was given four capsules of aureomycin in divided doses over 20 hours (1,000 mg.). When seen two days later the discharge had gone and the urine was completely clear apart from some threads in the first glass; the inguinal adenitis had entirely subsided. The urethral smear showed no pus cells, and the culture was negative for gonococci. He did not trouble to attend again until the 26th day, when he had no discharge, his urine was clear, and his prostatic secretion was free from pus.

Discussion

The results here recorded confirm those from America, and suggest that aureomycin is a satisfactory treatment both for gonococcal urethritis and for non-specific urethritis, pleuropneumonia-like organisms disappearing rapidly from the urethral discharge.

Aureomycin has also been shown to be effective in lymphogranuloma venereum (Wright *et al.*, 1948a, 1948b) and in granuloma inguinale (Greenblatt *et al.*, 1948). In addition O'Leary *et al.* (1948) have reported that doses of 40 to 50 g. of aureomycin rapidly cleared up the clinical symptoms in two cases of syphilis with early secondary lesions: serological reactions were unaffected. This antibiotic therefore seems capable of influencing all the common venereal infections.

Summary and Conclusions

Two cases of gonococcal and four cases of non-specific urethritis have been treated by oral aureomycin. One of the gonococcal cases and one of the non-specific cases received 2,000 mg. and the remainder 1,000 mg. over 24-60 hours.

Both the gonococcal cases responded, as did three of those with non-specific urethritis. Although one of the latter relapsed, it reacted favourably to further treatment. There was one failure.

In addition to the routine tests special examinations were made for pleuropneumonia-like organisms in patients with non-specific urethritis. These organisms were recovered before treatment in three cases and after treatment in none.

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The effect of vaccination during pregnancy on the incidence of malformations has been studied by Greenberg and his colleagues (*Paediatrics*, 1949, **3**, 456). More than 5,000,000 people were vaccinated following the outbreak of smallpox in New York early in 1947. Among these were 4,172 women in the first three months of pregnancy. They gave birth to 68 children with malformations, an incidence of 1.63%. A control non-vaccinated group of 2,186 women in the same period of pregnancy gave birth to 30 malformed infants, an incidence of 1.37%. These studies have shown that vaccination of women in the first three months of pregnancy does not appear to have any deleterious effect on the developing embryo.

NEUROLOGICAL COMPLICATIONS OF MUMPS

BY

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AND

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Hamilton (1781) first recorded cerebral manifestations associated with mumps; since then the subject, without becoming properly crystallized, has commanded medical interest as a comparative rarity.

Dopter (1910) reported that 9.8% of 1,705 cases of mumps showed meningeal symptoms, but admitted that "real" meningitis might be very rare. When Acker (1913) studied details of 30 fatal cases of cerebral mumps he considered that true meningo-encephalitis had been present. During and after the 1914-18 war French and American physicians described meningo-encephalitis complicating mumps, and details of isolated cases continue to appear in medical journals.

Coe (1945) agreed with Paddock (1932) that clinical meningitis accompanied mumps in from 0.15 to 0.5% of cases. Frankland (1941), in discussing a mumps epidemic involving 234 cases, put the occurrence of meningitis as high as 30% and reckoned that meningeal symptoms in contact cases of mumps could be presumed to be due to mumps infection. Five of Frankland's cases gave a meningeal reaction in the cerebrospinal fluid. Another epidemic of mumps, among men of the New Zealand Expeditionary Force in Japan, was noted by Laurence and McGavin (1948), who considered that out of 208 cases 60 had symptoms suggestive of meningeal involvement and six had definite meningo-encephalitis.

Ford (1937) has collected information demonstrating the widespread neurological lesions which may be expected in mumps, lesions involving almost any part of the central nervous system.

While it is generally agreed that the cerebral symptoms usually occur after the ordinary signs of mumps have shown themselves, Colomb and Mary-Mercier (1912), Bedingfield (1927), and Frankland (1941) described cases with neurological signs before there was any suspicion of mumps. Also, Howard (1919) and Frankland (1941) reported cases in which meningo-encephalitis occurred during a mumps epidemic and suggested that these were cases of mumps with the neurological signs as the only clinical manifestations.

Dopter (1910), Frankland (1941), and Lightwood (1946) tend to hold that the virus of mumps can be primarily neurotropic, and this view is given tentative authority by Harries and Mitman (1947) on experimental evidence. Similarly, Box (1946) ascribes the virus with possible neurotropic qualities.

In reviewing this considerable literature and remembering that individual cases of mumps meningo-encephalitis are still reported in some detail from time to time, we feel that a group of 14 cases occurring in a restricted area and during a short period of time merits attention.

The Present Series

With one exception all the cases developed in the Bristol area in May (1 case), June (3 cases), July (3 cases),

TABLE I

Case No.	Sex	Age	Day of Disease on Admission	History							Admission Findings										Progress of Disease							State on Discharge	Remarks		
				Headache	Parotitis	Orchitis	Vomiting	Delirium	Drowsiness	Shivering	Paralysis	Meningitis Symptoms	Parotitis	Orchitis	Abdominal Pain	Vomiting	Frontal Headache	Pain in Back	Nystagmus	W.B.C. 1,000/c.mm.	Polymorphs %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Day of Disease Temp. Settled	Day of Disease Dev. Orchitis			Day of Disease Lost Nuchal Rigidity	Day of Disease Dev. Parotitis
1	M	19	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	6.5	73	22	4	1	—	10	9	9	3	1	22	Well	Submaxillary mumps
2	M	29	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	8.7	69	25	6	—	—	9	2	9	1	5	15	—	—
3	M	15	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	6.7	72	22	3	2	1	5	—	6	2	3	13	—	—
4	M	9	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	8.7	76	23	1	—	—	5	—	9	3	1	11	—	—
5	M	4	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	9.1	65	26	7	1	1	9	—	13	1	6	16	—	Submaxillary mumps
6	M	26	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	6.8	70	25	4	—	—	11	7	9	3	1	22	—	—
7	F	18	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	7.9	66	23	8	2	1	7	—	8	1	3	15	—	—
8	M	25	5	+	+	+	+	+	+	+	+	+	+	+	+	+	+	10	75	20	4	—	—	8	5	11	1	5	16	—	—
9	F	2	4	+	+	+	+	+	+	+	+	+	+	+	+	+	+	6.1	63	31	2	1	3	11	—	13	3	4	16	—	—
10	M	14	4	+	+	+	+	+	+	+	+	+	+	+	+	+	+	7.3	66	27	7	—	—	16	—	17	6	12	13	—	Ext rectus paralysis
11	F	34	7	+	+	+	+	+	+	+	+	+	+	+	+	+	+	—	—	—	—	—	—	11	—	—	2	7	10	—	Ext. rectus paralysis
12	F	6	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	9.7	50	34	7	9	—	13	—	—	7	1	14	—	Paresis of legs
13	M	1	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	—	—	—	—	—	—	—	—	6	3	16	—	Facial palsy	
14	M	15	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	8	55	32	6	4	3	4	—	5	1	16	—	—	—

August (6 cases), and September, 1948 (1 case). During the same period 23 cases of anterior poliomyelitis were admitted to hospital—more than during the general epidemic period of 1947. Otherwise there was no marked prevalence of virus infections. It was noted that 18 out of 48 cases of known anterior poliomyelitis had long previously had mumps.

Since mumps is not notifiable and cases are not usually admitted to hospital, it is impossible to compute the total number of cases in the area during the time that we received these 14 cases, but hearsay evidence did not suggest even a moderate mumps epidemic. Table I gives details of the cases.

It will be seen that Cases 1, 4, 6, 12, 13, and 14 had signs of involvement of the central nervous system before there was any other indication of mumps. All the patients appeared to be alarmingly ill on admission, and the majority entered hospital under a quite justifiable diagnosis of meningitis. Four cases showed paralysis, and nystagmus was a common feature. Pyrexia on admission was constantly in the region of 102° F. (38.9° C.). Bradycardia, reported as common by French writers, was not noted. Severe frontal headache was a distinctive feature. All the patients were discharged well and without sequelae. Table II gives details of cerebrospinal fluids on admission.

In all cases the fluid pressure was raised and the general picture was that noted in other types of virus encephalitis.

The emphasis laid by Frankland (1941) on the occurrence of a purely lymphocytic reaction was not sustained; in fact,

the polymorphonuclear percentages were welcomed in differentiating some of the cases from benign lymphocytic meningitis; but these polymorphonuclear findings made a differential diagnosis from tuberculous meningitis more difficult, and in view of the necessity for early treatment of this condition with streptomycin the problem is important. The recent emphasis on the lowering of the cerebrospinal fluid sugar concentration in tuberculous meningitis should be a valuable differentiating point, for the sugar concentration in mumps meningitis is not low. It is worth noting that two of our cases were admitted as cases of tuberculous meningitis for streptomycin treatment.

Most of the cases of mumps meningitis give a history of previous contact with a case of mumps, which is not always inquired about. It is of interest to note that Case 7 was that of a nurse who came in contact with Case 11 and might well have had the same strain of virus. A further contact with this nurse was a surgeon working in the same hospital, who also developed a severe meningitic reaction, coming on nine days before the appearance of orchitis. As this surgeon refused lumbar puncture we are unable to include him in this series. It does seem that this strain of virus was highly neurotropic.

These three cases bear some resemblance to the cases of mumps meningitis in twin brothers quoted by Paddock (1932). These two brothers developed typical severe meningitis with increased cellular responses in the cerebrospinal fluid, but neither case showed any parotitis. Three sisters in the same family, however, showed the typical parotid symptoms found in mumps. It would seem, therefore, that the virus can have a predilection for the nervous tissue in certain people, but it more usually reacts on the parotid.

Comment

Although it has been suggested that a cerebrospinal reaction exists in cases of orthodox mumps, and Lavergne *et al.* (1938) have even shown many instances of a cerebrospinal fluid pleocytosis in asymptomatic contacts of mumps, most commonly during the last three days of the incubation period, yet a grouping of 14 cases, such as put forward in this article, suggests the presence of an organism more than usually neurotropic. It might also suggest a population more than usually susceptible to a neurotropic virus, and this might have some bearing on the unusual prevalence of poliomyelitis during the same period.

TABLE II

Case No.	Globulin (+ = Increase)	Sugar (+ = Present)	Protein, mg./100 ml.	Chlorides, mg./100 ml.	Cells per c.mm.	Polymorphs %	Lymphocytes %	Monocytes %	Organisms	Culture	Day of Disease Lumbar Puncture Performed
1	++	++	60	730	110	3	97	—	—	—	2
2	++	++	35	725	100	3	92	—	—	—	2
3	++	++	80	720	380	14	85	—	—	—	2
4	++	++	45	735	84	10	90	—	—	—	2
5	++	++	95	700	1,050	10	92	—	—	—	2
6	++	++	85	730	213	10	90	—	—	—	2
7	++	++	35	730	110	8	92	—	—	—	2
8	++	++	40	740	45	10	90	—	—	—	2
9	++	++	35	720	25	—	100	—	—	—	2
10	++	++	60	710	800	30	63	7	—	—	15
11	++	++	45	625	390	45	55	—	—	—	7
12	++	++	—	760	150	5	58	—	—	—	4
13	++	++	20	760	113	5	95	—	—	—	4
14	+	+	75	750	940	17	80	3	—	—	2

Donohue (1941) has described perivascular demyelination, similar to that seen in other cases of post-infective encephalitis, when he reported the pathology of a case of fulminating mumps meningo-encephalitis. Gordon (1927) experimentally produced mumps encephalomyelitis in a monkey (*M. cynomolgus*), and noted a cerebrospinal fluid reaction similar to that seen in the cases described here. He also described histological parotitis at necropsy in four cases of encephalitis lethargica (Gordon, 1913). Armstrong *et al.* (1936) similarly demonstrated the virus of choriomeningitis in the testes of experimentally infected monkeys.

There are authenticated cases of orchitis (Humphries, 1947) and pancreatitis (Box, 1946) as the only signs of mumps. We may therefore be but guessing at the tissue predilections of virus organisms. It may well happen that cases loosely described as aseptic meningitis may in reality be mumps meningo-encephalitis. If, however, after study of the other manifold manifestations of mumps it is considered that this virus infection is generalized and apt to influence any tissue—even the foetus *in utero* (Humphries, 1947)—then it is quite understandable that the central nervous system can at times be affected too, and possibly in preponderance. Thus it would no longer be necessary to postulate a neurotropic virus but rather one which settles where it will, and, depending on the speed of immunity production, the salivary glands, central nervous system, pancreas, ovaries, testicles, or pericardium may one or all produce clinical signs of virus inflammation.

Summary

The literature concerning the central nervous system manifestations of mumps is reviewed.

Fourteen cases of mumps meningo-encephalitis are presented, six of which occurred before other signs of mumps developed. The place of the neurological signs of mumps in the picture of the disease is discussed, and it is suggested that, being a general infection, central nervous types of the disease are apt to occur more by accident than because the virus is necessarily essentially neurotropic.

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LEUCOCYTE COUNTS IN THE PREVENTION OF DRUG AGRANULOCYTOSIS

BY

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Himsworth (1948) stated that he and Morgans (1947) had come to the conclusion that frequent blood counts for the early detection of agranulocytosis during treatment with thiouracil are worse than useless, because agranulocytosis develops like a bolt from the blue, and a normal count may impart a quite unjustifiable sense of security. This has long been known in the case of the sulphonamides, but the evidence has been generally disregarded, and leucocyte counts for purposes of prophylaxis are still considered desirable. Roberts (1948) and Hendry (1948) have drawn attention to the greatly increased demands being made on clinical pathological departments of hospitals, and leucocyte counts, requested under the mistaken impression of their value in the prevention of agranulocytosis, constitute an unnecessary and wasteful part of such demands.

I drew attention to the failure of serial leucocyte counts during sulphanilamide administration either to give warning of an impending agranulocytosis or to prevent a fatal outcome (Young, 1937). Later I collected evidence supporting this observation (Young, 1944). On the other hand, Britton and Howkins (1938) carried out leucocyte counts during 14 days of sulphonamide treatment in 50 patients, and found that the polymorphs fell during treatment in 46% of cases—in 10% to fewer than 2,000 per c.mm—but they did not observe agranulocytosis. Also Bigler *et al.* (1938) carried out counts in 33 persons during short courses of sulphonamide treatment, and concluded that sulphonamides seemed to cause depression of white blood cells even to a point at which leucopenia developed, but agranulocytosis did not occur with this depression.

It might be anticipated that leucocyte counts would be useful in the prophylaxis of agranulocytosis in two ways: (1) in preventing the occurrence of agranulocytosis, and (2) in reducing case mortality through earlier diagnosis.

Influence of Counts on the Occurrence of Agranulocytosis

It has been assumed that the detection of a drop in the leucocyte count to a leucopenic level during treatment would enable agranulocytosis to be averted by stopping administration at this stage, and it has been claimed that this has been achieved (Hohmann, 1938). Plum (1937), by administering amidopyrine to patients who had recovered from agranulocytosis due to the same drug, showed that the changes in the marrow are well established before the peripheral blood gives any warning, and that, although administration of the drug was stopped long before this warning in the blood, agranulocytosis followed. His experiments, and other evidence (Sheket and Price, 1939; Agranat *et al.*, 1939; Filler, 1941), indicate that when a leucopenia is due to an imminent agranulocytosis the latter will follow whether the drug is stopped or not. If a rise in granulocytes occurs immediately after administration ceases the condition merely represents the mild leucopenia which occurs in about 50% of persons, as demonstrated by Britton and Howkins (1938) and Bigler *et al.* (1938) with sulphonamides.