depend on the absence of calcium ions from the medium rather than on the presence of strontium (see also ref. 8). On the contrary, the time course of the hyperpolarising transient of the cones at the onset of the stimulus is not significantly different in the three conditions.

Previous work has shown that the transmission of electrical signals from photoreceptors to horizontal cells depends critically on the presence of calcium in the extracellular fluid[7] and is blocked either by excess magnesium[6-8] or by the presence of cobalt ions[7]. In this paper I have demonstrated that the addition of strontium ions to the retinal medium restores the response of horizontal cells to light abolished by calcium removal. All these properties are characteristic of the chemical transmission in conventional synapses and therefore these results strongly support the chemical nature of the signal transmission from photoreceptors to horizontal cells.

As to the modifications in the time course of the depolarising transient and in the $V/\log I$ curves observed in the response of the horizontal cells during the perfusion with calcium-free strontium Ringer, these seem to depend on similar changes in the behaviour of the cones in the same conditions. On the contrary, the prolongation of the time course of the hyperpolarising onset in the horizontal cells responses has no counterpart in cone responses. At the neuromuscular junction Sr^{2+} ions are known to increase, by way of a postsynaptic effect, the duration of transmitter action. If one assumes that the hyperpolarising responses to light of horizontal cells result from a reduction in the release of a depolarising transmitter[15] continuously flowing in darkness from the receptor pedicle, increasing the duration of transmitter action would result in a slower time course of the hyperpolarising phase at the light onset.

I thank Dr L. Cervetto for suggestions and Drs L. Maffei, A. Fiorentini and A. Cangiano for reading the manuscript.

M. Piccolino

Laboratorio di Neurofisiologia del CNR, Pisa, Italy

Received February 24; accepted March 25, 1976.

1 Lasansky, A., *Phil. Trans. R. Soc.*, B262, 365–381 (1971).
2 Gray, E. G., and Pease, H. L., *Brain Res.*, 35, 1–15 (1971).
3 Raviola, E., and Gilula, N. B., *J. Cell Biol.*, 65, 192–222 (1975).
4 del Castillo, J., and Katz, D., *Progr. Biophys. Biophys. Chem.*, 6, 121–170 (1956).
5 Weakly, J. N., *J. Physiol., Lond.*, 234, 597–612 (1973).
6 Dowling, J. E., and Ripps, H., *Nature*, 242, 101–103 (1973).
7 Cervetto, L., and Piccolino, M., *Science*, 183, 417–419 (1974).
8 Kaneko, A., and Shimazaki, H., *J. Physiol., Lond.*, 252, 509–522 (1975).
9 Miledi, R., *Nature*, 212, 1233–1234 (1966).
10 Dodge, F. A., Jr, Miledi, R., and Rahamimoff, R., *J. Physiol., Lond.*, 200, 267–283 (1969).
11 Meiri, U., and Rahamimoff, R., *J. Physiol., Lond.*, 215, 709–726 (1971).
12 Cervetto, L., and MacNichol, E. F., Jr, *Science*, 178, 767–768 (1972).
13 Heisey, S. R., *Fedn Proc.*, 27, 287 (1968).
14 Baylor, D. A., and Fuortes, M. G. F., *J. Physiol., Lond.*, 207, 77–92 (1970).
15 Byzov, A. L., and Trifonov, Yu. A., *Vision Res.*, 8, 817–822 (1968).

Postexposure serum prophylaxis of neonatal herpes simplex virus infection of mice

Perinatal infections with herpes simplex virus (HSV) cause death or permanent disability in most reported cases[1-5]. In theory, control of this disease by immunotherapy might be feasible, much like postexposure serum prophylaxis of rabies, since the time of HSV infection in the birth canal is usually known and antibody can be administered soon thereafter. Treatment with antibody has not been encouraged, however, because (1) many investigators consider this immunity cell-mediated rather than humoral[6-11]; (2) effective administration of human immune globulin in neonatal herpes of man has not been demonstrated[1,3,12], and (3) transplacental antibody conferred only partial protection in human neonatal infections[1]. There is further discouragement in animal studies which failed to show protection by antibody[9-11], although antibody was protective in some animal studies[13-20]. The findings reported here raise again the possibility that antibody treatment might be effective in specific conditions.

The concept that cell-mediated immunity, rather than humoral immunity, is the major host defence has been based in part on increased severity of HSV infection after impairment of T-lymphocyte function[6-11]. But, findings that HSV antibody production is T-cell dependent[9,20,21] suggest that exacerbation of some of these infections by impaired T-lymphocyte function could have been due to decreased antibody formation[20]. Furthermore, protection of mice that received syngeneic, immune spleen cells and were infected with HSV might, in some cases, be due to the transfer of antibody-producing or helper cells, since high levels of antibody were produced more rapidly in these mice than in control mice (unpublished observations). Consistent with this view is the protection of nude[20], immunosuppressed, and normal mice (unpublished observations) against HSV infection by sufficiently high levels of passively administered antibody and apparent protection against HSV by maternal antibody of infants (excluding newborns) under 11 months of age[22].

Re-examination of antibody potential in a model of neonatal HSV infection is indicated by these findings, even though they do not establish the importance of antibody in all conditions. For example, strains of HSV that spread principally through the blood stream might be affected by antibody, but not strains of HSV that are transmitted through nerve pathways which exclude antibody.

Our study was designed to determine whether administration of various units of neutralising antibody could achieve post-exposure prophylaxis of experimental neonatal HSV infection[20]. Mice (Swiss, CDF-1 or BALB/c), age 1–4 d, were infected subcutaneously with from 1 to 300 newborn mouse LD_{50} of HSV, either type 1 (VR3 strain) or type 2 (MS strain). One hour after infection, the experimental mice were injected intraperitoneally with 0.1 or 0.2 ml of type-specific hyperimmune rabbit antiserum. Controls were injected with normal rabbit or foetal bovine serum, or Eagle's tissue culture medium containing 2% foetal bovine serum. Mice were observed for at least 12 d. Percentage protection was calculated as follows:

$$\frac{\%\text{ mortality of controls} - \%\text{ mortality of treated}}{\%\text{ mortality of controls}} \times 100$$

Rabbit antisera were prepared by initial injections of HSV virus either type 1 or type 2 (grown in rabbit kidney cultures and emulsified with Freund's incomplete adjuvant) into the footpads and back (0.25 ml containing $10^{5.4}$ PFUs of HSV), followed by four to eight weekly subcutaneous and intravenous injections of virus without adjuvant.

Protection consistently occurred in newborn mice infected with 1–20 LD_{50} of either type of HSV and treated with a total of 12,000 U of antibody (Table 1). No protection occurred when the large dose of antibody was administered to mice infected with a high challenge dose (100–300 LD_{50}) of HSV. Little or no protection followed treatment with 600 U of antibody. Better results attained against HSV type 1 warrant further study.

Our findings demonstrate good protection against experimental neonatal HSV infection by large doses of antibody in mice infected with low challenge doses of virus. Failure of antibody in some animal studies[9-11], but not in others[13-20], could conceivably be due to such variables as antibody dose[17], virus challenge dose[14], portal of entry HSV, and difference in pathogenesis, depending on the virus strain used. These same factors might account for the reported failures of human immune globulin to protect newborn infants against HSV nfection[1,3,12]. Additional study of these and other variables may further determine the optimum conditions for antibody protection of newborns.

Although our results were obtained using mice infected subcutaneously, other studies have shown antibody protection

Table 1 Protection by antiserum of newborn mice against HSV infection

Expt	Mouse strain (Age, d)	HSV type (strain)	Challenge dose (LD_{50})	Dose of antibody (U per mouse)	Dead mice/ Total mice	% Mortality	% Protection	Combined% protection*
1	CDF-1 (1)	1 (VR3)	10	0	7/7	100		
			10	12,000	1/8	13	87	
2	Swiss (1)	1 (VR3)	2	0	6/9	67		
				12,000	0/10	0	100	
3	Swiss (1)	1 (VR3)	20	0	19/21	90		
				12,000	1/19	5	94	94†
4	CDF-1 (1)	1	100	0	6/7	86		
			100	12,000	6/7	86	0	0
5	BALB/c (1)	2 (MS)	2	0	3/8	38		
				600	5/5	100	0	
			20	0	7/7	100		
				600	7/7	100	0	
6	Swiss (1)	2 (MS)	20	0	18/22	82		
				600	9/22	41	50	18
7	Swiss (4)	2 (MS)	1	0	3/5	60		
				12,000	0/6	0	100	
		2 (MS)	3	0	5/5	100		
				12,000	4/8	50	50	
8	Swiss (2)	2 (MS)	2	0‡	3/5	60		
				12,000	2/8	25	58	
9	Swiss (1)	2 (MS)	3	0	5/5	100		
				12,000	2/6	33	67	
10	Swiss (1–2)	2 (MS)	3	0‡	7/8	88		
				12,000	2/14	14	84	71†
11	Swiss (1–3)	2 (MS)	300	0	18/18	100	0	
			300	12,000	25/25	100	0	0

* Average % protection for preceding experimental group.
† $P < 0.005$.
‡ Normal rabbit serum.

of newborn or young animals infected intranasally[13,19], intradermally[13], intracerebrally[14,15,17], intraperitoneally[14], intravaginally[18] or subcutaneously[16]. Because of these earlier findings, human immune globulin treatment in man had been considered[1,12,19,24]. If proper conditions can be defined to protect newborn infants with hyperimmune human globulin, this treatment would offer several advantages over present methods: for example, administration of human immune globulin to newborns is much safer than surgical delivery of the babies or than use of toxic drugs. Finally, combination of protective antibody with other antiviral agents, such as interferon, might enhance protection as with vaccinia virus infection of mice[23].

We thank Thomas K. Hughes Jr for technical assistance.

SAMUEL BARON
University of Texas School of Medicine, Galveston, Texas 77550

MICHAEL G. WORTHINGTON
St Elizabeth's Hospital, Boston, Massachusetts 02135

JULIANN WILLIAMS
JAMES W. GAINES
National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20014

Received February 19; accepted April 20, 1976.

1 Nahmias, A. J., Alford, C. A., and Korones, S. B., *Adv. Peds.*, **17**, 185–226 (1970).
2 Nahmias, A. J., *et al.*, *Am. J. Obstet. Gynec.*, **110** (6), 825–837 (1971).
3 Hanshaw, J. B., *Am. J. Dis. Childh.*, **126**, 546–555 (1973).
4 Nahmias, A. J., and Roizman, B., *New Engl. J. Med.*, **289** (15), 781–789 (1973).
5 Hare, M. J., *Proc. R. Soc. Med.*, **67**, 15–16 (1974).
6 Mori, R., *et al.*, *Proc. Jap. Acad.*, **41**, 975–978 (1965).
7 Nahmias, A. J., *et al.*, *Proc. Soc. exp. Biol. Med.*, **132**, 696–698 (1969).
8 Allison, A. C., *Transplant. Rev.*, **19**, 3–55 (1974).
9 Allison, A. C., *Monogr. Allergy*, **9**, 259–271 (1975).
10 Oakes, J. E., *Infect. Immun.*, **12**, 166–172 (1975).
11 Koyama, H., and Kassahara, S., *Infect. Immun.*, **12**, 1472–1474 (1975).
12 Wheeler, C. E., Jr, and Huffines, W. D., *J. Am. med. Ass.*, **191**, 111–116 (1965).
13 Berry, G. P. and Slavia, H. B., *J. exp. Med.*, **78**, 305–320 (1943).
14 Cheever, F. S., and Daikos, G., *J. Immun.*, **65**, 135–141 (1950).
15 Tokumaru, T., *Arch. ges. Virusforsch.*, **22**, 332–348 (1967).
16 Gruia, M., *et al.*, *Rev. Roum. Virol.*, **10**, 47–58 (1973).
17 Akerfeldt, S., Lofberg, E., and Fuchs, G., *Biochem. Pharmac.*, **22**, 2911–2917 (1973).
18 Baker, M. B., Larson, C. L., Ushijima, R. N., and Anderson, F. D., *Infect. Immun.*, **10**, 1230–1234 (1974).
19 Luyet, F., Samra, D., Soneji, A., and Marks, M. I., *Infect. Immun.*, **12**, 1258–1261 (1975).
20 Worthington, M. G., Williams, J., Baron, S., and Conliffe, M. A., *IRCS Medical Science: Cell and Membrane Biology; Immunology and Allergy; Parasitology and Infectious Diseases*, **3**, 370 (1975).
21 Burns, W. H., Billups, L. C., and Notkins, A. L., *Nature*, **256**, 654–656 (1975).
22 Anderson, S. G., and Hamilton, J., *Med. J. Austr.*, **1**, 308–311 (1949).
23 Worthington, M., and Baron, S., *J. infect. Dis.*, **128**, 308–311 (1973).
24 White, J. G., *New Engl. J. Med.*, **269** (9), 455–460 (1963).

Type C virus in lymphosarcoma in northern pike *(Esox lucius)*

THE northern pike (*Esox lucius*) is a highly prized freshwater fish, both as a game fish and as a commerical species. Epizootics of lymphosarcoma occur widely in North American pike[1] and in the Old World[2,3]. The tumour in pike has been found with an overall frequency of 20.9%, which is the highest frequency of a malignant neoplasm in any known free living vertebrate[1]. All pike with the tumour have cutaneous lesions, and epizootiological evidence suggests that the disease is transmitted horizontally by contact during spawning[1]. The tumour is transplantable and evidence of cell-free transmission has been found[1,4]. In an attempt to resolve the aetiology of the disease, we have investigated the presence of oncornavirus in pike lymphoma. Since all known RNA tumour viruses possess the enzyme reverse transcriptase, we have sought the activity of this enzyme in post-mitochondrial particulate fractions prepared from pike lymphoma tissue.

Pike lymphomas were analysed as described in the legend