

1956 Summary of R.M.D. Diseases - 1

# THE LANCET

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## A New Clinical Entity?

IN 1917 VON ECONOMO<sup>1</sup> reported a small outbreak of an illness in which the main features were fever, stupor, and ophthalmoplegia: 2 of his 13 patients died and at necropsy there was evidence of inflammation of the brain substance. During the next two years a great many similar outbreaks were recorded and by 1921 the disease had reached epidemic proportions in almost every country in Europe.<sup>2</sup> In spite of perplexing variations in the clinical picture from case to case, locality to locality, and even from season to season,<sup>2</sup> it soon became clear that for practical purposes a new clinical entity had appeared.<sup>3</sup> In 1924, 5039 cases of encephalitis lethargica were notified in England and Wales alone,<sup>4</sup> but by the beginning of the next decade confirmed cases of this dangerous disease had become sporadic and by 1939 they were extremely rare.<sup>5</sup> By the end of the late war, the centre of interest had shifted to poliomyelitis as by far the most prevalent and disabling infection of the nervous system. The work of RITCHIE RUSSELL and others<sup>6</sup> focused attention on the importance of diagnosis in the pre-paralytic stage; and from other sources<sup>7, 8</sup> there was evidence of a change in the epidemiology of poliomyelitis.

Against this background of intense interest in poliomyelitis and its problems came reports of outbreaks<sup>9-11</sup> and isolated cases<sup>12, 13</sup> which, for one reason or another, led to difficulties in diagnosis. Broadly, these can be divided into those in which the cerebrospinal fluid (C.S.F.) is abnormal and those in which it is normal. Of the abnormal group (group I), only in the series described by LAURENT<sup>10</sup> was no convincing causative organism isolated. The conditions described by KELLEHER<sup>12</sup> and JENNINGS<sup>13</sup> proved to be aberrant poliomyelitis, and there was presumptive evidence of the same disease in the outbreak reported by BARRETT<sup>9</sup> from Cambridgeshire in 1949. The Coxsackie group of viruses has also been implicated in this group<sup>11, 14</sup>: in such cases

pleocytosis is the rule and signs of parenchymal damage to the nervous system are very uncommon. Much more perplexing outbreaks are those in which no changes are found in the C.S.F. (group II). Since we discussed these illnesses in 1954 under the non-committal title, Not Poliomyelitis,<sup>15</sup> another epidemic with similar features has been reported from Durban<sup>16, 17</sup> and two further outbreaks are described in this issue by Dr. SUMNER and by Dr. RAMSAY and Dr. O'SULLIVAN. Only a brief description<sup>18</sup> has so far been published of the alarming outbreak at the Royal Free Hospital last year, but there are arguments for including it in this group. In none of these cases has it been possible to incriminate the poliomyelitis or Coxsackie virus, nor indeed has any other known infective agent been isolated.

There seem good reasons, in our present state of ignorance, for placing in a third and intermediate group the epidemic which took place in Akureyri, Iceland, in the winter of 1948-49,<sup>19</sup> and about which Dr. SIGURDSSON and Dr. GUDMUNDSSON write on p. 766. In all 8 cases examined the C.S.F. was abnormal; on the other hand, the protracted course and mental symptoms described by Dr. SIGURDSSON are prominent symptoms in group II. The outbreak in the nurses training school in the University of Pennsylvania in 1945<sup>20</sup> is also difficult to classify since it happened before the isolation of the Coxsackie viruses: there was pleocytosis in 2 out of 5 cases. The unusual epidemic reported by WALLIS from Cumberland in 1955<sup>21</sup> has many features of group II—notably vertigo, diplopia, myalgia, cervical lymphadenopathy, and protracted convalescence with mental symptoms. Unfortunately there is no information about the C.S.F. The recorded atypical outbreaks can thus be grouped as follows:

		Virus	C.S.F.
Group I	Laurent <sup>10</sup> (1947)	Unknown	Usually abnormal
	Kelleher et al. <sup>12</sup> (1949)	Poliomyelitis	
	Curnen et al. <sup>11</sup> (1949)	Coxsackie	
	Jennings et al. <sup>13</sup> (1949)	Poliomyelitis	
	Barrett et al. <sup>9</sup> (1952)	Poliomyelitis	
	Galpine and Macrae <sup>14</sup> (1953) and others	Coxsackie	
Group II	Adelaide <sup>22</sup> (1949)	Unknown	Normal in nearly all cases
	New York State <sup>23</sup> (1950)	Unknown	
	Middlesex Hospital <sup>24</sup> (1952)	Uncertain	
	Coventry <sup>25</sup> (1953)	Unknown	
	Berlin (1954) (Summer)	Unknown	
	Durban <sup>17</sup> (1955)	Unknown	
	Royal Free Hospital <sup>18</sup> (1955)	Unknown	
Hampstead (1955) (Ramsay and O'Sullivan)	Unknown		
Group III	Pennsylvania <sup>20</sup> (1945)	Unknown	Abnormal 2/5
	Akureyri, Iceland <sup>19</sup> (1948)	Unknown	Abnormal 8/8
	Cumberland <sup>21</sup> (1955)	Unknown	Unknown

Of the 8 outbreaks in group II, all except that at the Royal Free were initially confused with polio-

1. von Economo, C. *Wien. klin. Wschr.* 1917, **30**, 581.  
 2. Hall, A. J. *Epidemic Encephalitis*. Bristol, 1924.  
 3. Kimmer Wilson, S. A. *Lancet*, 1918, **ii**, 7.  
 4. MacNalty, A. S. *Epidemic Diseases of the Central Nervous System*. London, 1927.  
 5. *Epidemic Encephalitis*. 3rd Report by Matheson Committee. New York, 1939.  
 6. Russell, W. R. *Poliomyelitis*. London, 1956.  
 7. Dauer, C. C. *Amer. J. Hyg.* 1948, **48**, 133.  
 8. MacLean, F. S. New Zealand Department of Health. Annual Report of Director General, 1945, p. 90.  
 9. Barrett, A. M., Gairdner, D., McFarlan, A. M. *Brit. med. J.* 1952, **i**, 1317.  
 10. Laurent, L. J. M. *Proc. R. Soc. Med.* 1947, **40**, 927.  
 11. Curnen, E. C., Shaw, E. W., Melnick, J. L. *J. Amer. med. Ass.* 1949, **141**, 894.  
 12. Kelleher, W. H., Bratton, A. B., MacCallum, F. O. *Brit. med. J.* 1949, **ii**, 213.  
 13. Jennings, G. H., Hamilton-Paterson, J. L., MacCallum, F. O. *Ibid.*, p. 210.  
 14. Galpine, J. F., Macrae, A. D. *Lancet*, 1953, **i**, 372.

15. See leading article. *Ibid.* 1954, **ii**, 1060.  
 16. Editorial. *S. Afr. med. J.* 1955, **i**, 331.  
 17. Hill, R. W. *Ibid.*, p. 344.  
 18. See *Lancet*, 1955, **ii**, 351.  
 19. Sigurdsson, B., Sigurjonsson, J., Sigurdsson, J., Thorkeklsson, J., Gudmundsson, K. R. *Amer. J. Hyg.* 1950, **52**, 222.  
 20. McConnell, J. *Amer. J. med. Sci.* 1945, **209**, 41.  
 21. Wallis, A. I. *Lancet*, 1955, **ii**, 290; *Ibid.*, p. 1091.  
 22. Pellow, R. A. A. *Med. J. Aust.* 1951, **i**, 944.  
 23. White, D. N., Burtch, R. B. *Neurology*, 1954, **4**, 506.  
 24. Acheson, E. D. *Lancet*, 1954, **ii**, 1044.  
 25. Macrae, A. D., Galpine, J. F. *Ibid.*, p. 350.

myelitis, and all occurred during or shortly after the seasonal period of prevalence of poliomyelitis. The three British outbreaks<sup>18 24 25</sup> were in late summer, in contrast to the former peak incidence of encephalitis lethargica in the first three months of the year.<sup>2</sup> Five outbreaks took the form of dramatic localised epidemics, four of which were in nurses' homes. Dr. RAMSAY and Dr. O'SULLIVAN describe cases in the neighbourhood of one of these outbreaks, and HILL<sup>17</sup> had a similar experience in Durban. The attack-rate in closed communities is high. The onset in this group is usually acute with systemic prodromata such as are common in poliomyelitis. In contrast, fever is usually low and may be absent.<sup>14 18 25</sup> The course is generally two to eight weeks but occasionally symptoms may last for months. Relapses are frequent. Usually the immediate outcome is favourable but in a few cases paresis or mental sequelae may be incapacitating for many months.<sup>22 23 26</sup> Depression, emotional lability, or irritability in convalescence have been a constant feature in all group-II outbreaks. Although previous experience has shown that a long period of observation will be necessary before the harmlessness of the disorder is assured, it can at least be said that the immediate mortality-rate of nil is in striking contrast to the epidemic infections of the nervous system previously described<sup>4</sup>; and this in itself is very encouraging.

Among the more characteristic features of group II are the severe muscular pains, often accompanied by exquisite tenderness, which often dominate the clinical picture.<sup>22-25</sup> As WHITE and BURTON<sup>23</sup> have pointed out, these pains differ from those of poliomyelitis in that they are not simply a short-lived precursor of paresis but may last for weeks. Most commonly they affect the neck, back, or limbs but there may also be Bornholm-like chest and abdominal pains.<sup>17 18 23 25</sup> Continuous or intermittent painful muscular spasms were noted in the outbreaks at the Middlesex and Royal Free Hospitals, and they are also reported by Dr. RAMSAY and Dr. O'SULLIVAN. In nearly every patient there are symptoms or signs of disease of the central nervous system, but the weight and site of the damage vary considerably from outbreak to outbreak. The Hampstead and Berlin epidemics illustrate this variation. The innervation of the eye muscles (diplopia and nystagmus) and the seventh and eighth cranial nerves (deafness, hyperacusis, vertigo, and facial weakness) suffer most commonly. Sensory symptoms and signs are common and pyramidal signs have also been observed. Some patients in Adelaide and Durban and at the Middlesex Hospital had retention of urine. The paresis, usually short-lived but occasionally persisting for weeks or months, is in itself an interesting problem, for in many cases it is not accompanied by the classical disturbances of tone and reflexes which would point to damage in the anterior horn or pyramidal tract.<sup>23 25 26</sup> Pain, muscular spasm, and involuntary movements often make the degree of palsy difficult to assess. In this connection the striking electromyographic records obtained by Dr. RAMSAY and Dr. O'SULLIVAN are of great interest. Although they do not as yet point to the exact nature of the lesions, they may provide evidence of organic paresis in patients who might otherwise be suspected of

hysteria, and in a disease at present so bereft of positive laboratory findings they may be a help in diagnosis in the future.

The outbreaks mainly differ in the severity and site of the damage to the nervous system; but the lymph-glands are another point of difference. Enlarged lymph-glands, particularly in the posterior cervical triangle, were prominent in the Hampstead and Royal Free cases, and they were also noted in 4 cases by WHITE and BURTON<sup>23</sup> and in the more doubtful Cumberland outbreak.<sup>21</sup> In retrospect lymphadenopathy was found to have been present in 2 of the 14 cases reported from the Middlesex.<sup>27</sup> Hepatitis and splenomegaly may also turn out to be part of the picture. It is doubtful whether the absence of these features in the other reports can be attributed entirely to observer error<sup>27</sup> and it must be accepted as a real discrepancy.

A study of the available material in group II shows sufficient common ground to suggest that this is a new clinical entity which may be expected to appear again here or elsewhere in the late summer and autumn. From the purely practical standpoint it would be useful to have a name for this syndrome. As the most helpful single feature in the recognition of this syndrome in the past has been the predominantly normal cerebrospinal fluid, the names which have already been suggested, "Iceland disease"<sup>16 23</sup> and "Akureyri disease," are not really appropriate. The objections to any but a purely descriptive name for a disorder without a known cause or established pathology are obvious. For this reason, the term "benign myalgic encephalomyelitis" may be acceptable. It in no way prejudices the arguments for or against a single or a related group of causal agents; and it does describe some of the striking features of a syndrome characterised by (1) symptoms and signs of damage to the brain and spinal cord, in a greater or lesser degree; (2) protracted muscle pain with paresis and cramp; (3) emotional disturbances in convalescence; (4) normal C.S.F.; (5) involvement, in some variants, of the reticuloendothelial system; (6) a protracted course with relapses in severe cases; and (7) a relatively benign outcome. It remains to identify this syndrome more precisely; but we believe that its characteristics are now sufficiently clear to differentiate it from poliomyelitis, epidemic myalgia, glandular fever, the forms of epidemic encephalitis already described, and, need it be said, hysteria.

### Antibiotic-resistant Staphylococci

IF bacteriologists are good judges of what is important, the direction and emphasis of much of their work suggests that it is high time we adopted whatever modifications of clinical practice are necessary to halt the spread of antibiotic-resistant staphylococci in hospital wards and outpatient departments. These infections in hospital are not only a cause of ill health, lost time, and wasted money, but also a source from which a veritable epidemic of staphylococcal infections may spread to the general community. There is no reason whatever to doubt the implications of ROUNTREE and RHEUBEN'S<sup>28</sup> evidence that in December, 1955, 25.7% of 101 nasal carriers of staphylococci among 200 Sydney blood-donors

26. Adnams J. N. Personal communication.

27. Acheson, E. D. *Lancet*, 1955, ii, 394.

28. Rountree, P. M., Rheuben, J. *Med. J. Aust.* 1956, i, 399.

## A NEW CLINICAL ENTITY ?

SIR,—In your leader of May 26 you suggest that the epidemic simulating poliomyelitis which occurred in Akureyri, Iceland, in 1948 be classified separately from clinically and epidemiologically similar outbreaks in various parts of the world since then. Your reason is that in the Akureyri epidemic the cerebrospinal fluid was abnormal, whereas in other outbreaks, which you classify as group II, it was usually normal. May I remind you that only 5 C.S.F. specimens from Akureyri were examined. The cell-counts were 3, 0, 80, 10, and 0 cells per c.mm. The protein was 50, 80, 59, and 75 mg. per 100 ml. in 4 samples (protein was not determined in 1 case). An increase in cells was thus found in 1 or 2 cases out of 5 and a slight increase in protein was found in the 4 cases examined.

The examination of 3 C.S.F. samples from patients in Reykjavík, ill at the time of the outbreak in Akureyri, revealed moderately raised cell-counts. It was assumed that the sporadic cases in Reykjavík were also Akureyri disease, but this unfortunately could not be proved.

This slight increase in protein and cells hardly justifies putting the Akureyri epidemic in a class separate from the other outbreaks which have been so strikingly similar both clinically and epidemiologically. Besides, abnormalities in the C.S.F. have also been found in certain cases in other outbreaks<sup>1-4</sup> which you classify in group II.

There is reason to believe that some of the lesions responsible for the signs and symptoms in all the outbreaks must have been in the spinal cord. If this is correct, one would expect that slight changes in the composition of the C.S.F. would be found in at least some cases at a certain stage of the infection, particularly in outbreaks of perhaps more than average severity.

You also suggest that this disease might be called "benign myalgic encephalomyelitis." Akureyri disease is benign in the sense that it does not kill, but in some cases it is not at all benign in other respects. Moreover, would it not be better to avoid the word encephalomyelitis until we know that inflammatory lesions are in fact present in the brain and spinal cord? It seems likely that such lesions may be present but so far nobody seems to have had an opportunity to look for them.

Previous authors seem to have hesitated to give this disease a descriptive name because they have felt the name might become unsuitable as knowledge of the nature and location of the morbid process increased.

I think this puzzling disease can hardly be adequately and permanently named until aetiological and anatomical studies have better identified its nature. Such studies would also help to distinguish it from related conditions, if they exist.

Reykjavík, Iceland.

BJÖRN SIGURDSSON.

1. White, D. N., Burch, R. B. *Neurology*, 1954, 4, 506.
2. Pellet, R. A. A. *Med. J. Aust.* 1951, i, 944.
3. Ramsay, A. M., O'Sullivan, E. *Lancet*, 1956, i, 761.
4. Sumner, D. W. *Ibid.*, p. 764.