, and has gone to typical flaccid paralysis and atrophy of several scattered muscle groups. The prospect of

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dealing with a "normal" incidence of poliomyelitis of 20 to 30 per 1,000 population in a semi-isolated community without specially trained personnel or special equipment was truly a grim one, relieved only by the presence in the community of an experienced physical therapist-turned-housewife. The development of 175 diagnosed cases in a population of 3,000 (or almost *60 per thousand*) in the next few months, along with the knowledge that many others had suffered a mild undiagnosed form of the disease, calls for a complete review of the situation.

Seward is a seaport town with predominantly white population which is somewhat transient. No full-blooded native was diagnosed as having either poliomyelitis or Iceland disease in this outbreak.

Early in the outbreak the cases seemed generally to fit one or another of the commonly recognized syndromes of typical poliomyelitis. Typical meningeal symptoms followed by varying degrees of muscular weakness and later atrophy were seen. Three patients developed bulbar paralysis and, though promptly transported to respirator care in Anchorage, two died. However, fairly early in the outbreak, cases began to appear which did not conform to any of the standard accepted syndromes of acute poliomyelitis infection, protean as they are known to be. After several weeks it became apparent that there was a graded series of symptom complexes ranging from the few obvious, severe cases of paralysis through those of less clear-cut symptomatology to a picture which slowly assumed a fairly definite pattern of mild to moderate chronic neurologic or neuromuscular illness not compatible with any of the available recorded descriptions of poliomyelitis—bulbar or spinal, paralytic, non-paralytic, or abortive.[9-11] Nor were these latter cases similar to any of the encephalitides previously described.

Clinical Picture

Clinical onset of the atypical cases took two forms: (1) abrupt or meningeal, and (2) insidious or influenzoid. (See table 2.)

The meningeal type of onset, more dramatic but less frequent, was heralded by rather sudden development of fever, malaise, severe headache, and definite stiffness and pain in the neck and back and usually one or more extremities. Use of the affected muscles caused pain and cramping. Tremor in the acute stage foretold prolonged disability. Most of the encephalomyelitic

Table 2. Comparison of Acute Phase Symptoms

Symptom	Polio	1954
Age	More common under 20	2 out of 3 over 15
Sex	Slightly more males	Females 5 to 2
Fever	Usually	Usually
Headache	Usually	Usually
Malaise	Usually	Always
Stiff neck	Usually severe	Usually moderate
Muscles on pressure	Very tender	Sore, especialy on motion
Paralysis	Prompt—either present or absent	Insidious weakness
Distribution	Patchy	All on one side
Sensory change	Hypersensitivity	Paresthesias, dysesthesias, photophobia, hyperacusis
Anxiety	In bulbar type	Marked to point of hysteria
C.S.F.	50-100 cells and up Pandy positive	0-50 cells Pandy occasionally positive. but weak

patients showed disturbed (usually increased) sensitivity of one or more senses (e.g., photophobia, hyperacusis, disturbed taste), extreme nervousness with tension, and occasionally near-hysteria. They complained of dysesthesias and paresthesias described as "bubbles under the skin" or the more prosaic formication. The extreme muscle tenderness common in the acute phase of poliomyelitis was not generally seen.

When the fever disappeared in three to five days, the patients were checked for muscle weakness. Distribution of affected muscle groups is shown in figure 2. The muscular weakness in the Seward patients was quite widespread, rather than discretely localized as described in Sigurdsson's original report. Usually an entire limb was affected and frequently an entire side of the body. Trunk and back muscles were affected and frequently an entire side of the body. Trunk and back muscles were affected more often than realized at first and have been the source of discomfort and scoliosis in later phases. A few isolated cranial nerve palsies occurred. Diplopia was not common. Stupor and coma did not appear. Testing of the affected muscles showed weakness down to the grades of "good" and "fair" and was followed regularly by a sensation described by the patients as cramping or "being about to cramp." Paralysis to the grades of "trace" and "zero" were not seen in those cases showing the pattern of chronic psychiatric and recurrent muscular dysfunction. Tremors and severe incoordination suggesting basal ganglionic involvement were common and in quite a few patients were complicated by sudden isolated convulsive jerks of large segments of the body.

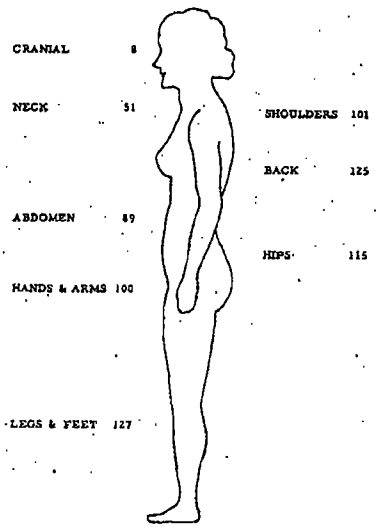

Fig. 2. Distribution of affected muscle groups.

such as the shoulders or one leg. Both the tremors at rest and the jerking were increased by fatigue of the muscles which occurred with slight physical exertion or mental excitement, and in some patients they became so severe as to make it impossible to drink from a full cup or glass although the muscles used were not greatly weakened. Vasomotor instability manifested by night sweats, flushing, pallor, and rarely by significant transient hypertension was noted in many of the victims.

As in polio, symptoms of bladder and gastrointestinal dysfunction were common in the acute stage with constipation and transient urinary retention appearing quite often. In 5 patients a severe substernal burning "explosive" pain resulted from swallowing anything at all. This symptom was attributed to esophageal muscle spasm, recurred for several weeks, and was relieved most efficiently by hot packs or tubs.

The insidious type of onset consisted of mild to moderate fever and malaise with moderate headache, and occasional localized muscle pain lasting a few days, often treated by aspirin and rest without medical assistance. Many of these patients did not consult a physician until some weeks or even months after the acute flu-like episode, when, usually during or just after a menstrual period, they came in quite bewildered by their psychiatric symptoms and ease of fatigue with its associated muscular discomfort and stiffness. On examination, muscular weakness down to "fair" was found in the painful areas.

Chronic Stage

It is in the post acute period that myalgic encephalomyelitis reveals its distinctive pattern from poliomyelitis infection. (See table 3.) The

Table 3. Comparison of Chronic Phase Symptoms

Symptom	Polio	1954
Parlysis	Fixed or slowly improving	Variable recurrent weakness
Muscle pain	No	Recurrent
Stiffness	No	Recurrent
Tenderness	No	Recurrent
"Can't think"	No	Very frequent
Forgetfulness	No	Very frequent
Emotional instability and irritability	No	Very frequent

post acute stage in true poliomyelitis is, in general, one of progressive improvement up to a definite point for each patient, eventuating in about 18 months in a variable degree of permanent weakness, without recurrence of the manifestations of earlier phases. The post acute phase of benign myalgic encephalomyelitis is characterized by cyclic recurrences of symptoms seen in previous weeks or months. Muscles showing weakness, stiffness, and soreness may respond encouragingly to treatment, but the disabilities will be found to be developing elsewhere. Later, treated and responsive muscles frequently relapse into pain and weakness. Relapses have continued to occur for two and one-half years in the Seward outbreak. The advent of cool weather has increased the intensity of recurrent symptoms in the fall of each year since the Seward outbreak.

Relations to Menstruation

The association of exacerbation of both physical and mental symptoms with the menstrual phase was striking, especially in the later stage of the disease. With the approach of the menstrual period, muscles—even those which had been responding well to physical therapy—again became weak and sore. Premenstrual tension increased to intolerable proportions. Women whose menstrual phase had not previously been marked by hyper-irritability and emotional tension complained that they could not control themselves, flew into rages at what they realized were really insignificant frustrations or annoyances. Many remarked that they were

concerned that their husbands might just give up and leave. The jerking of spasmodic involuntary contractions of the limbs and back increased and the tremors became more noticeable. This relapse persisted through the menstrual period and as the period was left behind, improvement again occurred, only to relapse again the next month.

In counterpoint to the effect of the menstrual cycle on the disease was the effect of the disease on the menses. Frequently, periods were delayed or skipped for several months. On the other hand, hypermenorrhea and increased frequency were also observed. Not uncommonly associated with these irregularities was pain and tenderness of the lower abdomen of considerable severity. The combination of the menometrorrhagia and severe lower abdominal pain, which did not respond to medical treatment, finally necessitated pelvic laparotomy in 4 of the women with removal of the uterus in 3 of them. In several others, the abdominal tenderness was confusing until it was discovered that the tenderness could be localized in the abdominal musculature by having the patient tense the abdominal muscles against the depressing fingertips with resultant increase rather than decrease in pain. Physical therapy brought relief to these patients as it did to those with pain and tenderness of the limb muscles.

Chronic Headache

A peculiarly distressing symptom in several patients was persistent and continuous headache related to involvement of the neck muscles. During the acute phase, padded support of the cervical spine gave partial or complete relief. Later, without the relief provided by a collar or by physical therapy including Sayre traction, this headache was sufficient, because of its unremitting nature, to bring the patient to the doctor in a near frenzy. Nor was physical therapy always successful in providing relief. There are patients who, two years after the original illness, must use cervical traction two to five times a week to remain comfortable. Associated with the recurrent muscular tension and pain in the neck and its resultant headache, disturbances of vision—especially on the periphery of the visual fields—were noted by several patients. These were described as "shimmering" and "like looking through a veil." They cleared on application of heat and passive stretching of the neck muscles.

Neuropsychiatric Symptoms

Inability to concentrate, loss of memory, forgetfulness and confusion in varying degrees afflicted most of these atypical patients. These symptoms have been among the most persistent and distressing effects of the infection. Several of the patients have described the almost physical effort required, months after the acute illness, to re-initiate their mental processes. Similar psychologic difficulties have been noted in other epidemics of this disease in various parts of the world.[7-8] Four of the adult women experienced more or less marked disturbances of consciousness for months after the original illness. One 7 year old girl fainted during physical therapy one year after onset. One 5 year old girl, four months after the onset of her illness (which has left definite paralysis, atrophy, and scoliosis) developed a grand mal seizure which has not been repeated. These disturbances of consciousness appear to be the result of vasomotor instability in at least some instances.

Laboratory

Among those seen in the acute phase, the white blood count showed no consistent picture, being normal in about 50 per cent and either slightly elevated or slightly lowered in the remainder; the sedimentation rate was elevated in about two-thirds of those few in whom it was performed. Spinal puncture was not performed in a large number because of the high case load; approximately one-third of those performed showed normal fluid; any cell increases were in the 10 to 30 level and it was our impression that there was a tendency for the protein to remain slightly elevated for a longer period than the cell count. Random single blood specimens were taken in November 1954 from 19 patients who were having subacute symptoms. Serum neutralization titers against the three types of poliomyelitis were generally low and showed no consistent pattern. The more complete viral studies reported from the Iceland, New York, and Australian oubreaks revealed negative results for all three types of poliomyelitis virus, the Coxsackie viruses, and various encephalitis viruses, except in Australia where an atypical virus, apparently related to the Coxsackie group, was identified in cases corresponding to ours.[12]

Two Years Later

Now, two years after the acute outbreak it is extremely difficult to draw the line between

those who had true poliomyelitis and those who had myalgic encephalomyelitis. There are certain cases which show typical poliomyelitic paralysis; others are clearly this new syndrome, but without virology and serology studies the diagnosis of some of the cases is still uncertain. Apparently, those with no atrophy or true decrease in strength, and with persistent muscular stiffness and ease of fatigue, and especially those with the persistent psychiatric dysfunctions and tremor can now be diagnosed as not polio, but myalgic encephalomyelitis or Iceland disease.

In 1955, Sigurdsson and Gudmundsson[11] returned to Akureyri and reexamined 39 of the patients from their previous study. Although nearly all were back at work, they found many of them still complaining of nervousness, tiredness, tender muscles, and pain. Though the Seward outbreak showed a low mortality and low incidence of true paralysis and atrophy, the incidence of chronic morbidity has been very distressing (table 4). Out of the 81 women of the 15 to 45 age group available for checking two years after the acute episode, 63 complain of ease of fatigue and tiredness; 54 have recurrent and frequent pain and stiffness of the affected areas; 33 complain of weakness of mild but noticeable degree; 22 of awkwardness and incoordination; 20 of tremor; 6 of gross jerking movements, and 2 show residual paralysis and atrophy. In the psychiatric area, emotional instability is significant in 34, tension in 27, poor concentration in 27, and disturbances of consciousness in 7.

Table 4. Residual Symptoms Two Years after Onset

	Males				Females				Both			
	0–15		15+		0–15		15+		0–15		15+	
	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases
Total	100	32	100	20	100	32	100	91	100	64	100	111
Ease of fatigue	47	15	70	14	35	11	75	69	39	26	76	84
Pain and stiffness	22	7	60	12	9	3	65	59	15	10	64	71
Muscle weakness	38	12	30	6	16	5	37	34	26	17	38	40
Paralysis	25	8	5	1	16	5	2	2	19	13	3	3
Scoliosis	32	10	0	0	25	8	6	5	27	18	4	5
Tremor	6	2	25	5	3	1	23	21	5	3	23	26
Incoordination	22	7	20	4	6	2	25	23	14	9	24	27
Jerking	0	0	0	0	0	0	7	6	0	0	5	6
Emotional instability	29	9	25	5	25	8	39	36	17	11	37	41
Tension	16	5	25	5	19	6	32	29	17	11	31	34
Poor concentration and memory	9	3	20	4	6	2	32	29	8	5	30	33
Disturbance of consciousness	0	0	10	2	6	2	8	7	3	2	8	9

Diagnosis

Diagnosis is usually made well after the acute phase of the disease has passed, because of the similarity to poliomyelitis in the acute phase. The syndrome of muscular pain and stiffness, ease of fatigue and psychiatric difficulties suggests neurosis to those inexperienced with this particular problem. The differentiating features are the acute influenzoid initiating episode and, in the untreated chronic case, definite though not marked weakness of the muscles affected, without atrophy.

Differentiation from non-paralytic or abortive anterior poliomyelitis is based on, in the acute cases, the lesser degree of spinal fluid changes in combination with sensory abnormalities. In the postacute period, the psychiatric and sensory symptoms and lack of atrophy of the affected areas serve to mark this disease as a separate syndrome.

Treatment

The only consistently effective treatment for the muscular symptoms has been heat and stretching exercises under the guidance of a physical therapist. Tolserol has been of benefit in an occasional patient and should be tried. The various psychotropic drugs, including chlorpromazine, reserpine, meprobamate, mephenesin and Ritalin were effective in a few patients who had to be discovered purely by trial and error. After the acute stage was well passed (six months or so) many of the patients found that they improved in their mental abilities by resuming work which necessitated resumption of concentration, memory, and thinking through, but the effort of will required to "start the wheels going round" again was apparently a great one.

Comment

Differentiation of encephalomyelitis from poliomyelitis is both qualitative and quantitative.

The pattern of poliomyelitis derives from pathologically proven involvement of the gray matter of the anterior horn cells and internuncial neurones in the motor segments of the cord and brain stem. Poliomyelitis involves essentially the final common pathway of motor impulses. The clinical picture of myalgic encephalomyelitis suggests involvement of this same final common pathway to a lesser degree and more common damage to structures above the medulla and to centers controlling vasomotor function.

Reference to older texts reveals that syndromes now known to be due to poliomyelitis virus and syndromes congruent with benign encephalomyelitis have formerly been grouped together due to lack of laboratory differentiation.[14] Virologic study of encephalomyelitic outbreaks in the future will be necessary to clarify with certainty the syndromes attributable to the individual diseases. You will recall that until bacteriologic evidence distinguished the boundaries of syphilis and gonorrhea, the two were thought of as one disease[15] on the fallacious clinical evidence adduced by John Hunter.[16]

Clinical differentiation of the syndromes will not be difficult to one who sees the two diseases for himself. The points mentioned in table 1 will serve to alert the diagnostician to the necessity for utilization of all laboratory aids. In the absence of specific treatments for either disease, therapy is of necessity limited to rest, physical therapy and symptomatic medication. The practical value of differentiation, therefore, lies in prognosis of the course of the individual patient and the individual outbreak. Recognition of the existence of benign encephalomyelitis as separate from anterior poliomyelitis is important in evaluating the effect of poliomyelitis preventive vaccines and in eventual development of preventive and curative therapy for another segment of the afflictions of mankind.

Conclusion

In conclusion, there are reports from Iceland, eastern United States, Australia, Great Britain, Europe, and Alaska—non-tropical areas well scattered over the earth's surface—of explosive outbreaks of an apparently new neurologic infectious disease, presumably of virus origin, occurring in conjunction with clinically typical poliomyelitis and leaving in its wake persistent and distressing mental and physical symptoms not of a paralytic nature. One could postulate that either there is developing a mutant of the poliomyelitis virus with marked encephalotropic properties, or there is at least one hitherto unidentified encephalomyelotropic virus, almost indistinguishable in its clinical manifestations from poliomyelitis in its early stages and not closely related to the familiar Coxsackie groups, that deserves study and identification in order to decrease the high degree of prolonged morbidity therefrom. Early reports of this type of outbreak should be encouraged and a real effort to obtain thorough and concentrated epidemiologic study is indicated since the disease—if it is a single entity—has been reported from widely scattered portions of the globe.

Addendum

Since my original report at the AMA clinical session in Seattle in 1956, I have been informed[17] that 18 major outbreaks falling within this general pattern have been under study by the Communicable Disease Center of the USPHS at Atlanta, Georgia. These have been scattered widely across the length and breadth of the United States and despite all efforts no etiologic agent has been identified in any of them. Personal contacts and correspondence with physicians, especially in Ohio, suggest that the picture of myalgic encephalitis occurred not infrequently in the Midwest in 1954 and 1955.

P.O. Box 247.

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