10. A. D. Dalton, Anat. Rec., 121, 281 (1955).
11. H. R. McDonald, H. D. Engers, G. C. Cerottini, et al., J. Exp. Med., 140, 718 (1974).
12. H. R. McDonald, B. Sordat, and G. C. Cerottini, J. J. Exp. Med., 142, 622 (1975).
13. W. Rosenau and H. D. Moon, J. Natl. Cancer Inst., 27, 471 (1961).

# THE IMMUNODEPRESSIVE ACTION OF VACCINIA VIRUS

O. S. Danilyuk, S. G. Dzagurov, and M. S. Berdinskikh

UDC 612.017.1.014.46:615.371:578.821.51

KEY WORDS: living and inactivated smallpox vaccine; antibody formation; immunodepression.

Virus diseases (measles, influenza, rubella, mumps, chicken pox, etc.) are known to weaken immunity both to each other and to bacterial infections. However, the experimental study of this phenomenon only began comparatively recently. It was shown, for instance, that in influenza the number of T lymphocytes in the blood of affected humans and animals is reduced [5, 15], as also is the number of antibody-forming cells (AFC) in the spleen [3, 9], and macrophages and neutrophils are injured [7]. There is a certain amount of experimental evidence on immunoinhibitory properties of adeno-, arbo-, and cytomegaloviruses [2, 6, 10], measles virus [13], and rabies street virus [14].

The object of this investigation was to study the possibility of an immunodepressive action of vaccinia virus (living or inactivated).

## EXPERIMENTAL METHOD

Noninbred albino mice weighing 12-14 g were used. Living vaccinia virus (batch 0342 produced by the Moscow Research Institute of Virus Preparations) in a titer of $10^{4.5}$ PFU was injected into the caudal vein in a volume of 0.2 ml. Inactivated smallpox vaccine (from the same producer, batch 8) was injected by the same route in a volume of 0.5 ml.

Sheep's red blood cells (SRBC) were injected into the caudal vein in a volume of 0.2 ml of 10% suspension. On the 4th day the number of AFC in the spleen was determined by Jerne's method [12].

The numerical results were subjected to statistical analysis by Student's t test and geometric means and confidence intervals were calculated [1].

## EXPERIMENTAL RESULTS

Preliminary experiments showed that after injection of living or inactivated smallpox vaccine alone into the animals without SRBC the number of AFC per weight of organ on the 4th day after injection of the preparation was 42 and 12, respectively.

Three principal experiments were carried out on 60 animals. Twenty animals were used in each experiment (five in a group). The results were consistent (Table 1). The number of nucleated cells in the spleens of mice of all groups was almost identical. The number of AFC per $1 \cdot 10^6$ splenic karyocytes on the 4th day after injection of SRBC in group 2 was indistinguishable from the control (group 1). Different results were obtained in the animals of group 3: in mice receiving the living vaccine and SRBC 2 days later the number of AFC per $1 \cdot 10^6$ karyocytes was significantly less than in the control ($P < 0.01$). When inactivated smallpox vaccine was used (group 4) the number of AFC per $1 \cdot 10^6$ splenic karyocytes was a little higher than in the control.

L. A. Tarasevich State Research Institute of Standardization and Control of Medical Biological Preparations, Ministry of Health of the USSR. Laboratory of Immunology, D. I. Ivanovskii Institute of Virology, Academy of Medical Sciences of the USSR, Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 94, No. 7, pp. 73-74, July, 1982. Original article submitted November 18, 1981.

 0007-4888/82/9407-0942$07.50 

TABLE 1. Effect of Living and Inactivated Smallpox Vaccine on Number of AFC in Mouse Spleens

| Preparation studied | Group of mice | Scheme of injection of antigens | Number of animals in group | Number of nucleated cells in spleen | Number of AFC | |
|---|---|---|---|---|---|---|
| | | | | | per $10^6$ nucleated spleen cells | per spleen |
| Control | 1 | SRBC | 15 | $2{,}2 \cdot 10^8$ ($1{,}8 \cdot 10^8$—$2{,}6 \cdot 10^8$) | 72,4 (55,0—95,5) | 27 540 (21 380—35 480) |
| Living smallpox vaccine | 2 | SRBC + vaccine (2 days later) | 15 | $2{,}6 \cdot 10^8$ ($2{,}1 \cdot 10^8$—$3{,}1 \cdot 10^8$) | 66,1 (43,7—102,3) | 34 670 (23 990—50 120) |
| | 3 | Vaccine + SRBC (2 days later) | 15 | $2{,}1 \cdot 10^8$ ($1{,}4 \cdot 10^8$—$3{,}2 \cdot 10^8$) | 20,9 (14,4—30,2) | 8 913 (6 607—12 020) |
| Inactivated smallpox vaccine | 4 | Vaccine + SRBC (2 days later) | 15 | $4{,}0 \cdot 10^8$ ($3{,}3 \cdot 10^8$—$4{,}8 \cdot 10^8$) | 85,1 (79,4—91,2) | 63 100 (51 290—77 620) |

The total number of AFC in the spleen of the animals of group 2 was the same as in the control. However, in animals of group 3 the number of AFC in the spleen was minimal, evidence of the marked immunodepressive action of the living virus on immunopoiesis ($P < 0.01$). Inhibition of AFC formation was not observed in the mice of group 4. The results of these experiments thus show that living smallpox vaccine, unlike inactivated, has a marked immunodepressive action.

The mechanism of this action of living smallpox vaccine is not clear, nor is it known for other viruses. Only in relation of influenza virus have experimental data been obtained to show that virionic neuraminidase participates in this process [4], but not ribonucleoprotein [8].

Vaccinia virus has been shown to be capable of inducing T suppressor cells in mice [11]. All that can be suggested is that the phenomenon of immunodepression, induced by living vaccinia virus, depends on the action of the virus on cooperation between immunocompetent cells, leading to the formation of a population of antibody-producing cells.

## LITERATURE CITED


1. I. P. Asmarin and A. A. Vorob'ev, Statistical Methods in Microbiological Research [in Russian], Leningrad (1962).
2. V. Sh. Nizamov and I. Kh. Shuratov, Vopr. Virusol., No. 1, 48 (1979).
3. V. Sh. Nizanov and I. Kh. Shuratov, Vopr. Virusol., No. 3, 284 (1980).
4. N. L. Novichenko, in: Problems in Microbiology and Virology (Seventh Conference of Junior Scientists) [in Russian], Riga (1977), p. 216.
5. G. I. Savitskii, T. Ya. Lyarskaya, and N. M. Savrasova, Vopr. Virusol., No. 3, 297 (1978).
6. B. F. Semenov, in: Abstracts of Proceedings of the 16th All-Union Congress of Microbiologists and Epidemiologists [in Russian], Part 2, Moscow (1977), p. 70.
7. L. V. Solilova, G. I. Il'in, L. Ya. Reikh, et al., Vopr. Virusol., No. 6, 682 (1973).
8. V. I. Struk, Z. D. Savtsova, and N. L. Novichenko, in: Viruses of Cancer and Leukemia [in Russian], Moscow (1977), p. 133.
9. L. V. Yakimenko, S. L. Rybalko, Z. D. Savtsova, et al., Vopr. Virusol., No. 1, 96 (1975).
10. J. Booss and E. F. Wheelock, J. Infect. Dis., 135, 478 (1977).
11. A. Ferrante, D. E. O'Keefe, and G. H. Thong, Med. Microbiol. Immunol., 168, 227 (1980).
12. N. K. Jerne and A. A. Nordin, Science, 140, 405 (1963).
13. C. J. Lucas, J. Ubels-Tostma, J. M. D. Galama, et al., Cell. Immunol., 37, 448 (1978).
14. T. J. Wiktor, P. C. Doherty, and H. Koprowski, J. Exp. Med., 145, 1617 (1977).
15. D. T. G. Yu, J. Immunol., 115, 91 (1975).