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LOCALIZATION OF SPECIFIC ANTIGEN IN ORGANS OF ANIMALS VACCINATED WITH LIVE MEASLES VACCINE

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Temporary localization of attenuated measles virus antigen in neurons and blood vessels of the brain of newborn mice and hamsters vaccinated subcutaneously with live measles vaccine was demonstrated by an immunofluorescence method. Virus-specific antigen was found in adult animals in the lymphoid system only. Signs of serous meningitis and also vascular disorders were observed for a short time in the brain tissue of any animal by biological testing in tissue culture.
KEY WORDS: attenuated measles virus; immunofluorescence.

As a result of the wide use of live measles vaccine in preventive medical practice the incidence of measles in children has been greatly reduced. However, reports have been published [1, 2, 5] indicating that measles vaccination may lead to the development of vaccinal reactions and sometimes of postvaccinal lesions of the nervous system. The pathogenesis of these complications is not clear and the few attempts that have been made to study their mechanism experimentally have yielded contradictory results [7, 8]. Other problems still awaiting solution are the ability of vaccinal strain L-16 to penetrate into the structures of human and animal nerve tissue, the dynamics of its accumulation in the organs, and the nature of the course of the vaccinal reaction and the histological changes following injection of measles vaccine into animals with altered reactivity, and so on.

The object of this investigation was to study the distribution of attenuated measles virus or its antigen and the histopathological changes in the brain tissue of newborn albino mice and Syrian hamsters, and also in intact guinea pigs and guinea pigs sensitized with AMDT vaccine, vaccinated with measles vaccine.

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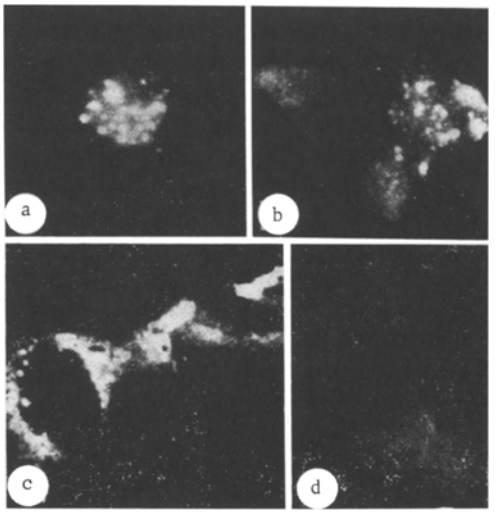

Fig. 1. Localization of virus-specific antigen in brain structures of newborn mice vaccinated with live measles vaccine, on fourth day after vaccination: a) glial cells; b) neuron; c) blood vessels; d) control (unvaccinated animals), squash preparation of brain. Indirect Coons' method, 720 ×.

EXPERIMENTAL METHOD

Experiments were carried out on 54 guinea pigs weighing 200-250 g, 40 newborn mice, and 40 hamsters aged 1-2 days. The guinea pigs of the experimental group were sensitized by three subcutaneous injections of DTP (diphtheria–tetanus–pertussis) vaccine at intervals of 1 day in a dose of 0.5 ml per injection. Fourteen days later the animals received an intracardiac injection of 5 vaccinal doses of live measles vaccine (batch 0679, Moscow Research Institute of Virus Preparations). The experimental scheme was chosen to fit in with the existing program of vaccination of the children. Guinea pigs sensitized with AMDT vaccine, recieving an intracardiac injection of physiological saline, and also intact animals receiving an intracardiac injection of measles vaccine served as the controls. The guinea pigs were killed by total exsanguination followed by perfusion of the organs with physiological saline through the systemic circulation 1, 3, 7, 14, 21, and 28 days after the injection of measles vaccine. The presence of measles vaccine virus in brain extracts was determined by biological tests in continuous L-41 tissue cultures, highly sensitive to measles virus [3]. Squash preparations were obtained from brain, liver, kidney, lung, and spleen tissue, fixed with acetone, and stained by the indirect Coons' method [6]. Normal human immunoglobulin with a high content of antibodies against measles virus was used as the immune antimeasles serum. The specificity of the immunofluorescence method was confirmed by the appropriate controls [6]. Pathomorphological changes in brain and spinal cord tissues were studied in histological sections stained with hematoxylin–eosin in the usual way.

Newborn animals were vaccinated subcutaneously with a single vaccinal dose of measles vaccine. The animals were killed 2, 4, 6, 8, 10, 12, 14, 21, and 28 days later and their brain tissue investigated by the methods described above.

EXPERIMENTAL RESULTS

In the intact and sensitized guinea pigs vaccinated by intracardiac injection of measles vaccine no clinical signs of damage to the nervous system were found. During attempts to infect tissue cultures no attenuated measles virus could be isolated from the brain of the vaccinated animals at any time of the experiment. During the experiment no virus-specific measles antigen could be detected by the immunofluorescence method in structures of the brain, kidneys, liver, and lung. Only occasionally, chiefly during the first few days after injection of the measles vaccine, were erythrocytes with measles antigen located on their surface found in the squash preparations of the brain. Specific fluorescence was regularly observed only in cells of the plasma series in the spleen, in which they were found as early as on the second day after injection of the measles vaccine. Virus-specific antigen was detected in the cytoplasm of the spleen as fluorescent granules, which increased in size considerably toward the third to seventh days of the experiment. The largest number of anti-

gen-containing cells was observed by the seventh day after injection of measles vaccine into the blood stream; by the 14th-21st days only single cells with specific fluorescence could be found in the preparations.

Pathomorphological investigations of the brain and spinal cord tissue of the intact and sensitized guinea pigs vaccinated by intracardiac injection of measles vaccine revealed temporary signs of perivascular and pericellular edema and also transient, weak manifestations of serous meningitis.

No evidence was thus obtained from these experiments to confirm that attenuated measles virus penetrates into tissue of the nervous system of adult guinea pigs.

In the experiments on newborn mice and hamsters vaccinated subcutaneously with measles vaccine none of the animals died. No vaccinal virus was isolated from the brain tissue of the animals at any time during the experiment, but specific measles antigen was regularly found in neurons, glial cells, and membranes of brain blood vessels as early as on the second day after vaccination, in the form of brightly fluorescent granules (Fig. 1). Toward the sixth day the intensity of fluorescence fell sharply, and by the eighth day no virus-specific antigen could be found in brain preparations of newborn vaccinated animals. Pathomorphological investigation of the brain tissue at this period showed temporary disorders of the circulation and slight serous meningitis; no damage to neurons was observed. No vaccinal virus or its antigen could be found in the brain tissue of adult mice vaccinated with measles vaccine.

The investigations thus revealed an affinity of attenuated measles virus for the cellular and vascular structures of the brain of newborn animals, probably attributable to the immaturity of the immunological mechanisms in the early postnatal period. According to observations by other workers [7, 8], attenuated measles virus adapts itself easily to the tissue of the neonatal nervous system. Evidently the quantity of virus in the brain tissue was minimal, or alternatively the vaccinal virus was present in a special form, for the results of the virological tests in these experiments were negative. In adult animals measles virus antigen was localized in the spleen cells, in agreement with the findings of Gusman et al. [4].

The development of circulatory disorders in the brain tissue of animals vaccinated with live measles vaccine could be due in the newborn animals to direct injury to the wall of the blood vessels by vaccinal virus, whereas in the adults it could be due to the toxic effect of the vaccination.

The results point to potential affinity of attenuated measles virus for nerve and lymphoid tissue and they provide a theoretical basis for the possible role of measles vaccinal virus in the pathogenesis of vaccinal lesions of the nervous system which develop in children after vaccination against measles.

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