LARGE EPIDEMIC OUTBREAK OF VOMITING ASSOCIATED WITH MENINGISM AND EXANTHEM

CLINICAL AND EPIDEMIOLOGICAL OBSERVATIONS

BY

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Early in October, 1956, the headmistress of an infants' school in Harlow, Essex, informed the Public Health Department of a sudden outbreak of vomiting and diarrhoea amongst her pupils. At first it was thought to be food-poisoning, but preliminary investigations did not confirm this diagnosis, especially as at the same time it was learned from one of the general practitioners that during the past fortnight he had seen a number of patients complaining of vomiting, severe headache, neck rigidity, and occasional diarrhoea. Other general practitioners were contacted and most of them confirmed the occurrence of similar cases. Notifications had also started coming in of non-paralytic poliomyelitis, but, although the clinical symptoms and C.S.F. findings seemed to corroborate the diagnosis, it was obvious from epidemiological observations that the disease was not poliomyelitis. It soon became apparent that there was in Harlow a sharp epidemic outbreak of an obscure infection believed to be caused by a virus.

It is difficult to estimate the extent of the epidemic because most of the cases were very mild, the patients recovering within 24 to 48 hours, without coming to the attention of either their family doctor or the Public Health Department. However, from the available information it can be deduced that there were several hundred cases in the town, over 170 of which were reported by the schools. Fourteen patients were admitted to hospital.

Clinical Features

In the mild cases vomiting was the most prominent symptom. The usual history was that of a child suddenly being sick at school or waking up at night or in the early hours of the morning and vomiting in bed. In adults such vomiting was usually less precipitous and was accompanied by headache. In some patients there was a short prodromal period of general malaise. The following are two fairly typical cases.

Case 1.—A boy aged 4 years. October 16: Suddenly woke up during the night and was sick in bed. Continued vomiting until late the next morning and complained of headache. Slight diarrhoea. Temperature 100° F. (37.8° C.). In the afternoon very listless but otherwise feeling all right. Completely recovered next day.

Case 2.—A male teacher aged 34. October 15: Woke up at 6 a.m. feeling intense nausea and frontal headache followed by repeated vomiting. Later in the morning went to work but returned home after two hours complaining of headache, shivering, thirst, and prostration. Temperature not taken. For a further two days was off colour and then returned to normal health.

Many patients presented a more complex clinical symptomatology, often with meningism and sometimes with exanthem. Over 80 non-hospital cases were investigated, but, as this is a relatively small proportion of the total number and because many cases were selected for investigation on account of their clinical interest, a detailed analysis of them tabulated according to age, sex, presence or severity

of certain symptoms, etc., would only give a biased and misleading picture of the whole epidemic. Therefore the following is simply a description of the main symptoms in their approximate order of frequency.

(1) *Nausea and/or Vomiting*: vomiting was projectile and sudden and consisted of bilious fluid with mucus; nausea at times preceded or replaced vomiting. (2) *Headache*: this was usually very severe and mainly post-orbital; less frequently it was occipital, particularly when associated with neck rigidity. (3) *Anorexia*. (4) *Upper respiratory symptoms*: injection of fauces was a very common finding, though only some patients actually complained of sore throat; a few had a cough. (5) *Pyrexia*: usually moderate, rarely reaching 103° F. (39.4° C.) and falling by lysis. (6) *Generalized aches and pains*. (7) *Sweating*: mainly at night and very profuse. (8) *Drowsiness*. (9) *Prostration*. (10) *Neck and back rigidity* in many cases was very pronounced and a positive Kernig's sign could often be elicited. (11) *Giddiness*: often pronounced in the more severe cases. (12) *Photophobia*: many patients also complained of pain on moving their eyes; diplopia in two cases. (13) *Abdominal pain*: more often complained of during the later stages of the epidemic, when it became very severe. (14) *Muscular tenderness* seldom associated with transient weakness of a group of muscles. (15) *Diarrhoea*: only mild and of short duration and not a common feature. (16) *Enlargement of lymph nodes*: the tonsillar and occipital glands were mostly involved. (17) *Exanthem* was observed in only 13 cases and was unrelated to the severity of the other symptoms. In fact, in some of the multiple cases occurring in families it was the only pathological symptom. The rash was usually rubella-like but of a deeper colour and more punctate, sometimes petechial. It affected the trunk, thighs, and face. The duration of the exanthem was on an average three to four days, but in one case it had appeared and disappeared within an hour. (18) *Otalgia* in a few cases. (19) *Retention of urine*: transient and in only two cases.

In cases with meningeal involvement the onset was less sudden than in those without. Complaints of anorexia, general malaise, headache, aches and pains, and sore throat preceded by several days the acute phase of the disease. In many cases the symptoms subsided on the second or third day of the illness, only to reappear with increased severity and meningism within 24 to 36 hours. The duration of the more severe cases was on an average five to eight days, and recovery was complete though lassitude persisted somewhat longer.

Case 3.—Housewife aged 37 years. October 16: Complained of general malaise and lassitude which with vague aches and pains in the back continued for two days. On the third day felt well but later in evening developed very severe headache which kept her awake at night. Temperature normal. During next four days the headache became worse and she complained of giddiness, photophobia, vomiting, and profuse sweating. Temperature around 100° F. (37.8° C.). Pronounced neck and back stiffness with positive Kernig's sign. All these symptoms completely disappeared on eighth day, leaving behind considerable prostration which lasted for a further three days.

Family Outbreak

In family outbreaks the variety and severity of symptoms differed from case to case.

Case 4.—Infant girl aged 10 months. September 4: Very restless in morning—later developed a fine punctate rash all over body. Showed signs of discomfort for another day and then completely recovered. Rash vanished four days after its appearance.

Case 5.—Sister of Case 4 aged 3½ years. September 6: Complained of abdominal pain and generalized aches. During the following day was very drowsy and in the evening developed a rash on her thighs and abdomen. During next four days all symptoms gradually cleared up and she recovered.

Case 6.—Brother of Cases 4 and 5 aged 2½ years. September 7: Woke up at night with abdominal pain. Next day complained of general malaise, drowsiness, and slight diarrhoea. A rubella-like rash appeared on the body. Gradual complete recovery in course of next three days.

Case 7.—Mother of Cases 4-6 aged 23. September 9: Woke up with a headache which got progressively worse. Next day felt very ill—complained of drowsiness, photophobia, headache, and stiffness of the neck. These symptoms gradually subsided during next few days and she made a complete recovery.

Case 8.—Salesman aged 24 (husband of Case 7 and father of Cases 4-6). September 9: In the evening felt cold and shivery. Next day had severe headache in occipital region with pain radiating down the neck, generalized aches and pains in whole body, sore throat, drowsiness, temperature 102° F. (38.9° C.). During the following day felt well except for residual slight headache. The day after again complained of severe headache, profuse sweating, and pyrexia with pain in the neck and sore throat. Vomited several times and was troubled by stiffness of neck and back. A slight rash appeared on face. Admitted to hospital on September 13. Temperature 101.8° F. (38.8° C.), pulse 110, respirations 28. Erythema of face, neck, and front of trunk. A coated tongue, injected throat, and neck and back rigidity. All reflexes present and equal. No other abnormal signs. Blood: Hb, 96%; white cells, 7,100/c.mm. (polymorphs 68%, lymphocytes 26%, monocytes 5%, eosinophils 1%); E.S.R., 7 mm. (Westergren). C.S.F.: protein, 40 mg./100 ml.; globulin, negative; chlorides, 720 mg./100 ml.; glucose normal; cells, 27/c.mm.; stained film small lymphocytes only. Throat swab: moderate growth of *Streptococcus viridans* and *Neisseria catarrhalis*. Stools: tissue culture negative. The pyrexia settled after 36 hours but there was a frequency of micturition due to a urinary infection with *Escherichia coli*. This condition cleared up in five days with sulphonamide treatment. Complete recovery.

Cases 4-7 were not seen by a doctor and their histories were obtained only after recovery and subsequent to the hospital admission of Case 8.

There were other similar family outbreaks in which some cases had pronounced meningeal symptoms and were admitted to hospital; others suffered from vomiting and headache only, or from an exanthem without any other pathological symptoms.

In the 14 hospital cases the symptoms were distributed as follows: pyrexia 14 cases, neck rigidity 11 (positive Kernig sign in 7), severe headache 10, congested fauces 10, nausea and vomiting 8, pains in limbs 5, drowsiness 5, abdominal pain 4, exanthem 3, profuse sweating 2, vertigo 2, photophobia 2, enlarged lymph nodes 2, otalgia 2, diarrhoea 1, diplopia 1.

Laboratory Findings

Blood.—Specimens from 17 patients were examined. Haemoglobin, white-cell count, and E.S.R. were mostly within normal limits. The differential count showed relative lymphocytosis of up to 54%, with an increase of monocytes up to 12% and a slight increase in eosinophils. There were no abnormal lymphocytes characteristic of glandular fever. Paired serum specimens of six patients were sent to the Central Public Health Laboratory, Colindale, where tests for mumps, lymphocytic choriomeningitis, influenza A and B, A.P.C. group, Q fever, psittacosis, *Streptococcus M.G.*, *Leptospira icterohaemorrhagiae*, and *L. canicola* were negative.

Cerebrospinal Fluid.—In only nine hospital cases were lumbar punctures done. The C.S.F. was sterile on culture and the only changes were occasionally increased protein (up to 140 mg./100 ml.) and pleocytosis with a cell count varying from 27 to 2,500/c.mm. In two of the cases the cells were at first mainly polymorphs (86% and 90%) but in subsequent specimens lymphocytes predominated in a similar proportion. In each of the other seven cases only one lumbar puncture was performed and the differential cell count showed lymphocytosis of between 75% and 100% in all but one of them. In the latter there were 75% polymorphs and 25% lymphocytes.

Faeces.—Bacterial cultures of 40 cases were negative for organisms of the salmonella and shigella groups. Virus investigations were carried out at the Central Public Health Laboratory, Colindale. One batch of 22 specimens came from children from the infants' school which had first reported an outbreak of vomiting. Rectal swabs of some close family contacts were also included. A cytopathogenic agent was isolated in three cultures. In two cases it was identified as Coxsackie B₁ and was grown from the stools of a 5-year-old girl and her father, both of whom had suffered only from sudden vomiting with headache lasting 24 hours. The virus isolated in a third case, also from a girl of 5 with similar symptoms, could not be identified

despite repeated attempts. However, it was not poliomyelitis virus and did not appear to fall within the Coxsackie B, Coxsackie A9, or ECHO group of viruses. Subsequently, when the epidemic had spread and cases with meningeal involvement and rashes had appeared, the laboratory, owing to pressure of work, could accept only four specimens of such cases and all were negative on tissue cultures.

Nose and Throat Swabs.—In only two cases was there a growth of *Str. viridans*. Four other bacterial cultures were negative.

Epidemiology

The earliest known case in the described outbreak occurred in May and was diagnosed at the hospital as lymphocytic choriomeningitis, presumably on the grounds of a predominantly lymphocytic pleocytosis in the C.S.F. No virus investigations or neutralization or complement-fixation tests against lymphocytic choriomeningitis were carried out. Between May and the last week in September only two more cases were admitted to hospital, one diagnosed as mild encephalitis, the other as non-paralytic poliomyelitis. Both were adults in their twenties. There is no indication that the minor form of the disease was widespread during that period.

On September 18 a 5-year-old girl attending a local infants' school was taken ill with severe headache, vomiting, pyrexia, drowsiness, and, later, neck and back stiffness. She was admitted to hospital on September 21 as a case of meningitis. Two days after this girl's first day of absence from school other children in the same classroom started having bouts of sudden vomiting, sometimes associated with mild diarrhoea and abdominal pain or with headache. The infection rapidly spread to other classrooms and to the adjoining junior school and later to practically all the schools in the town. A number of teaching and non-teaching staff were also affected. The epidemic reached its peak in October, when not only the total incidence was high but the proportion of patients with meningeal involvement was considerable. Only relatively few cases, however, were admitted to hospital, because by then all general practitioners in the area knew of the outbreak and of its clinical features and were therefore less alarmed by symptoms which at times suggested poliomyelitis.

In November and December there were only isolated cases with meningeal involvement, although the number of abortive cases was still quite high. At that time it was also noticed that besides vomiting severe abdominal pain of a myalgic type had become a prominent feature. By early January, 1957, the epidemic had spent itself.

The disease mainly affected children and young adults of either sex, meningism being both more frequent and more severe in the latter. Infectivity was very high and multiple cases in families were common. The incubation period was around two days. This could be deduced from the fact that when the infection was first introduced into a family or a school subsequent cases appeared at an interval of one to three days. It was also established in three cases that the first symptoms developed two days after a known and only contact with an infected person.

It is interesting to note that in those schools which rigorously enforced the exclusion for a week of all children who had suffered from sudden unaccountable vomiting the incidence of the disease decreased very considerably. A transient drop in the number of children affected was also observed in all schools for a short time after the mid-term break at the end of October.

The frequent finding of injected fauces points to an upper respiratory portal of entry of the infection.

During the first weeks of the epidemic there were no other infectious diseases in the area except a few sporadic cases of whooping-cough and measles. In the third week of October, however, the incidence of measles increased sharply and continued to do so with fluctuations until it reached a peak of 273 cases during the week ending January 5, 1957.

Discussion

Most of the Harlow cases were mild and in many ways resembled "epidemic nausea and vomiting" ("winter vomiting disease"). The common features were very short incubation period, precipitate vomiting, abdominal pain, anorexia, headache, injected fauces, and occasional diarrhoea. This disease has been known as a definite syndrome since its first description by Zahorsky (1929) in the U.S.A. In this country outbreaks have been reported by various authors, including Bradley (1943), who made an extensive study of the disease. The causative agent of epidemic nausea and vomiting is believed to be a virus, but it has not yet been isolated. Neither meningism nor exanthems have ever been directly associated with the disease, though Haworth *et al.* (1956) have described as "winter vomiting disease with meningeal involvement" cases in which there were changes in the C.S.F. but not physical signs of meningitis.

The more severe of the Harlow cases had the appearance of non-paralytic poliomyelitis because of their diphasic character, the C.S.F. findings, and other clinical features. However, the very short incubation period and high infectivity, the frequency of multiple cases in households, the absence of paralytic disease (except in one doubtful case mentioned below), and the failure to recover poliomyelitis virus in tissue cultures speak against this diagnosis.

Aseptic meningitis simulating poliomyelitis was first described by Wallgren (1925). Since then, and particularly in recent years, poliomyelitis-like outbreaks have been reported in this and several other countries. Although they had many features in common they nevertheless differed in some important respects. One of the main differences was in the findings of the C.S.F., and a suggestion has been made (Lancet, 1956) to classify the syndrome according to the presence or absence of changes in the C.S.F. Pleocytosis in cases with pronounced meningism and without encephalitic signs and sequelae is found in aseptic virus meningitis. Such cases have been reported by Parry and Good (1949), Coverton and Miles (1953), Tyrrell and Snell (1956), Pickles (1956), Garnett *et al.* (1957), Rotem (1957), and others. In some outbreaks the poliomyelitis-like disease was regarded as encephalomyelitis because the C.S.F. was normal and there were muscular weaknesses and psychological disturbances, usually transient but at times of long duration (Pellw, 1951; Sigurdsson and Gudmundsson, 1956; Ramsay and O'Sullivan, 1956; Sumner, 1956; Jelinek, 1956; Galpine and Brady, 1957; and others).

Symptomatically the distinction between meningitis and encephalitis is not always clear-cut and some cases have been described as meningo-encephalitis (Lyle, 1956; Langdale-Smith *et al.*, 1957).

In the Harlow outbreak most cases with meningeal involvement had the clinical appearance of aseptic meningitis. Pleocytosis was found in nine cases in which lumbar puncture was done. No mental changes were observed and transient muscular weakness was seen in only a few patients. In one case, however, there was slight residual paresis of the abdominal muscles. This was diagnosed at the time as paralytic poliomyelitis, but in the light of further knowledge the diagnosis is open to doubt.

Symptoms such as mouth lesions (Tyrrell and Snell, 1956) were absent from the Harlow and other outbreaks. Acute myalgia, more prominent in cases of benign encephalomyelitis than in aseptic meningitis, appeared in the later stages of the Harlow epidemic and affected the abdominal muscles.

Virus investigations have yielded varying results. Such cytopathogenic organisms as have been isolated were from cases in which the C.S.F. showed pleocytosis and which could be described as aseptic meningitis. Crawford *et al.* (1956) reported the recovery of five strains of virus from the stools of their cases. These were small babies 3 to 14 months old who presented a clinical picture of irritability, pyrexia, vomiting, diarrhoea, and a maculopapular rash but no meningism. There was pleocytosis in the C.S.F. The

strains of virus were morphologically closely related to each other but distinct from poliomyelitis, Coxsackie, and other known viruses. Tyrrell and Snell (1956) isolated a virus related to Coxsackie A, and other authors found ECHO viruses or viruses akin to this group (Boissard *et al.*, 1957; Rotem, 1957).

Coxsackie B viruses have for some time been known to be associated with certain outbreaks of aseptic meningitis (Hummeler *et al.*, 1954; Wilkins *et al.*, 1955; McLeod *et al.*, 1956). Viruses of this group are, according to Rhodes (1956), rarely found in healthy persons, so that their recovery from two of the Harlow cases may be significant though inconclusive.

It appears that different groups of viruses may be responsible for outbreaks which present a similar general clinical picture but differ in some aspects from each other. Further careful investigations will no doubt throw more light on this infection.

Summary

An account is given of a large outbreak of a disease closely resembling epidemic nausea and vomiting but with a proportion of cases exhibiting meningism and other symptoms simulating non-paralytic poliomyelitis and some with an exanthem. The differences in the clinical features of this and other outbreaks simulating poliomyelitis are discussed.

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The problem of the rheumatic diseases was twofold, said Dr. W. S. C. COPEMAN, chairman of the Empire Rheumatism Council, when addressing the Royal Society of Health on January 15. The first aspect was financial, as the present state of knowledge necessitated a large expenditure on basic research, much of which had to come from voluntary sources, chief amongst which was the Empire Rheumatism Council. The second main aspect was the provision of adequate treatment centres of high standard within the present regional organization of the National Health Service. Although two university chairs in rheumatology had been established, consultant posts in this specialty were not yet recognized by the Ministry of Health.