American Journal of Diseases of Children

VOLUME 71			JANU	ARY 19	946	•	Number	1
	COPYRIGHT.	1946.	BY THE	AMERICAN	MEDICAL	Association		

MUMPS

Use of Convalescent Serum in the Treatment and Prophylaxis of Orchitis COMMANDER ALWIN C. RAMBAR (MC), U.S.N.R.

M UMPS is a specific virus disease that is rarely serious in children but that produces a high percentage of severe manifestations in adults. In normal times, the study of patients admitted to contagious disease hospitals yields results probably not representative of the average disease, since these patients are usually a selected group with more severe types of mumps. The mobilization of large numbers of men in military service or an institutional outbreak provides an opportunity to make surveys and note the effects of specific therapy on this disease.

Mumps usually occurs between the ages of 5 and 15 years, the incidence being 10 to 20 per cent among persons who have spent their childhood in rural areas, while 80 per cent of those who have lived in urban districts had mumps in childhood. The high morbidity in the armed services is due, in the main, to the large number of susceptible persons from rural districts and to the intimate contact caused by necessary crowding. Under these conditions both the susceptible persons and those relatively immune have the disease during epidemics.

Johnson and Goodpasture¹ are generally credited with proving the existence of the specific virus in mumps. They showed that a filtrable virus exists in the saliva during the first forty-eight hours of the disease, that it is resistant to neutral glycerin, freezing and drying and that it is transmissible to rhesus monkeys through many generations and back to human beings. Granata² in 1908, Nicolle and Conseil³ in 1913 and Martha Wollstein⁴ in 1918 noted the evidence of a filtrable

1. Johnson, C. D., and Goodpasture, E. W.: An Investigation of the Etiology of Mumps, J. Exper. Med. **59**:1 (Jan.) 1934; Experimental Immunity to the Virus of Mumps in Monkeys, Am. J. Hyg. **23**:329 (March) 1936.

2. Granata, S.: Sulla etiologia degli orecchioni da virus filtrable, Med. ital. **6**:647, 1908.

3. Nicolle, C., and Conseil, E.: Essai de reproduction expérimentale des oreillons chez le singe, Compt. rend. Soc. de biol. 75:217, 1913.

4. Wollstein, M.: An Experimental Study of Parotitis, J. A. M. A. 71:639 (Aug. 24) 1918.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

virus in this disease. Johnson and Goodpasture¹ in 1936 examined the parotid glands of rhesus monkeys to which they had transmitted the disease and described the pathologic changes during the acute stage. They found an edematous swelling of the salivary glands involved and the tissues surrounding, with pinpoint hemorrhages in the capsule. The glands showed parenchymal lesions and disintegration of the acinar cells and infiltration of mononuclear cells and lymphocytes.

It is probable that the virus enters the body by way of the mouth or nose. Gordon 5 stated that the most consistently entertained conception of mumps is that of a primary local disease of the parotid glands which arises from invasion of the buccal cavity, with progression of the virus along Stensen's duct and eventual production of a nonsuppurative swelling of the gland. Wesselhoeft 6 expressed the belief that it may reach the salivary glands by a roundabout course involving the blood stream. Philibert ⁷ originally proposed the theory that the virus finds its way first to the central nervous system by way of the conjunctiva and, being of a low neurotropic order, does not manifest itself clinically, but after an appropriate incubation period it enters the blood stream and produces its familiar symptomatology. This hypothesis would explain the fact that orchitis, encephalitis and pancreatitis can occur before, with or after an involvement of the salivary glands. He explained the involvement of the salivary glands on the theory that the virus is eliminated through them.

The most frequent complications are involvement of the gonads in men and of the pancreas, breasts, thyroid gland, thymus, lachrymal glands and Bartholin's gland.⁶ Since it is probable that the virus enters the blood stream, the many so-called complications are more likely a part of the systemic manifestations of the disease proper.

Since the clinical signs of orchitis are so obvious, statistics concerning this condition are probably more accurate than those concerning other associated manifestations of this disease. Unless the observer was particularly interested in carefully noting all symptoms, many other statistics are of questionable value.

Orchitis occurs in an average of 18 per cent of men affected with mumps in epidemics,⁶ although in individual groups the percentage reported has been as high as 66 per cent.⁸ Wesselhoeft ⁶ stated that

8. Bang, H. O., and Bang, J.: Involvement of the Central Nervous System in Mumps, Acta med. Scandinav. 113:467 (April 17) 1943.

^{5.} Gordon, J. E., and Heeren, R. H.: The Epidemiology of Mumps, Am. J. M. Sc. 200:412 (Sept.) 1940.

^{6.} Wesselhoeft, C.: Medical Progress: Mumps, New England J. Med. 226: 530 (March 26) 1942.

^{7.} Philibert, A.: Nouvelle conception de la pathogénie des oreillons, Progrés méd. 23:145 (Jan. 23) 1932.

RAMBAR---MUMPS

in different epidemics strains have a wide variation in their predilection for the testicle. In Radin's ⁹ series of 4,397 cases, 611, or 13.91 per cent, of the patients had orchitis. Bailey and Haerum ¹⁰ have reported 110 cases of orchitis in 551 patients with mumps, an incidence of 19.9 per cent. Potter and Bronstein ¹¹ noted 13 cases of orchitis in 112 adults. Dermon and Le Hew ¹² found 44 cases of orchitis, or 35 per cent, in 126 men. McGuinness and Gall ¹³ reported 494 cases of orchitis, or 36.2 per cent, in 1,364 patients with mumps at Camp McCoy, Wis. Worden,¹⁴ in his series, noted 41 cases, or 16.4 per cent, of orchitis in a group of 250 patients with mumps, and in the Bangs'⁸ series of 74 males over 13 years of age, 49, or 66 per cent, had orchitis.

ENCEPHALITIS

Involvement of the central nervous system is probably directly due to the virus in the same manner that encephalitis occurs in equine encephalitis, lymphocytic meningitis and poliomyelitis. Wollstein,¹⁵ was able to produce a mild meningitis in cats by using filtered saliva from patients with mumps and injecting it suboccipitally. Gordon ¹⁶ has produced severe, and, in a few cases fatal, lymphocytic meningitis by injecting filtered mumps saliva intracerebrally into monkeys. While the involvement of the central nervous system is generally mild, Donohue ¹⁷ reported a death in a 5 year old child and reviewed the previous reports in the literature, finding 10 authenticated cases. Autopsy revealed a perivascular demyelination similar to that seen in the postinfectious encephalitides. Urechia¹⁸ described the changes

9. Radin, M. J.: The Epidemic of Mumps at Camp Wheeler, October, 1917-March, 1918, Arch. Int. Med. 22:354 (Sept.) 1918.

10. Bailey, W. H., and Haerum, A. T.: Some Observations on the Efficacy of Convalescent Mumps Serum, Mil. Surgeon 90:134 (Feb.) 1942.

11. Potter, H. W., and Bronstein, L. H.: Some Clinical Characteristics of Mumps and the Effect of Belladonna in Treatment: A Study Made at the Station Hospital, Fort George G. Meade, Md., Ann. Int. Med. **21**:469 (Sept.) 1944.

12. Dermon, H., and Le Hew, E. W.: A Mumps Epidemic in a Small Task Force, Am. J. M. Sc. 208:240 (Aug.) 1944.

13. McGuinness, A. C., and Gall, E. A.: Mumps at Army Camps in 1943, War Med. 5:95 (Feb.) 1944.

14. Worden, E. M.: Epidemic Parotitis: An Analysis of 250 Cases in Male Adults, Canad. M. A. J. 50:47 (Jan.) 1944.

15. Wollstein, M.: Experimental Mumps Meningitis, J. Exper. Med. 34:537 (Dec.) 1921.

16. Gordon, M. H.: Report of the Medical Officer, Great Britain Local Gov. Public Health and Medical Subjects, London, 1914, p. 96.

17. Donohue, W. L.: The Pathology of Mumps Encephalitis with Report of a Fatal Case, J. Pediat. 19:42 (July) 1941.

18. Urechia, C. J.: Parotidite épidémique à forme psychosique; autopsie, Encéphale 2:144 (Sept.-Oct.) 1938.

in the rare fatal cases of encephalitis as characterized by slight lesions of nerve cells, perivascular infiltrations predominately lymphocytic, neuroglial reactions, foci with demyelination and small capillary hemorrhages. Myelitis, optic neuritis, nystagmus, neuritis and polyneuritis have been reported ¹⁹ as complications of this disease.

The terminology of the disease process involving the central nervous system is not standardized. The manifestations of fever, headache and drowsiness, associated at times with nuchal rigidity and with the presence of Kernig and Brudzinski signs, plus a positive Pandy reaction and a lymphocytic pleocytosis of the spinal fluid, have been variously called encephalitis, meningitis and meningoencephalitis. Since the same symptom complex associated with other virus diseases is classified as encephalitis, it seems proper that this manifestation should also be called encephalitis.

Since pleocytosis may occur with or without symptoms, mumps encephalitis is classified as either latent or manifest. In this asymptomatic reaction, there appears to exist the mildest form of involvement of the central nervous system. Finkelstein²⁰ examined the spinal fluid of 40 patients with mumps and found pleocytosis in 16. Of these, 10 had encephalitic symptoms, while 6 were asymptomatic. Cell counts varied from 15 to 1,250, mainly lymphocytes, with no correlation between the number and the severity of the symptoms. Dopter ²¹ reported a 9.8 per cent incidence of encephalitis among 1,705 men with mumps in the French army. Dermon and Le Hew 12 found only 1 case of encephalitis in 129 adults: Potter and Bronstein¹¹ noted 2 cases of encephalitis in 112 persons with mumps. Wesselhoeft 6 stated that clinical evidence of involvement of the central nervous system occurs in 10 per cent of the cases. The Bangs 8 have made an excellent study of 458 patients with mumps hospitalized in Copenhagen in the winter of 1941-1942. Examinations of the spinal fluid were made for all of the patients, and it was found that 235, or 65 per cent, showed an increased cell count. One hundred and six, or 45 per cent, revealed manifest encephalitis, while in 129, or 55 per cent, the encephalitis was latent. The time of onset of manifest symptoms was usually the fifth day, although cases were reported from as long as seven days before to thirty-eight days after involvement of the salivary glands occurred.

It can be seen that statistics for mumps encephalitis depend on the type of observation made. When diagnostic examination of the spinal fluid is made, the incidence of pleocytosis may be as high as

^{19.} McKaig, C. B., and Woltman, H. W.: Neurologic Complications of Epidemic Parotitis, Arch. Neurol. & Psychiat. 31:794 (April) 1934.

^{20.} Finkelstein, H.: Meningo-Encephalitis in Mumps, J. A. M. A. 111:17 (July 2) 1938.

^{21.} Dopter, C.: La méningite ourlienne, Paris méd. 1:35, 1910.

100 per cent, as in de Massary's ²² series, or when clinical symptoms alone are considered it may be as low as that recorded in Radin's ⁹ report, in which he noted only 1 case of encephalitis in 5,756 cases of mumps in soldiers at Camp Wheeler in 1918.

Pancreatitis is an unusual manifestation, or at least its diagnosis is rarely made. Sinclair²³ stated that only 26 cases are on record in the United States Army during the World War. Greene and Heeren²⁴ found 7 instances in their series of 100 adults with mumps. Brahdy and Schefer²⁵ reported 13 cases of pancreatitis in 252 patients, and Haerem²⁶ reported 6 cases of this disease in 500 patients with mumps.

Ocular complications have been described frequently.²⁷ Conjunctivitis, keratitis, dacryoadenitis, optic neuritis, muscular paralysis, nystagmus, neuroretinitis and disturbances of accommodation have been noted.

CLINICAL STUDY

An epidemic of mumps during the winter of 1945 in a specialized school of the Navy provided the material for this study. From March 1 to July 1, 1945, 249 men were admitted to the hospital with mumps. A study of the effect of convalescent serum in the prevention of associated manifestations and of the effect of convalescent serum and normal pooled plasma in the treatment of orchitis was made. Pooled serum was made from various groups of these patients by the Samuel Deutsch Serum Center of Michael Reese Hospital, blood being drawn three to six weeks after recovery. One hundred and fifty-seven of these men were 17 to 21 years of age; 80 were 21 to 30, and 12 were in the 31 to 39 year age group. These groups corresponded to the proportionate age groups of the men in the school and are not indicative

25. Brahdy, M. B., and Schefer, I. H.: Pancreatitis Complicating Mumps, Am. J. M. Sc. 181:255 (Feb.) 1931.

26. Haerem, A. T.: Treatment of Measles and Mumps with Three Well Known Sulfonamides, Mil. Surgeon 92:306 (March) 1943

^{22.} de Massary, E., and Tockmann, L.: Statistique portant sur 243 militaires atteintes d'oreillons, soignés à l'hôpital Andral: Fréquence des orchites et des réactions méningées, Bull. et mém. Soc. méd. d. hôp. de Paris **40**:1035, 1916.

^{23.} Sinclair, C. G.: Mumps: Epidemiology and Influence of the Disease on the Non-Effective Rate in the Army, Mil. Surgeon **50**:626 (June) 1922.

^{24.} Greene, J. A., and Heeren, R. H.: Mumps, J. Lab. & Clin. Med. 23:129 (Nov.) 1937.

^{27.} Wesselhoeft, C., in Virus and Rickettsial Diseases, Harvard School of Public Health, Symposium, Cambridge, Mass., Harvard University Press, 1940, p. 309. Lippman, O.: Keratitis Due to Mumps, South. M. J. **36**:654 (Sept.) 1943. Danielson, R. W., and Long, J. C.: Keratitis Due to Mumps, Am. J. Ophth. **24**: 655 (June) 1941. Powell, L. S., and Dunlap, R. L.: Report of Two Cases with Visual Disturbances Complicating Epidemic Parotitis, J. Kansas M. Soc. **41**:432 (Oct.) 1940.

of age immunity. No age is considered exempt from this disease, but as the age increases more persons have had mumps, with a resulting decrease in the number of susceptible persons. In general, it can be said that one attack produces immunity, regardless of the number of glands involved, although second and even third attacks do infrequently occur.

Bilateral parotitis was noted in 112 men, unilateral parotitis in 75, parotitis and involvement of the submaxillary or sublingual glands in 54 and involvement of the submaxillary glands alone in 8. Thus, involvement of the parotid glands was present in 97 per cent of the patients, of whom 45 per cent had bilateral involvement, 30 per cent had unilateral involvement and 25 per cent had involvement of the parotid glands. Radin's ⁹ figures, compiled in a study of 4,274 cases, showed involvement of the parotid glands in 99 per cent (unilateral in 59 per cent, bilateral in 30 per cent and associated with involvement of the submaxillary and the sublingual glands. Radin's ⁹ figures, compiled in a study of 4,274 cases, showed involvement of the parotid glands in 99 per cent (unilateral in 59 per cent, bilateral in 30 per cent and associated with involvement of the submaxillary glands in 10 per cent). Feer ²⁸ noted involvement of the submaxillary glands in 25 per cent of his 146 patients.

One hundred and sixty-three men constituted the control group, while 86 received convalescent serum on the first day of clinical symptoms. Serum was administered as it became available, so that the two groups were mixed throughout the months of study. Forty cubic centimeters of convalescent serum was given intravenously on admission to each of the treated patients. Orchitis occurred in 14, or 16.27 per cent, of the 86 men given serum, while it occurred in 47, or 28.83 per cent, of the 163 controls. Bilateral orchitis occurred in 2 of the treated and in 5 of the control group. Statistical analysis, employing the chi-square test, indicates that serum treatment reduced the incidence of orchitis.

Clinical symptoms of encephalitis were present in 14, or 16.27 per cent, of the 86 men of the serum-treated group and in 26, or 15.23 per cent, of the 163 controls. The diagnosis of encephalitis was made on the basis of clinical symptoms, the absence of other complicating factors and the presence of pleocytosis in the spinal fluid. Examinations of the spinal fluid were not made on asymptomatic patients, and therefore the number of patients with latent encephalitis is unknown. Four of the treated group had both orchitis and encephalitis, while 11 of the controls had both. Conjunctivitis was noted in 6 of the serumtreated group and in 7 of the controls. Presternal edema of a high degree was noted in 4 patients. It is probable that this condition

^{28.} Feer, W.: Beobachtungen bei Parotitis epidemica, Schweiz. med. Wchnschr. 78:1569 (Dec. 31) 1943.

would have been noted more frequently, but examinations were not made specifically for this. Gellis and Peters²⁹ reported its presence in 30, of 6 per cent, of 502 cases. Barker³⁰ noted its incidence in 3 of 438 cases. This phenomenon is explained on the basis of lymphatic obstruction by pressure of the enlarged salivary glands (table 1).

The diagnosis of pancreatitis could not be definitely made for any of the patients observed during this study.

The effect of convalescent serum on the clinical manifestations was studied. The average temperature of the treated group was 101.18 F. and of the control group 101.16 F.; the average number of days of fever of the treated group was 2.98 and of the control group 3.03. The average stay in the hospital for the treated group was 10.8 days, while for the controls it was 11.87 days.

TABLE 1.—Clinical Manifestations in 249 Cases of Mumps

Patients	Orchitis	Encephalitis	Orchitis and Encephalitis	Conjunc- tivitis	Presternal Edema
Serum treated (86)	14	14	4	6	1
Controls (163)	47	26	11	7	3

 TABLE 2.—Relationship of Involvement of Salivary Glands to

 Associated Manifestations

Glands Involved	Orchitis	Encephalitis	Orchitis and Encephalitis	Conjunc- tivitis	Presternal Edema
Parotid bilaterally (112)	23	10	10	7	1
Parotid unilaterally (75) Parotid and submaxillary or	11	7	ō	2	ō
sublingual (54)	9	7	0,	4	3
Submaxillary alone (8)	3	1	0	0	0

The average time of onset of orchitis was six days in each group. The average time of appearance of encephalitis in the serum-treated group was 5.8 days after onset and 4.8 days in the controls. Conjunctivitis appeared on the average of 6.2 days after onset in both groups, and symptoms were present about fourteen days in both. Presternal edema was noted on the average of six days after the onset.

A study of the associated conditions in relation to each type of involvement of salivary glands was made. The various percentages of cases of orchitis, encephalitis and conjunctivitis appear approximately proportionate to the total number of various involvements of salivary glands (table 2).

30. Barker, C. S.: Complication of Mumps-Swelling over Manubrium Sterni, Canad. M. A. J. 48:22 (Jan.) 1943.

^{29.} Gellis, S. S., and Peters, M.: Mumps with Pre-Sternal Edema, Bull. Johns Hopkins Hosp. 75:241 (Oct.) 1944.

8

TREATMENT OF ORCHITIS

The use of convalescent serum and plasma in the treatment of mumps orchitis was studied. Gradwohl and co-workers³¹ reported excellent therapeutic results with only 5 cc. of convalescent serum in the treatment of orchitis. In 1944, I 32 reported 2 cases of mumps orchitis in which there was a dramatic response to the use of 500 cc. (1 unit) of pooled normal plasma. The temperature of each patient dropped by crisis within twenty-four hours. This report stimulated the study of Smith,³³ who had similar results in 5 cases. In the present study, there were a total of 61 cases of orchitis. In 5 of these, the patients were afebrile and were not included in the control group, since all patients who were treated with either plasma or serum were febrile. In the control group of 30 patients, the temperatures dropped by crisis in three days or less in 7 instances; a drop by lysis in three days or less was noted in 3, and in 20 men the fever defervesced by lysis in more than three days. Thirteen men were treated with

Patients	Temperature Dropped by Crisis in Three Days or Less	Temperature Dropped by Lysis in Three Days or Less	Temperature Dropped in More Than Three Days	Average Number Days of Fever
Serum treated (13)	3	4	6 Ì	
Plasma treated (10)	6	1	3 }	4.52
Serum and plasma treated (3)	2	0	1 J	
Controls (30)	7	3	20	5.40

TABLE 3.-Effect of Treatment on Orchitis

500 cc. of pooled normal plasma. In 6 the temperatures dropped by crisis in three days or less; in 1, by lysis in three days or less, and in 6, by lysis in more than three days. Ten patients with orchitis were treated with 40 cc. of convalescent serum; in 3 of these the temperatures dropped by crisis and in 4 by lysis in three days or less, while in 3 the fever lasted more than three days. Three patients were treated with 500 cc. of plasma and 40 cc. of serum, both being adminstered on the day of onset. In 2 of these the temperatures dropped by crisis in less than three days, and in 1 the fever lasted five days. The average number of febrile days in the treated group was 4.5 and in the untreated group 5.5. In summarizing these figures, it is found that of the treated group 16 had fever for three days or less and 10 had longer febrile courses, as compared with 10 with fever of three days or less and 20 for more than three days in the untreated group (table 3).

31. Gradwohl, R. B. H.: Study of an Epidemic of Mumps, U. S. Nav. M. Bull. 13:723 (Oct.) 1919.

32. Rambar, A. C.: Pooled Plasma Treatment of Mumps Orchitis, U. S. Nav. M. Bull. 42:871 (April) 1944.

33. Smith, R. G.: Plasma Treatment of Mumps Orchitis, U. S. Nav. M. Bull. 44:159 (Jan.) 1945.

RAMBAR—MUMPS

THE PROPHYLACTIC USE OF CONVALESCENT SERUM

The value of convalescent serum as a protective agent appears to be fairly well substantiated. The earliest report is that of Hess,³⁴ who treated 17 exposed nonimmune children with an intramuscular injection of 6 to 8 cc. each of convalescent whole blood obtained from donors who had recently recovered from mumps. The disease did not develop in any of these 17. Regan³⁵ administered 2 to 4 cc. of convalescent serum to each of 70 children; only 1 had mumps. Skrotzky³⁶ gave injections of 5 to 15 cc. of convalescent serum to 179 exposed children, of whom only 2 had mumps and their disease was Zeligs ³⁷ reported the successful protection of all 44 children mild. in contact with the disease to whom he gave injections of 5 cc. of serum from donors recently recovered from mumps. Cambessédès 38 reported 100 per cent success, using an injection of 10 to 20 cc. of convalescent serum. Dwyer 39 obtained 100 per cent protection for 31 schoolboys by using 4 cc. of convalescent serum for each. Teissier's 40 report was similar, he having used 10 to 20 cc. of convalescent serum for each of 22 girls. Levinson and Wolfe's ⁴¹ figures showed that of 23 nonimmune persons in contact with the disease in their homes given injections of 10 cc. of convalescent serum mumps developed in 4; by using 15 cc. each in 4 susceptible persons, no mumps developed; by using 20 cc. of serum each in 157 susceptible persons, no disease appeared in 144, or there was 92 per cent success. Ruhrah 42 stated that the disease should be expected to develop in one fourth to one third of the susceptible persons in contact. Barenberg and Ostroff 48 gave 40 children in an institution 5 cc. of convalescent serum each.

34. Hess, A. F.: A Protective Therapy for Mumps, Am. J. Dis. Child. 10:99 (Aug.) 1915.

35. Regan, J. C.: Serum Prophylaxis of Epidemic Parotitis, J. A. M. A. 84: 279 (Jan. 24) 1925.

36. Skrotzky, A. I.: The Seroprophylaxis of Epidemic Parotitis, Odessky M. J. 4:8, 1929; abstracted, J. A. M. A. 93:345 (July 27) 1929.

37. Zeligs, M.: Convalescent Serum in the Prevention of Mumps, J. Pediat. 1: 727 (Dec.) 1932.

38. Cambessédès, H.: L'emploi du sérum de convalescents dans les oreillons, Ann. d'hyg. 11:83 (Feb.) 1933.

39. Dwyer, H. L.: Convalescent Serum in the Prophylaxis of Mumps, J. Kansas M. Soc. 25:257 (Aug.) 1925.

40. Teissier, P.: Prophylactic Value of Convalescents' Serum in Mumps, Bull. Acad. de méd., Paris 93:369 (April 7) 1925; abstracted, J. A. M. A. 84:1701 (May 30) 1925.

41. Levinson, S. O., and Wolfe, A.: Personal communication to the author.

42. Ruhrah, J., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 6, p. 277.

43. Barenberg, L. H., and Ostroff, J.: Use of Human Blood in the Protection Against Mumps, Am. J. Dis. Child. 42:1109 (Nov.) 1931.

The disease developed in 39 per cent of 125 untreated controls in the same institution, while only 15 per cent of the treated group came down with mumps and these had a milder form. Gunn 44 gave injections of 5 cc. of serum to 22 susceptible persons who escaped the disease, but a few weeks later mumps developed in 3 after secondary exposures. Lyday,⁴⁵ using 10 cc. of convalescent serum, reported 11 failures to immunize in 86 children given injections. Odenius 46 reported 100 per cent success for the use of serum in men of the Swedish army, using 10 cc. in each repeated once in three to five davs. Smaller amounts used before had been unsuccessful. This was noted by Vasquez 47 who used injections of 0.1 to 2.5 cc. of serum subcutaneously and had 20 failures in immunization among 175 exposed Chilean soldiers. Beeson and co-workers 48 used injections of 4.5 and 6 cc. of pooled plasma for a group of soldiers in England. Six days later 8 cc. of another plasma was given. A decrease in the incidence of mumps occurred, but this was not striking.

However, they observed that hepatitis occurred in 101 of 266 men given this serum and concluded from epidemologic studies that it was due to a hepatotoxic agent present. MacNalty⁴⁹ reported this condition in a group of children given measles convalescent serum. Morgan and Williamson⁵⁰ noted its appearance after the giving of pooled and dried reconstituted human adult serum. Whole blood transfusions have also produced it. Neefe and co-workers⁵¹ reported its occurrence in a male physician eleven weeks after the intravenous injection of 200 cc. of pooled mumps human convalescent serum.

The administration of convalescent serum to patients with parotitis as a prophylactic measure against other manifestations has been reported by many observers. Gordon and Heeren⁵ have reviewed these reports

44. Gunn, W.: Convalescent Serum in Prophylaxis of Measles, Chickenpox, and Mumps, Brit. M. J. 1:183 (Jan. 30) 1932.

45. Lyday, J. H.: An Evaluation of Convalescent Serum in the Prevention of Mumps, J. Pediat. 18:473 (April) 1941.

46. Odenius, R.: Attempt at Immunization Against Mumps in Royal Norrland Regiment, 1926, Tidskr. i mil. Hälsov. 51:177, 1926.

47. Vasquez, A.: Seroprofilaxis de la parotiditis epidemica con suero de convalesciente, in Actas y trabajos de Primer congresso de medicina y cirugia naval y militar de Chile, Valparaiso, 1929, p. 675.

48. Beeson, P. B.; Chesney, G., and McFarlan, A. M.: Hepatitis Following Injection of Mumps Convalescent Plasma, Lancet 1:814 (June 24) 1944.

49. MacNalty, A. S.: Report of the Chief Medical Officer, 1937, Great Britain Ministry of Health, London, 1938.

50. Morgan, H. V., and Williamson, D. A. J.: Jaundice Following Administration of Human Blood Products, Brit. M. J. 1:750 (June 19) 1943.

51. Neefe, J. R.; Miller, T. G., and Chornock, F. W.: Homologous Serum Jaundice: A Review of the Literature and Report of a Case, Am. J. M. Sc. **207**:626 (May) 1944.

and have expressed the opinion that they lack proof of any worth while knowledge. Bailey and Haerum¹⁰ studied a group of patients and noted that of 551 controls orchitis developed in 110, or 19.9 per cent, while of 183 who received 10 to 20 cc. of serum each 28, or 15.3 per cent, had orchitis. Of the 183 patients who received serum, 135 had serum from donors who had not had orchitis. The disease developed in 26, or 19.2 per cent, of these, while of the 48 who had serum from donors who had orchitis this manifestation developed in only 2, or 4.2 per cent. They suggested that blood from patients with orchitis contains specific antibodies against this condition. Teisser ⁵² gave 20 to 40 cc. of serum to each of 172 patients with the disease and found that orchitis developed in 8.13 per cent, while in a group of 174 controls it developed in 23.29 per cent. De Lavergne and Florentin 53 treated 113 patients with injections of 20 cc. of convalescent serum, with an additional 10 cc. five days later. Orchitis occurred in 5 instances and meningitis in 2, while in 107 controls orchitis occurred in 25 and meningitis in 9. Odenius 46 noted that of 18 patients each given 20 cc. of convalescent serum at the onset of swelling of the parotid glands orchitis developed in 1, or 5.5 per cent, while of 52 untreated patients 5, or 9.5 per cent, had this disease. Cambessédès 38 used a dose of 20 to 40 cc. of serum in 171 cases of mumps, with orchitis resulting in 7 per cent of the patients. Of 176 controls orchitis developed in 23 per cent. Iversen 54 administered 40 cc. of mumps serum to alternate persons in a group of soldiers with mumps. Of the 56 serum-treated patients, orchitis in 20 per cent developed while of the 56 controls 30 per cent were involved. Hinckley 55 noted that 13 per cent of his 23 serum-treated patients had complications as compared with 40 per cent of the 55 controls. The serum-treated patients had a shorter and milder course, with an average of 10.17 days in the hospital with 4.26 febrile days in the treated, as compared with 12.24 hospital days with six febrile days in the controls. Candel⁵⁶ used 100 cc. of pooled plasma intravenously in each of 30 patients, of whom 6, or 20 per cent, had orchitis. They concluded that 100 cc. of pooled normal plasma does not lower the

52. Teissier, P.: Epidemiology and Prophylaxis of Mumps, Bull. méd., Paris **39**:349 (March 28) 1925; abstracted, J. A. M. A. **84**:1701 (May 30) 1925.

53. de Lavergne, V., and Florentin, P.: Convalescents' Serum in Prevention of Orchitis in Mumps, Bull. Acad. de méd., Paris 93:362 (March 31) 1925; abstracted, J. A. M. A. 84:1701 (May 30) 1925.

54. Iversen, P.: Complications of Epidemic Parotitis and Experimental Treatment with Convalescent Serum, Ugesk. f. læger 92:167 (Feb. 13) 1930.

55. Hinckley, R. G.: Therapeutic Use of Convalescent Serum in Mumps, Minnesota Med. 20:227 (April) 1937.

56. Candel, S.; Wheelock, M. C., and Grimaldi, G. J.: Mumps Orchitis, with a Discussion of Plasma Prophylaxis, U. S. Nav. M. Bull. **45**:97 (July) 1945.

incidence of orchitis. Haerem ²⁸ gave 10 cc. of serum intramuscularly to each of 100 patients with mumps in the course of a study comparing this method of therapy with the use of the sulfonamide compounds. The serum was obtained from donors who had recovered from orchitis. Thirty per cent of those receiving the serum had orchitis, while 27 per cent of the control group and only 21 per cent of the group receiving sulfonamide compounds had it. However the majority of these reports show a definite decrease in orchitis after the use of serum.

COMMENT

Convalescent serum appears to be the best available means of preventing mumps and of decreasing the incidence of orchitis. The reports in the literature are difficult to evaluate, since varied doses of serum and means of administering it have been used, and there is no agreement on the time period when donors should be bled. Wesselhoeft⁶ expressed the belief that after the symptoms are established the virus has already become attached to the cells of the involved organs and is well out of reach of antibodies supplied in the form of therapeutic He questioned some favorable conclusions reported, because serum. Bonnamour and Bardin⁵⁷ have observed equally good results from the prophylactic use of diphtheria antitoxin. At one time Wesselhoeft 58 noted 82 consecutive cases of mumps without orchitis, followed by 6 cases of orchitis among the next 18 patients with mumps. In the present group of sailors studied, the incidence of orchitis was constant throughout the study. Bailey and Haerem 10 noted that the consensus of various observers may vary because the incidence of orchitis differs with different epidemics. The severity of the epidemic does not always parallel the incidence of orchitis. In this series, the reduction of orchitis from 28.83 per cent in the control group to 16.27 per cent in the treated group, when subjected to statistical analysis, is significant. The encephalitis observed, however, is of the same order, 16 per cent The association of orchitis with meningitis, while in each group. higher than with meningitis-free patients, is not of significant magnitude. It is interesting that no differences were found between the groups in range of temperature, number of days of fever or length of stav in the hospital.

The use of serum or plasma in the treatment of orchitis did not produce the spectacular results reported for very small series. However, in 26 treated patients the temperature of 16 dropped to normal

^{57.} Bonnamour, S., and Bardin, J.: Le sérum antidiphtérique dans le traitement des oreillons comme préventif de l'orchite ourlienne, Presse méd. **28**:929 (Dec. 22) 1920.

^{58.} Wesselhoeft, C.: Mumps, in Christian, H. A.: Oxford Medicine, New York, Oxford University Press, 1941, vol. 5, pt. 2, p. 497.

in three days or less, while of 30 controls this occurred in only 10. Since the subjective feeling of illness in mumps orchitis is directly related to the fever, it would appear that these men were benefited by this procedure. Stengel ⁵⁹ stated that in patients with orchitis, although the fever may end by crisis, slow subsidence, or lysis, is usually seen. Of 249 patients with mumps who were studied in this epidemic, 101 had either orchitis or manifest encephalitis or both.

There is sufficient clinical statistical evidence to show that this disease does little damage to boys below the age of puberty, and Wesselhoeft²⁷ is sound in his conclusion that familiarity with mumps tends to breed a respect for the advantages of early active immunity. One should weigh the few dangers of the disease in children with the great chances of serious involvements in adults before instituting protective measures in children.

SUMMARY

1. Of 249 men with mumps, orchitis developed in 61, or 24.5 per cent. In 86, to whom 40 cc. mumps convalescent serum was given intravenously on admission, orchitis developed in 14, or 16.27 per cent. In 163 controls, orchitis developed in 47, or 28.83 per cent. These figures are significant when subjected to statistical analysis.

2. There was manifest encephalitis in 40 of the 249 patients, no difference being noted between the serum-treated patients and the control groups. In 15 instances, both orchitis and encephalitis occurred together. Thus 86, or 35.3 per cent, of the 249 patients had orchitis. encephalitis or both.

3. Convalescent serum and pooled plasma were used in the treatment of orchitis. Sixteen of the 26 treated patients had fever three days or less, the temperature of all of them dropping by crisis, as compared with a group of 30 control patients, in 10 of whom the fever lasted three days or less while in only 7 the temperature dropped by crisis. Since the total number of days of fever in the treated group averaged 4.52 as compared with 5.4 in the controls, the value of serum or plasma as a therapeutic procedure cannot be definitely demonstrated.

Dr. Sidney O. Levinson, director of the Samuel Deutsch Serum Center of Michael Reese Hospital, Chicago, gave suggestions and assisted in the preparation of these data.

1525 East Fifty-Third Street, Chicago.

59. Stengel, A., Jr.: Mumps Orchitis, Am. J. M. Sc. 191:340 (March) 1936.