

# Meningitis and Encephalitis Associated with Mumps Infection

## A 10-Year Survey

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**Johnstone, J. A., Ross, C. A. C., and Dunn, M. (1972).** *Archives of Disease in Childhood*, 47, 647. **Meningitis and encephalitis associated with mumps infection: a 10-year survey.** During the 10-year period 1960–69, 137 patients in Ruchill Hospital were diagnosed by clinical and laboratory findings as mumps meningitis. Parotitis was detected in only 51 (37%). There was a male preponderance, 97 : 40. 96% of the males were under 10 years old compared with 78% of the females. The peak incidence of patients with meningitis alone was in June–July, parotitis with meningitis was from November to January. All 137 meningitis patients made a good recovery.

Of the 2 definite cases of mumps encephalitis 1 showed severe psychomotor sequelae.

More of the total 139 patients showed rising titres to mumps 'V' envelope antigen than to mumps 'S' nucleoprotein antigen.

Live attenuated mumps vaccines have been developed recently and used in the U.S.S.R. and U.S.A. (Hilleman *et al.*, 1968). The advisability of introducing a mumps vaccine for routine use in Britain has been questioned by Dick (1969) on the grounds that there are practically no data on the incidence of mumps or its complications on which to base a rational and logical immunization programme. He also claims that mumps is relatively mild in children and that serious sequelae appear to be rare.

The most common complication of mumps is aseptic meningitis; indeed mumps is the commonest perennial cause of aseptic meningitis in Britain. The most serious complication of mumps is encephalitis. It therefore seemed relevant to analyse our clinical and laboratory findings for mumps meningitis and encephalitis over the 10-year period 1960–69. Also, since deafness sometimes follows mumps infection (Fowler, 1960; Lindsay, Davey, and Ward, 1960; Whettnall and Fry, 1964), a follow-up study to investigate hearing was attempted.

In establishing a laboratory diagnosis of mumps infection serological demonstration of a rising antibody titre for mumps is more reliable than virus isolation, and the most practical serological method for mumps diagnosis is complement-fixation (CF). During infection with mumps two distinct CF antibodies appear in the patient's blood, one against the envelope of the virus (anti-V) and the other against 'soluble' viral nucleoprotein (anti-S). In early convalescence the titre of both antibodies is high, but anti-S usually disappears within a few months whereas anti-V persists for many years (Henle, Harris, and Henle, 1948).

Slight antigenic relation between mumps and parainfluenza viruses has been reported (Cook *et al.*, 1959). However, meningitis has not to our knowledge been associated with parainfluenza infections. Thus a rising mumps CF antibody titre in a patient with meningitis can be regarded as indicative of current mumps infection, and a high but not rising mumps S titre as indicating recent infection.

### Patients and Methods

The present study comprised patients admitted to Ruchill Hospital from 1960–69 with meningitis and/or

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encephalitis, in whom a serological diagnosis of mumps infection was made by the demonstration of rising or high mumps CF antibody levels.

Mumps S and V antibodies were measured in paired sera, with an interval usually of 10 to 14 days, by the CF method described by Grist *et al.* (1966). A serological diagnosis of mumps infection comprised a fourfold or greater rise in titre for mumps S and or mumps V, or high titres for mumps S ( $\geq 64$ ). All titres are expressed as reciprocals.

### Results

A total of 139 patients was diagnosed by clinical and laboratory findings as mumps meningitis or encephalitis. Many of these 139 were admitted with a diagnosis of meningoencephalitis; however, only 6 (all males aged from 2 to 7 years) showed evidence of cerebral involvement. In 4 of these 6 the clinical features suggesting encephalitis comprised one or more of the following: convulsions, drowsiness, twitching or rigidity of limbs, slurred speech. These features were transient and each of these 4 patients made a full speedy recovery; since they all had pleocytosis in cerebrospinal fluid (CSF), they have been considered as cases of mumps meningitis. The remaining 2 with more severe evidence of cerebral involvement had residual neurological signs on discharge from hospital; in this study they have been considered as cases of mumps encephalitis (see below). One of these 2 showed normal CSF findings.

**Meningitis cases.** These comprised 137 patients in whom meningitis was confirmed by the presence of pleocytosis in CSF. Parotitis, the accepted clinical criterion of mumps infection, was detected in only 51 (37%) of the total 137 patients. Thus, in most cases virological tests were necessary to establish the diagnosis. Rising antibody titres for mumps were obtained in 105 (73%) of the 137 patients: 68 for both S and V, 27 for V only, and 10 for S only (Table I). In both groups more patients showed rising titres to the V than to the S antigen, more in Group M than in Group MP.

TABLE I  
*Antibody Response in Patients with Meningitis (M)  
and Meningitis with Parotitis (MP)*

Group	Rising Titres			High Titres	Totals
	S and V	S only	V only	(S $\geq$ 64)	
M	41	4	17	24	86
MP	27	6	10	8	51
Totals	68	10	27	32	137

*Age, sex, and parotitis.* Table II shows that of the total 137 patients 97 (71%) were males and 40 (29%) females, i.e. a male preponderance. Males seemed to acquire this illness earlier than females: 88 (96%) of the total 97 males being under 10 years old compared with 31 (78%) of the total 40 females. Only three patients (all females) were in the group 10-14 years old. Parotitis was also more frequently detected in the males: 45 (46%) compared with 6 (15%) of the females; the male age-group showing the highest proportion of cases with parotitis was 5 to 9 years.

*Month of illness.* The cumulative number of cases with onset of illness by month is shown in Table III. Cases occurred in each month, but the peak incidence of Group M patients was in June-July (34 (39%) of the 86), whereas the peak of Group MP was from November to January (27 (53%) of the 51).

*CSF examination.* The range of the initial cell counts is shown in Table IV. Counts of over 200 were obtained in 43 (50%) of Group M patients and in 31 (61%) of Group MP; this difference between the two groups is not statistically significant. A lymphocytic preponderance was the usual finding in both groups.

CSF protein levels showed little difference between both groups (Table V), most patients having only a small rise. Protein values over 60

TABLE II  
*Age and Sex Distribution of Patients with Mumps Meningitis (M) and Meningitis with Parotitis (MP)*

Age	0-4		5-9		10-14		15+		Totals		M and MP
	M	MP	M	MP	M	MP	M	MP	M	MP	
Sex											
Male	25	11	25	27	0	0	2	7	52	45	97
Female	11	2	15	3	3	0	5	1	34	6	40
Total	36	13	40	30	3	0	7	8	86	51	137

TABLE III

Monthly Distribution of Cases of Mumps Meningitis (M) and Meningitis with Parotitis (MP)

Group	J	F	M	A	M	J	J	A	S	O	N	D	Total
M	6	6	6	2	6	19	15	7	4	6	7	2	86
MP	12	1	5	3	6	3	1	1	2	2	8	7	51
Totals	18	7	11	5	12	22	16	8	6	8	15	9	137

TABLE IV  
CSF Cell Count

Count (cells/mm <sup>3</sup> )	Meningitis	Meningitis with Parotitis
—20	9	2
—100	17	8
—200	17	10
—500	28	19
—1000	12	8
Over 1000	3	4
Total	86	51

TABLE V  
CSF Protein

Protein (mg/100 ml)	Meningitis	Meningitis with Parotitis
—30	46	26
—60	27	10
—100	8	8
100+	3	4
Not stated	2	3
Total	86	51

mg/100 ml were found in 13 (15%) of Group M compared with 15 (29%) of group MP; again the difference between the two groups is not significant.

An abnormally low CSF sugar (<40 mg/100 ml), generally considered suggestive of bacterial and not viral infection, was found in 8 (6%) of the 137 patients: 7 in Group M and 1 in Group MP.

*Follow-up of mumps meningitis.* An attempt was made in 1970–71 to contact by letter 122 individuals in Groups M and MP, and give them appointments for audiometric assessment. The response was poor: only 5 over 16 years of age and 8 under 15 agreed to be reviewed; all 13 had normal hearing.

**Encephalitis cases.** The 2 patients with encephalitis were both admitted to hospital in December 1960. It was of interest that in both children there was a history of recent head injury. Their case histories were as follows.

*Case 1.* A male, aged two years. This child, the youngest of 5 sibs, became ill on 8 December 1960, and was admitted to hospital two days later in a coma. On 5 December he had fallen and struck the right side of his head, without loss of consciousness or other apparent ill effect. On 8 December, he vomited a few times and the next day he was noticed to have swelling of the left jaw; he was fevered and shivering and in the afternoon became suddenly unconscious with twitching of the left side of the mouth and the left leg. After a period of unconsciousness lasting 2 hours he recovered and remained well until the next morning when he again became unconscious, with eyes staring to the right and twitching of the right arm. On admission he was found to be comatose, with minimal parotid gland enlargement, and bruising and swelling of the right forehead. Plantars were extensor, but tendon reflexes could not be satisfactorily elicited. The left arm and leg were not moving and there was stiffness of the right leg. The possibility of a subdural haematoma or cerebral abscess was considered and he was transferred to another hospital for ventriculography and x-ray of skull, which showed symmetrical dilatation of both lateral ventricles. Further convulsive and twitching movements were noted. He was readmitted to hospital on 12 December. Phenobarbitone and paraldehyde failed to control his twitching, which continued until 15 December. Tracheostomy was performed on 13 December. A course of prednisolone was given from 12 to 19 December. The child remained in coma until 17/18 December, when flaccid paralysis of the left hand and arm was recorded. He was slow to feed and did not speak, but recovered sufficiently to be dismissed home on 5 February 1961. 3 months later he was still retarded and there seemed no doubt that severe cerebral damage had occurred. When last seen aged 7 he responded to sounds of various frequencies and moderate intensities, could not speak, was incontinent, and unable to feed himself, and came into the educational category of ineducable and untrainable.

During the acute illness no virus was isolated from CSF or faeces. Sera of 13 and 27 December 1960, respectively, gave titres of 32 and 512 for mumps 'S', 8 and 512 for mumps 'V'; all other serological tests were negative.

*Case 2.* A male, aged 5 years. This child was admitted to hospital on 24 December 1960, with a history of headache and vomiting since the 22nd, and of generalized twitching on the 23rd. He had been

unconscious for almost 12 hours before admission to hospital, by which time bilateral facial swelling, particularly marked on the right side, had developed. He was reported to have injured his head 2 weeks before the onset of illness. Apart from pallor on the night of the injury, no abnormal signs had been noted. Cases of mumps were prevalent in his home area, some 130 miles from Glasgow. On admission the child was semicomatose and had marked meningismus. Jerky movements of all four limbs were frequent. The parotid glands were swollen and an erythematous rash was present on the face and limbs. Herpes lesions were found on the upper lip. His temperature was 37 °C, pulse 138/min, respiration 28/min. CSF: cells 306/mm<sup>3</sup>, protein 40, and sugar 51 mg/100 ml. Temperature continued raised (maximum 38.2 °C) during the first 5 days in hospital and the child remained semiconscious for the first 3 days. On 29 December, he was able to sit up though still showing some neck stiffness. Thereafter recovery was straightforward, but on discharge on 21 January 1961, his gait was clumsy. When reviewed in 1971, at the age of 16 years, he had no disability.

Mumps virus was isolated from the CSF taken on admission. Sera of 26 December 1960, and 6 January 1961, respectively, gave titres of 128 and 128 for mumps 'S', 128 and 512 for mumps 'V'; all other serological tests were negative. No virus was isolated from faeces.

### Discussion

In the present study both groups, i.e. patients with meningitis (Group M) and patients with meningitis and parotitis (Group MP), had more with rising CF titres to the V antigen than to the S antigen. Moreover, anti-V antibody usually appeared earlier in the illness than anti-S. This is not in keeping with the findings of Henle *et al.* (1948) who reported that in mumps parotitis S antibody appeared earlier than mumps V. The difference between their results and ours may lie in different methods of preparation of antigens. Though our antigens like those of Henle *et al.*, were prepared in embryonated hen eggs, they used dialysed and irradiated material, whereas our antigens (Grist *et al.*, 1966) were not treated by these procedures.

Several previous workers have shown that mumps meningitis is generally benign with few sequelae (Afzelius-Alm, 1951; Russell and Donald, 1958). The present study has confirmed this, since all patients admitted to Ruchill Hospital during the 10-year period 1960-69 with mumps meningitis made a good recovery. Our attempt in 1970-71 to find out if some patients might have delayed sequelae such as deafness was limited by the poor acceptance rate for reassessment. From this it could be inferred that those unwilling to be reassessed considered that their hearing was adequate; however, this does not exclude the possibility of a

monaural hearing deficit. Of the 8 children and 5 adults who were investigated by audiometry all showed normal hearing.

Only two definite cases of mumps encephalitis were observed during this 10-year period in Ruchill, one of whom had no signs of meningitis despite severe cerebral involvement. Further, it was of interest that the only child admitted to hospital with deafness associated with mumps infection during the period of this study had neither meningitis nor parotitis. Her mother noticed one day that the child was neither responding to the spoken word nor to sounds. The father, a doctor, sought otological opinion immediately and the diagnosis of severe, bilateral perceptive deafness was confirmed. This child showed no CSF abnormality. Serological tests on a single serum gave evidence of recent infection with mumps, antibody titres for mumps 'S' and mumps 'V' being 128 and 512 respectively. The child's two older male sibs were at this point recovering from clinical mumps. Further details of this case have already been described by one of us (Dunn, 1966). The occurrence of encephalitis without meningitis has also been observed by previous workers (Miller, Stanton, and Gibbons, 1956). This suggests that mumps encephalitis may be caused by direct invasion of the central nervous system from the nasopharynx, as suggested for herpes simplex encephalitis by the studies of Johnson (1964). It would also be in keeping with the suggestion of several previous workers (Russell and Donald, 1958) that mumps virus is primarily neurotropic and that involvement of the parotid glands occurs as a secondary and not invariable complication.

Miller *et al.* (1956) collected data on 27 cases of so-called 'mumps encephalomyelitis' reported since 1934. Of these, 6 had died; of the 21 survivors, 9 recovered fully, 5 had minor sequelae, and 7 had major sequelae. From these findings and from the present study it seems that mumps meningitis is a benign complication of mumps infection, but that encephalitis sometimes without evidence of meningitis, has a much graver prognosis. The term 'meningoencephalitis' should therefore be used with caution. The rarity of severe neurological involvement in mumps infection lends no support to the routine use of mumps vaccine in Britain.

The reason for the preponderance of males over females with mumps meningitis, and the earlier age of mumps meningitis in males than in females, is unknown. It may be that males and females are equally liable to mumps infection but that females may have more subclinical infections. In the present study the marked excess of parotitis in the males

with meningitis as compared with the females suggests that in mumps infection a sex-linked genetic or hormone-mediated mechanism may be concerned in parotid enlargement. On the other hand, the greater prevalence of parotitis accompanying meningitis in males during the winter months suggests that development of clinical parotitis may be associated with colder temperatures (with the possibility that thicker subcutaneous fat in females may maintain higher temperatures in parotid tissues) or with some weather-related factor such as respiratory virus infections.

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