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SPECIFIC PROPHYLAXIS HOOF AND MOUTH DISEASE

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SPECIFIC PROPHYLAXIS HOOF AND MOUTH DISEASE

by

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SPECIFIC PROPHYLAXIS HOOF AND MOUTH DISEASE

The feasibility of protective vaccination of animals with attenuated hoof and mouth disease virus was established by N. N. Ekkert (1902), while he served as the Chairman of the All-Russian Anti-Hoof and Mouth Disease Commission in 1900-1901 in the Stavropol district. Analogous research was carried out in Germany by F. Löffler, who determined the virus nature of the causative agent of hoof and mouth disease and proved that the economic advantage in the prevention of hoof and mouth disease was not with medical, but with prophylactic agents [29].

Wide study of hoof and mouth problems in our country became possible only after the Great October Socialist Revolution. At first, in the All-Union Research Institute of Experimental Veterinary Science, under the leadership of Professor S. N. Vyshelesskiy, and then in a specially established hoof and mouth disease institute, with the active participation of Professor A. L. Skomorokov, a complex of quarantine-restrictive measures were developed. However, extreme measures permitted inoculation in a strictly isolated herd of horned cattle by scarification of the surfaces of the upper lip membrane with live virus. However, positive effects were not obtained from this inoculation. In 1934, a search was begun for more economical means of specific prophylaxis (serus from convalescents, formaldehyde-killed aphthous vaccines, and others). These methods were not sufficiently perfected at that time, and therefore did not receive wide use.

In Western European countries, especially in Germany, (on Romo Island) very significant work in hoof and mouth disease was carried out, specifically concerning etiology of the disease, resistance of the virus, and the mechanism for transmitting the infection (Val'dman, Paniye, Trautveyn, Ben, Vagener, Gallouey, Pikolau, Negel' and others[1]). In 1934,

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Danish researchers (Schmidt et al.[1]) proposed the adsorbed aphthous "GOAL" vaccine, which, according to the data of Papulovskoi (1934), created immunity against virus types "A" and "O" for a period of two to three months. This vaccine was improved by Val'dman and Kebe[1] (1937) at the Rimsov[1] Institute in Germany, after which the International Epizootic Bureau in Paris recommended the vaccination of animals with Schmidt - Waldman's[1] GOAL vaccine be used in a complex of measures to combat hoof and mouth disease.

Thus, mass production of hoof and mouth disease virus on the mucous of the tongues of horned cattle became the earliest method for commercially producing virus for preparation of anti-hoof and mouth disease vaccine.

The Great Patriotic War and a series of technical reasons prevented the organized production of anti-hoof and mouth disease vaccine in our country. Only in 1949 did L. D. Ratner and V. N. Gribanov begin to prepare an experimental series of aphthous vaccine at the All-Union Institute of Plant Protection, but with several changes and improvements over the Schmidt-Waldman method. In 1951, this vaccine was first tested in experiments extensively carried out in White Russia, and positive results were obtained. In 1953, preparation of this biological preparation was begun at the Kursk[1] biofactory from virus (tongue epithelium) obtained from slaughtered animals at meat combines adapted for this purpose. A similar vaccine prepared by the classic method of Schmidt-Waldman is used at the present time in a series of countries in Western Europe and Latin America. However, great difficulties have been associated with their production. Since the place for harvesting the virus (meat-packing plants), according to the conclusions of a series of foreign and Doviet authors (S. G. Poplavkhina[1], 1962), served as a constant source of hoof and mouth disease. Also, there is a danger of variation in the standard properties of virus used in producing residual immunity in the animals.

The method of propagating hoof and mouth disease virus in the organisms of laboratory animals, i.e., guinea pigs and rabbits [5, 7, 9, 13, 16, 17] was a promising method for obtaining cheaper raw materials (virus) for producing vaccine in our country. New-born rabbits proved to be the best subject for the propagation of hoof and mouth disease virus for preparation of sufficiently effective vaccines in the amounts required.

Scientists in our country deserve great credit for developing a method for obtaining inactivated vaccine from lapinized hoof and mouth disease virus. This became possible because of multiple research carried

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out mainly in our country, and also in France [43, 44], Brazil [23], Italy [39] and Argentina [38].

Primarily, formol-aluminum hydroxide mono- and di-valent vaccine [8], stabilized in glycerine, was prepared from the lapinized virus. This vaccine is used on a wide scale in our country for the specific prophylaxis of hoof and mouth disease of various types and in a series of production tests in some other countries [33, 38]. Lapinized vaccine creates immunity in animals which lasts for two to three months.

This vaccine is not a absolutely perfect preparation and therefore it requires further improvement to increase its effectiveness. However, the use of this vaccine in large quantities in a complex of veterinary-sanitary measures has been a great advantage and during the last five years has prevented the development of an epizootic outbreak of hoof and mouth disease from the European "O" and "A" types.

Recently, the heat-inactivation of lapinized virus has been attempted. According to preliminary data, that vaccine is more active and can be preserved better than formaldehyde-killed vaccine.

In 1947, the Dutch scientist Frenkel, based on research by the Maitlands [32] developed a commercially cultivated hoof and mouth disease virus in cattle tongue epithelium explants, and in 1952-1953, the author had already prepared a cultivated virus in 600-litre reaction vessels. This method is widely employed for manufacturing vaccine in Holland [25], Denmark [24], Italy [41], France [35] and other countries.

At the present time in the USSR, the preparation of an inactivated vaccine from hoof and mouth disease virus, cultivated by the Frenkel method on the surviving epithelium of the tongues of horned cattle and pigs [3, 14, 18] has been adopted in production.

Vaccine obtained by the Frenkel method is a highly effective and imparted immunity to the animals for 4 to 5 months, but according to the reports of a series of authors [36 and 42], it was less effective than the vaccine from natural (aphthous) virus.

Recently, for production of inactivated vaccine, mass cultivation of hoof and mouth disease virus was begun in mono-layer cultures of kidney cells from cattle and pigs, and also of transplantable cell lines. For example, in Italy a method was developed for growing hoof and mouth disease virus which permits one to obtain 200 to 500 litres of virus-containing material within a week, and in the Democratic Republic of Germany [2] a special production line was created guaranteeing the growth of virus in tissue culture.

Subsequently in Italy [40], Belgium [31] and our country [15], the technological production of virus in mono-layer cultures was perfected with rotating vessels, proposed for this purpose. That was a major step in making it possible to increase the area for growing cells and to increase the concentration of new virus in the culture medium. Moreover, considerable mechanization of the production operations was achieved.

Besides the inactivated vaccine indicated, other preparations have been widely used abroad. Thus, in France a vaccine has been produced for many years (but used primarily in Africa), which is prepared according to the Billin [21] method in a variolous hoof and mouth disease complex. But in the opinion of this author, this vaccine, including the tri-valent one, is not as effective as vaccine from aphthous stock and surpasses the cultured vaccine.

In India [26], a crystal-violet vaccine is used, which is prepared from virus contained in the blood of animals infected with the hoof and mouth disease. In [illegible]ntry, positive results were obtained from studies on such vaccine. [illegible]owever, it is not produced for sanitary reasons.

Basset (1951), in evaluating positive vaccinations against hoof and mouth disease, noted, that in France every year 6 million animals (nearly 20% of all horned cattle livestock) were inoculated against hoof and mouth disease in a two-stage program. Mono-valent vaccine against virus of types O, A, S and di-valents O_2/A_5 and A_5/C were prepared in France at three biofactories and the Institute for the Study of Hoof and Mouth Disease in Lyons.

Lucam, Makkovyak and Magat[1] (1958) by applying a statistical method, carried out investigations of the results in the immunization of animals against hoof and mouth disease in France for 10 years, and came to the conclusion that vaccination was harmless, and economically effective, and that it created dependable immunity in 80% of the animals, and 1/5 of those vaccinated, if they did have the disease, were without signs of generalization of the process. Cases of hoof and mouth disease among vaccinated animals were recorded only on those farms where the sanitary measures were unsatisfactory.

Argentina's Department of Agriculture also rates the vaccine as highly effective, although it indicates that vaccine does not always work in helping to protect small calves and swine from the hoof and mouth disease.

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In Switzerland in 1943, (Flyukkiger, 1955) mass vaccination was begun against the hoof and mouth disease coupled with slaughtering of large animals in primary force. Here all cattle are inoculated every spring with di-valent vaccine, but upon the threat of an appearance of hoof and mouth disease, repeated inoculations are conducted. Vaccine is prepared from variants O/O_4 and O/A_5, O/C and A_5/C.

The following indications are presented of the economical effectiveness of mass immuno-prophylaxis against hoof and mouth disease; during the epidemic in 1938-1939, when only serum from convelescents was used, the loss from hoof and mouth disease was 30 million francs, and in 1951-1952 (when vaccine was used) losses from this disease were only 3.5 million francs.

Moosbrugger (1958) considered that under contemporary conditions, prophylaxis of hoof and mouth disease on the European continent, without active immunization, was practically impossible [34].

The State Institute of Denmark located on the Island of Lindkholm[1], prepares di-valent vaccine O/A_5 and A_5/C, while a large reserve stock of it is not usually created, since when a new variant of the virus emerges, expenditure on its production may seem wasted. Here there is a small reserve of hoof and mouth virus of various types and variants, which of necessity, differe from expensive commercial vaccines. When the hoof and mouth disease poses a threat in our country, horned cattle, sheep and billy-goats are vaccinated on a wide scale. In Denmark, as in other countries, unsatisfactory results were often recorded upon vaccination of calves and swine.

In Holland, according to the data of Van den Born[1], a vaccine against hoof and mouth disease, prepared by the Frenkel method, has been used since 1949. At first, animals were vaccinated on only 8-10% of the farms, but after the epidemic in 1951-1952, all horned cattle were vaccinated every six months. At the same time, the sick animals, isolated from those inoculated, were killed. Vaccination in conjunction with killing the sick can, in the opinion of the author, ensure eradication of the disease. Mono-valent vaccines are prepared from types A, O, and S. When necessary, vaccines of different types of infection are mixed before injection.

In the Democratic Republic of Germany vaccine is prepared on the Island of Rims from aphthous virus of hoof and mouth disease, and virus grown in tissue culture. Inoculations are carried out here in a methodical manner, twice a year.

In the West German Federal Republic mass immunization is also conducted against two or three types of virus with the help of aphthous and

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cultured vaccine. In the opinion of many researchers (Pilz and others) polyvalent vaccines create immunity more rapidly than mono-vaccine.

In England the eradication of hoof and mouth disease was accomplished by killing the sick animals and paying their owners a compensation.

However, in the Scientific Research Institute of Pirbraite, work is intensively carried out in the search for effective vaccines. The best results in that institute were obtained in 90% of the animals receiving a vaccine from attenuated strains of virus (Gallouey, 1961).

An extremely promising method of preparing virus vaccine using mice was proposed by Skinner (1963). He and his co-workers discovered a method for obtaining more than 5,000 doses of vaccine daily from one 3-5 day old mouse. Using this method, the Pirbraite Institute prepared vaccine for African countries against types SAT-1, SAT-2, and SAT-3 of hoof and mouth disease. However, a period of 1 - 1.5 years was required to obtain attenuated strains of virus in mice. English investigators attach special importance to repeated vaccination of animals. Many scientists have established that repeated injection both of inactivated and especially of live vaccine 20-30 days after the first injection creates several times more intense and more prolonged immunity in inoculated animals than one-time immunization. This characteristic of immunogenesis should be considered during the vaccination of animals in zones which are threatened for a long time by hoof and mouth disease.

Vaccine prophylaxis of hoof and mouth disease is ofen complicated by the immunological incompatibility of commerical (from a biological manufacturing plant) and epizootic strains of virus, which is caused by the multiplicity of types and variations of virus. As indicated by the epizooty of hoof and mouth disease in the Republics of Central Asia and Caucasus, and also in a series of regions of the Russian Soviet Federated Socialist Republic, the creation of an effective anti-hoof and mouth disease vaccine requires clear work to typify the strains of virus, and rapid organization of the release of an effective biological preparation.

At the present time, the basic origin of virus stock for preparation of vaccine from inactivated hoof and mouth disease virus is 2-3 day old rabbits and tongue epithelium from killed animals.

The basic efficacy of a vaccine is revealed by its capacity to provide specific immunological re-organization in the organism, creating non-susceptibility to infection.

When high-quality vaccine is utilized, immunity is achieved comparatively slowly--in approximately 10 to 12 days in most of the inoculated animals. If vaccine possesses average immunizing qualities, immunity is achieved still more slowly--in 16 - 20 days. Highest intensity of post-vaccinal immunity is reached by the 30th to 40th day, and often later. Continuation of immunity depends upon the individual characteristics of the animals and the quality of the vaccine. In 50% of mature animals vaccinated, enough immunity of sufficient intensity develones and is retained up to 5-8 months. The intensity of immunity usually depends on the immunogenicity of the strain of virus manufactured, and often also on the type of equipment and method of vaccine preparation. Wider variations have been recorded in other directions.

Concerning the relative merits of anti-hoof and mouth disease vaccines, prepared from aphthous (natural), lapinized, and cultured virus, and also the effectiveness of mono-, di-, and tri-valent vaccines, there is no agreement among researchers. This is explained by the fact that scientists work with various preparations in animals with different immunological characteristics. The majority of investigators consider that vaccines from cultured virus create immunity for a shorter period than aphthous vaccine.

N. I. Gushchin[1] (1960) has analyzed the effectiveness of the use of agents for specific prophylaxis according to the data of the veternary account in the Voronezh region, where in 1959, two vaccines were used: aphthous GOAL-vaccine VIEV and lapinized (4%) GOAL-vaccine of the Kirgiz Scientific Research Institute Journal of Voronezh. In sum, it has been established that no vaccine has been created which confers 100% immunity.

Aphthous concentrate-vaccine in a series of farms has produced "vaccinated" hoof and mouth disease, and in several animals in foci of HMD, the lapinized vaccine did not create immunity.

Röhrer, evaluating vaccine-prophylais, considers it positively necessary to use vaccine only massively with a coverage of all susceptible livestock [37].

During the past decade, the search for a live virus vaccine against hoof and mouth disease was expanded [19]. With that goal, the most widely employed method is attenuation of virus via its passaging in the organism of naturally unsusceptible animals and also in tissue culture.

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Virus vaccine against hoof and mouth disease possesses a series of advantages over inactivated-vaccine. However, not one of the modified variants of the virus obtained has come out of experimental research.

By means of long passaging of hoof and mouth disease virus, type A in mono-layer culture of rabbit kidney, A. A. Sviridov (Novo Sibirsk Scientific Institute Medical Department) obtained an avirulent variant of the virus, which is being used in production conditions. Analogous work has also been begun there with virus type O.

Experiments in attenuation of hoof and mouth disease virus types SAT-1 and A in culture of transplantable cell lines were carried-out at The All-Union Scientific Research Institute on Hoof and Mouth Disease.

An attenuated variant of hoof and mouth disease virus types A, O, and S was obtained in the West German Federated Republic by means of long passaging (518-558) in a culture of calf kidney cells, in France experiments have also been carried out with types A and S in a culture of rabbit kidney cells, in the German Democratic Republic with type S in a transplantable cell line of pig embryo brain cells.

In the USSR, Brazil and France, the attenuated variant virus has been obtained by means of long passaging in rabbits. In our country, a modified variant of the virus was successfully obtained by means of adaptation to mice of gradually increasing age. An experiment with immunization against hoof and mouth disease of large and small horned cattle in the Autonomous Republics of Bashkir and Tartar and in the Central Regions of the Soviet Russian Federated Socialist Republic with avirulent virus vaccine of the State Scientific Agricultural Institute directly at unsafe localities [1, 6], confirms the possibility of rapid eradication (terminating) of epizooty at the origins of infection, without resorting to obsolete and dangerous methods of aphthization (artifical superinfection).

Regarding serological prophylaxis of hoof and mouth disease, there is no doubt about its practical value. However, the preparation of such serum on a commercial basis in our country has not yet been fixed, although appropriate proposals have been made [4, 10].

Taking into account the lability of the antigenic characteristics of hoof and mouth disease virus, regulations have been developed for the preparation of polyvalent immune serum and immune gamma-globulins, which protect animals, especially the young, from many types of virus encountered in the territory of the USSR.

Control of the manufactured series of vaccines and sera before their release in practice is one of the most important and responsible features

of the work. Fundamental control of vaccine is conducted on avirulence and immonogenicity. In England [28], West German Federated Republic [27] and other countries, analysis of avirulence is achieved by introduction of vaccine in sub-mucosa of the tongue of horned cattle or by infecting suckling mice and by not releasing any series of vaccine from which live virus is successfully isolated. It was necessary for us to review methods of controlling the harmlessness of anti-hoof and mouth disease preparations. For practical application, every series of vaccine must be released only after positive results of testing for sensitivity of hoof and mouth disease of horned cattle.

In order to verify the immunogenic characteristics of anti-hoof and mouth vaccine some methods have been proposed, on the basis of which principles were established for protecting horned cattle from the generalized hoof and mouth disease process [40], comparative titration of virus in vaccinated animals [30], determination of titer of virus-neutralizing antibodies in serum of vaccinated animals [20] and titration of hoof and mouth disease virus in vaccinated and unvaccinated adult mice [11, 22].

Our country borders on many other countries of Asia, the Near and Middle East, in which hoof and mouth disease shows stationary morbidity. While in these countries, the extremely dangerous exotic types of the virus: SAT, Asia, and the especially virulent Near-Eastern variant of Type A, which was arbitrarily designated Ai. Over a period of two years entry of the indicated types of hoof and mouth disease into the USSR occurred twice and several biofactories had to prepare an adequate quantity of agents for specific prophylaxis -- vaccine and serum of convalescents for extensive systematic immunization of animals were distributed in threatened zones of the country.

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13. ABSTRACT

Specific prophylaxis by inoculating animals was established as early as 1902, by N.N. Ekkert. Research by other scientists followed, with F. Loffler concluding that it was more economical to prevent hoof and mouth disease with medical than with prophylactic agents. Danish researchers (Schmidt and others) prepared the aphthous "GOAL" vaccine created by Papulovskoi, which was created against civirus types "A" and "O" and lengthened the period from two to three months. This vaccine was improved by Waldman and Kyebye at the Rimsov Institute in Germany. Then it became possible to mass reproduce virus of hoof and mouth disease in the mucous of the tongues of cattle.

A vaccine resulting from the Frenkel method was highly effective and protected the animals from 4 to 5 months, but on re-evaluating the series the author noted that it was less effective than the vaccine from a natrual aphthous virus. Continuance of immunity was dependent on the individual characteristics of the animals and the quality of vaccine. The intensity of immunity usually depended on the immunization strains of virus manufactured and often also on the type of implementation and method of vaccine preparation.

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