Incidence of Reactions To Antirabies Horse Serum

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THE REAWAKENING of interest in the development of hyperimmune rabies serum has made available a new approach to the prevention of rabies in man. Several groups of workers are now, or have been, exploring the use of serum as an adjunct to the classic vaccination procedure or possibly even as an outright replacement of vaccination (*1–3*).

During a recent outbreak of rabies in Birmingham, Ala., two children died from rabies, despite prompt and intensive vaccination with 14 Semple treatments. The incubation time was 17 days in one child and 19 in the other. Such short incubation periods allow very little time for the development of immunity. The Alabama State Department of Public Health laboratory in Birmingham, therefore, made available, first, hyperimmune antirabies rabbit serum and, later, a hyperimmune antirabies horse serum concentrate, to supplement vaccination.

This report deals with the use of the horse serum concentrate, which was provided by Lederle Laboratories with the request that the incidence of serum sickness following its use be assessed. The horse serum concentrate was used only on patients having face, neck, arm, and hand bites, the patients having been skin-tested before administration of the serum. Serum was not used if the bite occurred longer than 72 hours prior to the time serum could be given. The dosage was 0.25 ml. per pound of body weight given intramuscularly, followed in 24 hours with at least a 7-course treatment of Semple vaccine unless a shorter course was indicated by the condition of the biting dog.

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Serum Reactions

Reactions to antirabies horse serum concentrate in 32 patients are presented in the table. Eight of the patients had attacks of serum sickness of varying intensity. Only three of these reactions were severe and two were moderate. The latter two reactions were on a mother and daughter. If the three slight reactions are discounted, the reaction rate is 15.6 percent, a figure which compares favorably with reported reaction rates following the use of rabbit serum and is far less than reported rates following the use of sheep serum (*3*). If this reaction rate is maintained with more extensive experience, the use of antirabies horse serum in the presence of a negative skin test would not be contraindicated.

Ten of the patients were bitten by dogs proved rabid. The presence or absence of virus in the submaxillary glands of the dogs, however, was not determined except for patient 32. In this instance, rabies virus was demonstrated in an LD_{50} titer of 10^{-4}. Four additional patients were bitten by dogs in which rabies was doubtful. In one instance the biting dog was not found, and in two instances the animals were killed and the brains found negative for Negri bodies. In the latter two cases, no animal inoculation was done. In one other instance, Negri bodies were found by one laboratory but not by another. Animal inoculation in this case, however, was negative. Of the patients bitten by dogs proved rabid, 7 had face bites; 2, finger bites; and 1, leg bites. Of those bitten by doubtful rabid animals, 2 had face bites; and 2, finger bites.

Discussion

Experimentally the use of antirabies serum has a good foundation (*2, 3*). One adverse report which has appeared is not based on recent experimental evidence (*4*). It is not possible, of course, to draw a definite conclusion as to the value of serum on the basis of this limited study. It is safe to say, however, that there are no serious contraindications to its use and that it may indeed have done some good.

In view of the fact that 7 patients with face or neck bites and 2 with finger bites from rabid

Data on 32 patients treated with hyperimmune rabies serum of horse extraction

Patient	Age (years)	Weight (pounds)	Location of bite	Nature of bite	Animal rabid	Number of days Semple vaccine given	Serum dosage (ml.)	Reaction
1	8	87	Face	Severe	No	9	20	None.
2	6	45	Legs	Mild	Yes	14	10	None.
3	6	46	Cheek, chin, and upper lip.	Moderate	Yes	14	10	None.
4	4	35	Finger	Mild	Yes	14	9	None.
5	3	28	Cheek	Mild	Yes	14	7	None.
6	4	40	Face and abdomen	Severe	Doubtful	14	10	None.
7	5	40	Face	Moderate	No	7	10	None.
8	4	42	Lip	Moderate	No	7	10	None.
9	6	50	Eyelid and scalp	Severe	No	0	20	None.
10	3	33	Lip	Mild	No	7	8	None.
11	4	37	Cheek	Mild	No	6	9	None.
12	9	50	Chin	Mild	No	7	12. 5	None.
13	14	40	Forehead and scalp	Severe	No	7	10	None.
14	4	37	Cheek	Moderate	No	6	9	None.
15	5	39	Lips	Mild	No	7	9. 75	None.
16	4	44	Forehead and eyelid	Severe	No	7	10	None.
17	16 (mo.)	40	Face	Mild	Yes	14	10	None.
18	4	41	Forehead	Mild	No	7	10	None.
19	6	43	Face	Severe	No	0	11	None.
20	3	30	Face	Moderate	No	7	10	None.
21	4	35	Cheek and lip	Severe	Yes	14	9	None.
22	3	30	Face	Severe	No	3	12	None.
23	13	80	Face	Severe	No	2	32	None.
24	8	60	Face	Severe	No	2	15	None.
25	28	160	Neck	Mild	Yes	14	40	Mild.[1]
26	8	60	Thumb	Moderate	Yes	14	15	Mild.[2]
27	4	32	Lip	Mild	No	7	8	Mild.[3]
28	31	128	Fingers	Moderate	Doubtful	14	32	Moderate.[4]
29	8 (mo.)	20	Face	Mild	Doubtful	14	5	Moderate.[5]
30	2	31	Forehead, eyelid, and leg.	Moderate	Yes	14	8	Severe.[6]
31	26	134	Two fingers	Mild	Doubtful	14	33	Severe.[7]
32[8]	6	40	Nose	Mild	Yes	14	10	Severe.[9]

[1] Slight urticaria 10 days later.
[2] Slight rash at site of injection 11 days later.
[3] Slight redness and itching around injection area 8 days after, lasting 2 days.
[4] Rash 4 hours after injection. Rash reappeared after 5 days, lasting 5 days.
[5] Urticarial rash 5 days after injection, lasting 5 days.
[6] Fever, nausea, and vomiting fifth through ninth day.
[7] Severe urticarial reaction with swelling, fever, pain, nausea. Cleared in 11 days.
[8] Virus isolated from submaxillary gland of dog, LD_{50} titer of 10^{-4}.
[9] Rash and swelling after third day. Cleared in 5 days.

dogs were treated with a low potency vaccine, as measured by the Habel test, and that Sellers (*5*) has shown that the risk of infection is 72 times greater in face bites than in leg bites and 5 times greater in hand bites than in leg bites, it may be assumed that these patients were at great risk. Certainly patient 32 was exposed to infection because of the large amount of virus present in the submaxillary gland. None of the patients have to date developed rabies.

At present, it is premature to rely on serum treatment alone. If its use, however, permits a reduction in the number of vaccine treatments from the usual 14 to perhaps 7 or less, this would in itself be a distinct advantage, since a shorter course of vaccine treatment should reduce the risk of postvaccination paralysis. Serum is also advantageous in cases in which the biting dog cannot be found immediately. Its use would allow time for a thorough search for the dog before vaccine treatment is initiated. When vaccine treatment is indicated only on the theory that any animal bite, no matter how trivial, can produce rabies, judicious use of serum might permit elimination of vaccination and at the same time offer the patient mental

relief. Finally, in the presence of severe face and hand bites, simultaneous use of serum and vaccine should materially reduce the danger of infection, if, in fact, the serum alone were not efficacious. The prolonging of the incubation period through the use of serum gives more time for active immunity to develop from the vaccine.

Conclusion

Further experience is needed to determine the value of antirabies serum. At present, however, it should be considered as another worthwhile tool in the prevention of rabies and should be used wherever indicated.

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REFERENCES

(1) Habel, K.: Seroprophylaxis in experimental rabies. Pub. Health Rep. 60: 545–560 (1945).

(2) Koprowski, H., Van der Scheer, J., and Black, J.: Use of hyperimmune antirabies serum concentrates in experimental rabies. Am. J. Med. 8: 412–420 (1950).

(3) Koprowski, H., and Cox, H. P.: Recent developments in the prophylaxis of rabies. Am. J. Pub. Health 41: 1483–1489 (1951).

(4) Remlinger, P., and Bailly, J.: Le traitment Pasteurien et les travaux Americains relatifs a la vaccination antirabique. Rev. Immun. Par. 14: 291–298 (1950).

(5) Sellers, T. F.: Limitations of antirabic treatment. J. M. A. Georgia 35: 130–133 (1946).

Municipal Sewage Treatment Plant Construction

A total of 515 communities in the United States were awarded contracts in 1952 involving an expenditure of $137 million for construction of municipal sewage treatment plants, according to a recent report released in May by the Public Health Service. Of these contracts, 314 were for new plants costing $78,419,556; and 201, costing $58,789,133, were for additions, enlargements, or replacements of existing plants.

The report compares the 1952 rate for this type of construction with the annual rate of from $450 million to $500 million estimated to be required over a 10-year period to bring the pollution caused by municipal wastes under reasonable control. The 1952 total of $137 million is less than that for any year since 1948. It also falls short of the long-term average of $141 million for the period 1915–50.

The report is available in the Division of Water Pollution Control, Bureau of State Services, Public Health Service, Department of Health, Education, and Welfare, Washington 25, D. C.

During the first quarter of 1953, $31 million was invested by 119 municipalities for sewage treatment projects. Of these, 61 contracts were for construction of new sewage treatment plants; 48 were for enlargement or improvement of existing plants, and 10 were for construction of interceptor sewers.

In Departmental Periodicals . . .

OCCUPATIONAL HEALTH

Radiation Exposures

In the July (and final issue) of Occupational Health, Duncan A. Holaday summarizes the potential health problem from exposure to radiation. For many of the biological effects of radiation, there is a threshold dose below which no permanent damage will occur, he writes. For certain effects, such as the production of mutations, shortening of the life span, and possibly carcinogenesis, there is no lower threshold.

"Animal experiments and such data as we have on humans indicate that moderate radiation doses will increase the normal radiation rate," Mr. Holaday points out. For this particular effect, all radiation exposures are additive. "Calculations of radiation doses from various sources, such as the industrial and medical use of radiation, indicate that it is possible for an average person to be exposed to biologically significant amounts of radiation."

Mr. Holaday, an engineer with the Occupational Health Field Station of the Public Health Service at Salt Lake City, advises "all health departments to obtain data on the location of sources of radiation in their areas, on the levels of radioactivity in air and water, and on control and protective measures employed." Such baseline information, he concludes, would permit an intelligent appraisal of the extent of the present and future problems which the use of radiation may create and would permit the responsible agencies to determine their future course of action.

Other items in the July issue include articles on:

"Occurrence of Radon in Non-Uranium Mines in Colorado" (by P. W. Jacoe). The finding of appreciable quantities of radon in mines located several hundred miles from the nearest known deposit of uranium-bearing ore might indicate the possibility of undiscovered ore bodies nearby.

"Industrial Medicine Services in Italy" (by R. Vigliani). The number of industries in Italy which have their own medical services is increasing, although there is as yet no law compelling every industry to organize a medical service in its factories or establishing the rights, duties, or professional training of factory physicians.

"Occupational Health—A Joint Industry and Public Health Responsibility" (by Charles D. Yaffe). Industry in recent years has come more than halfway to meet the health agency in shouldering the responsibility for occupational health work.

"Occupation and Health" (by Seward E. Miller). Health hazards are reviewed in selected industries, such as chromate-producing, and in certain occupations, such as arc-welding in the steel shipbuilding industry.

Suspension Notice

Publication of *Occupational Health*, a monthly since 1940, has been suspended with its July 1953 issue as the result of reduction in appropriations. However, *Public Health Reports*—which in recent issues has presented papers on air pollution, human relations in industry, occupational and environmental aspects of various diseases, and industrial dentistry—will give increased attention to technical topics in occupational health. Official agencies, professional organizations, and teaching institutions not now receiving *Public Health Reports* should inquire of the Public Health Service as to their eligibility for official or free subscriptions. Other groups—and individuals wishing personal copies—should purchase subscriptions. *Use the subscription blank on the inside back cover of this issue.*

Recent issues of *Occupational Health* are available at 10¢ a copy from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.