OUTBREAK OF ASEPTIC MENINGITIS WITH EXANTHEM

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Wallgren (1925) postulated the existence of "acute epidemic aseptic meningitis" as distinct from non-paralytic poliomyelitis. Aseptic meningitis is now regarded as a syndrome which includes non-paralytic poliomyelitis and of which the list of causal viruses is lengthening, newcomers being Cocksackie (B) virus and, more recently, ECHO virus type 6 (Karzon *et al.*, 1956). Canicola fever may produce a similar picture (Ramsay, 1955). Encephalitic manifestations may on occasion suggest the term "meningo-encephalitis" (Galpine and Macrae, 1953).

Several reports of aseptic meningitis associated with an exanthem have been made in the last few years (*Monthly Bulletin*, 1956), including one described by Crawford *et al.* (1956) from which an enteric virus was isolated. In 1955 and especially 1956 outbreaks of aseptic meningitis associated with a rash occurred in various parts of the country (*Lancet*, 1956; Garnett *et al.*, 1957; Rotem, 1957) and strains of virus related to ECHO virus type 9 were recovered from throat washings, cerebrospinal fluid, and faeces in a number of instances (Boissard *et al.*, 1957). A comparable illness has been reported on the Continent by Nihoul and Quersin-Thiry (1957), who isolated a virus typed as ECHO 9. In a similar report from Sweden (Johnsson, 1957) a virus related to ECHO 4 is mentioned in addition to ECHO 9. The following account is of an outbreak of this type in Coventry in the autumn of 1956.

Epidemiology

From July 28 to August 31, 1956, one case of paralytic poliomyelitis was notified in Coventry, compared with seven clinically resembling "non-paralytic poliomyelitis." Examinations of faeces and sera from five of the latter were subsequently reported negative for poliomyelitis, and, although lacking the rash or familial tendency shown later, it is likely that these cases belong to the outbreak of aseptic meningitis which followed.

In September 19 cases, in October 17 cases, in November 14 cases, and in December 3 cases of aseptic meningitis,

TABLE I.—Incidence by Age and Sex

Age	Males	Females
0-11 months	0	0
12-23	1	1
2-4 years	7	1
5-14	15	12
15-24	3	2
25-34	1	6
35	1	0
36	1	0
Total	29	22

some with a rash, were admitted to hospital from Coventry—a period when only four cases of paralytic poliomyelitis occurred in the city. If we exclude a case with poliomyelitis type 1 virus in the faeces and a case having close contact with a paralytic case, 51 of these cases remain to be considered. Inquiries showed that a number of family contacts

were unwell but remained at home, and children in adjacent houses had illnesses but sought no medical advice. Twenty-three of the series were familial, being derived from nine families. Study of consecutive illnesses in several families suggested an incubation period of five or six days. Children preponderated, although a number of young adults were also affected (Table I). In the various age groups in all the families involved in the epidemic it was seen that 54% of the pre-school children exposed to risk, 56% of the schoolchildren, and only 17% of the adults became victims of the disease. The youngest patient was 15 months old and only two were under 2 years.

The majority (42) of the cases arose in neighbouring districts in the north-east of the city. The chief concentration was in a modern housing estate where 12 families were affected, and a group of houses surrounding a grassy area about the size of a village green provided 14 cases between September 17 and 23 with up to four cases from the same house. A near-by stagnant pool—a favourite spot for the local children—was blamed by several parents for the spread of the infection. Just before this time the persistently dull wet weather had relented to give a short Indian summer with a maximum shade temperature on September 13 of 75.8° F. (24.3° C.) and over 70° F. (21.1° C.) on September 22 to 25. Nine cases of aseptic meningitis occurred in areas of Coventry remote from the main focus, a direct link with the latter being established in three cases. It is remarkable that these scattered cases did not give rise to any known secondary foci.

The main incidence of aseptic meningitis followed quickly on the start of school term in early September and was accompanied by an increase in Sonne dysentery centred in the same area (Fig. 1), the two curves of incidence following closely for time and place (Fig. 2). Eleven of the 12 families mentioned above had a child attending the same school. The absence rate at this school was about 10%, approximately double that of the current average for all local authority schools in Coventry, presumably owing to the combined influence of Sonne dysentery and aseptic meningitis. In the nine families having more than one member in hospital a school child was clearly the first household case three times, a pre-school child once, an adult once, and in the remainder members fell ill approximately simultaneously.

FIG. 1.—Showing incidence of aseptic meningitis (above) and of Sonne dysentery (below) from September to December, 1956.

FIG. 2.—Showing the curves of incidence.

It is interesting that 73% of the cases of aseptic meningitis and 46% of all Sonne dysentery in the city in the last quarter of 1956 arose in a part of the city where housing standards are high, the estates being of comparatively recent development and the schools equally satisfactory. Following the onset of colder weather in early December the incidence of meningitis declined but Sonne dysentery showed a sharp increase, due mainly to an outbreak in another school in the area.

TABLE II.—Symptoms and Signs in 51 Cases

Pyrexia	49	Cough	6
Headache	51	Nasal discharge	4
Vomiting	41	Limb pains (usually legs)	8
Neck and/or back rigidity	37	Abdominal pain	4
Kernig's sign	18	Photophobia	9
Rash	19	Drowsiness	2
Backache and general aches	16	Delirium	1
Mild sore throat (no exudate)	13	Diarrhoea	1

Clinical Description of 51 Cases (Table II)

In at least 18 cases (admitted in the first and second day of the disease) there was early onset of meningeal symptoms. Another 19 cases were admitted in their third and fourth day and 14 cases on the fifth day or later. In four of the latter the history suggested a distinct pre-meningeal phase followed by a remission before onset of meningeal symptoms. The duration of illness (estimated from day of onset to final return of temperature to normal) varied from 2 to 13 days, but 41 cases lasted four to nine days. Pyrexia was usually considerable, and reached 101 to 103° F. (38.3 to 39.4° C.) in 35 cases, the maximum recorded being 103.8° F. (39.9° C.). In 20 cases a remission or intermission of pyrexia lasting one to three days occurred whilst in hospital, the final elevation being sometimes the higher. Fall of temperature was by rapid lysis, taking one to two days to reach normal.

The patients typically presented with headache (often severe, irritability, pyrexia, and unimpaired consciousness. Neck or back rigidity was recorded in 37 cases only, and in nine of these it was slight, as was Kernig's sign when present. In at least 20 cases, therefore, these signs were slight or absent. No nystagmus was seen. Superficial and tendon reflexes were usually brisk and plantar responses always flexor. Vomiting was common before admission but seldom gave much trouble afterwards. Limb pains sometimes caused fear of poliomyelitis, and in two cases with abdominal pain anxiety was caused in one by its severity (with vomiting) and in the other by localization in the right iliac fossa. No thoracic pains were noted.

In 12 out of 32 cases where special search was made small shotty lymphatic nodes were palpated in the posterior triangles of the neck, but they were deemed to be too small to be of special significance. Splenic enlargement was not recorded.

An exanthem was seen in 19 cases. It was unaccompanied by enanthem, conjunctival congestion, or adenopathy, and was commonest in the sharpest phase of the outbreak when 7 rashes were seen in 14 cases. The appearance of 17 of the rashes in relation to day of disease was: first day, 2; second day, 3; third day, 2; fourth day, 6; fifth day, 3; sixth day, 1. In relation to pyrexia the rash was observed in 11 cases when the temperature was falling, in four when intermitting or remitting, in three when destined to fall within 24 hours, and in one when finally resolved. Where an intermission or remission of temperature occurred in the same patient the rash appeared in relation to the first peak in six cases and the second peak in one case.

In 17 cases the rash was erythematous, in one case mixed erythematous and petechial, and in one solely petechial. The erythema consisted of small pink discrete macules or maculo-papules resembling those of rubella. It always invaded the face, to which it was limited in nine cases, often affecting the cheeks only (Fig. 3), but the chin and mid-forehead were also affected in one or two cases and the whole face in two others. On the face the rash took up to

as many as five days to disappear; in such cases the spots became semi-confluent and of a violaceous tint. In these respects it recalled the description of the rash in "fifth disease" (Harries and Mitman, 1951). In six cases it spread on to neck, shoulders, and upper part of the trunk. In two cases (one with trunk involvement) isolated areas of

FIG. 3.—Showing rash limited to the cheeks.

rash were seen in the distal parts of the limbs. In one case (that of the youngest patient, aged 15 months) the rash was generalized. On trunk and limbs the rash tended to be short-lived, often altering greatly within a few hours.

In one of the two cases with petechiae these were scattered on the shoulders at the same time as the usual erythematous rash was present on the cheeks; in the other a striking petechial rash appeared in the submental area, with scattered lesions on the trunk and no erythema.

Symptomatic treatment only was given except in one of the more severe cases in which chloramphenicol was used. No complications were observed and convalescence was rapid in all cases.

Clinical Pathology

Fifty-three Specimens of Cerebrospinal Fluid.—Pleocytosis (Table III) did not commonly exceed 500 per c.mm., although it could be much higher. Over the series polymorphonuclears and lymphocytes were approximately equal, with much individual variation. Two C.S.F.s with higher

TABLE III.—White-cell Counts in 53 Specimens of Cerebrospinal Fluid Taken from 48 Patients (Includes 5 Double Examinations)

Cells per c.mm.	No. of Samples	Polymorphs Predominant	Lymphocytes Predominant	Polymorphs and Lymphocytes about Equal
0-5 (normal)	5	—	—	—
6-20	2	1	1	0
21-100	11	4	5	2
101-500	28	11	14	3
501-1,000	3	1	1	1
1,001-2,000	2	1	1	0
2,001-3,000	1	0	0	1
3,760	1	1	0	0
Total	53	19	22	7

counts were opalescent and one (3 760 cells per c.mm., 94% polymorphonuclears) was frankly turbid. Repeat lumbar punctures in five patients (four with normal first specimens) all showed marked increase of cells. In about half the specimens a rise of protein above the high normal level of 40 mg./100 ml. was found, usually to less than 100 mg./100 ml., but three cases fell in the range 100–200 mg./100 ml. and there was one of 240 mg./100 ml. (associated with the count of 3,760 cells per c.mm. mentioned above).

White Blood Cell Counts in 33 Patients (Table IV).—About half the counts were either low normal or leucopenic owing to a tendency to relative neutropenia. No example of leucocytosis was found. Atypical lymphocytes were seldom reported. The erythrocyte sedimentation rate (Westergren) was estimated in 18 cases and showed an increase in half the number—three in the range 8–15 mm. in the first hour and six in the range 16–30 mm.

Virus Investigations.—Specimens of faeces from 27 patients were examined at the Virus Reference Laboratory, and in 19 instances a virus related to ECHO virus type 9 was isolated. This experience resembles that found in a number of outbreaks of aseptic meningitis during 1956 (Boissard *et al.*, 1957). In addition, 18 of the patients showed fourfold or greater rises in antibody titre against ECHO virus type 9 during the course of their illness. These laboratory studies will be reported in greater detail separately (A. D. Macrae, to be published).

TABLE IV.—Total White-cell Counts (Normal, 4,000–11,000 per c.mm.) and Neutrophil Counts (Normal 2,500–7,500 per c.mm.) of 33 Patients

White Cells per c.mm.	No. of Patients	Neutrophils per c.mm.	No. of Patients
3,000–4,000	5	Under 2,500	7
4,001–5,000	11	2,501–3,000	12
5,001–11,000	17	3,001–9,600	14

Discussion

The occurrence in Coventry in 1956 of aseptic meningitis associated with an exanthem was similar to the experience in a number of other places in that year. A syndrome of this kind had been noted as far back as 1948 (Parry and Good, 1949). The pattern of the Coventry outbreak was consistent with the existence of considerable immunity in the adult and infant populations, children above the age of 2 years being preponderantly affected. The presumed early cases did not have the characteristic rash or the familial incidence of the later ones. These considerations might suggest a variation in the clinical picture of a usually less distinguishable endemic infection.

The Coventry outbreak occurred mainly in one part of the city, and, although it followed the opening of schools for the autumn term, other evidence seemed as much in favour of the home being the theatre of spread as the school. A few cases arose singly in scattered areas in the city but did not give rise to secondary foci, and the factors which encourage the disease to flourish only in one area of the city remain conjectural. It was noticeable that Sonne dysentery was concentrated in the same area, and it is interesting to speculate whether the same environment merely favoured both diseases or whether the causal agent of the meningeal infection profited by the opportunity for faecal spread created by the diarrhoeal disease. There was no clinical evidence that Sonne dysentery predisposed to the meningeal infection, as a history of diarrhoea in the latter was uncommon and in only one household was the coexistence of the two diseases confirmed.

An erythematous rash was observed in every second or third of the Coventry cases and its distribution was characteristic enough to have diagnostic value. The occasional petechial elements and the not uncommon polymorphonuclear predominance in the C.S.F. suggest grounds for occasional confusion with meningococcal meningitis. The occurrence of rashes and of familial cases was commonest at the peak of the outbreak. If the rash can be taken as

evidence of viraemia it may indicate that the central nervous system is infected via the blood stream; the development of solid immunity after an attack is also to be expected—as in other virus diseases associated with a rash. The illness was benign and only occasionally acute enough to cause temporary anxiety. Encephalitic signs were absent. Recovery was rapid and complete.

In considering transmission of this type of aseptic meningitis it is tempting to draw a parallel with poliomyelitis. In both diseases virus has been found in pharyngeal washings as well as the faeces—the commonest view in poliomyelitis being that infection may be transmitted at different times by respiratory and alimentary routes (Taylor and Knowelden, 1957). The meningitis outbreak in Coventry occurred in the season favoured by poliomyelitis. Apart from the seasonal predilection, Bradley and Richmond (1953) could not correlate any specific meteorological factor with the incidence of poliomyelitis; likewise the association of a warm spell with the peak of the Coventry outbreak of meningitis may have been fortuitous, but it at least encouraged the mixing of children. Familial illnesses in poliomyelitis are uncommon compared with the frequency seen in this meningeal outbreak, but this may be misleading, as inapparent family infection is not uncommon in poliomyelitis (Francis, 1952).

Summary

In 1956 there were outbreaks in this and other countries of aseptic meningitis associated with an exanthem in a proportion of cases. One of these occurred in Coventry and 51 cases were admitted to hospital. From 19 out of 27 cases a virus related to ECHO virus type 9 was isolated, resembling the experience in a number of other outbreaks in 1956. Eighteen of these cases showed a significant rise of antibody titre to ECHO virus type 9 during their illness.

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The number of cases of plague in the world reported in 1957—namely, 514—was the lowest annual total since the beginning of the century, states the World Health Organization. This is mainly because the incidence in India was unusually low. There were 44 cases there as compared with 262 in 1956, 542 in 1955, and 8,230 in 1951. The world total in 1951 was 15,399. In America, one case was reported in the U.S.A. (Texas) in 1957, and active foci of the disease were detected in Ecuador, Peru, and Brazil. In Indonesia, only 15 cases were notified in Java against 113 in 1956 and 354 in 1955. Most of the cases reported from Asia outside China and the U.S.S.R. were in Burma. In Africa the highest frequency of cases was in the north-eastern part of the Belgian Congo. Sporadic cases were also reported in Kenya, Tanganyika, and South Africa.