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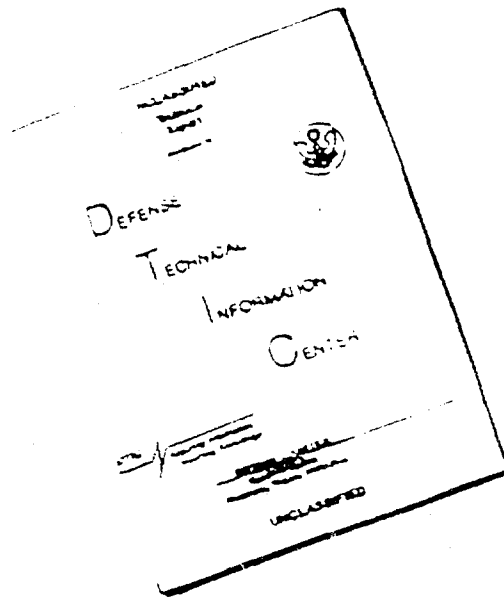
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# AEROSOL IMMUNIZATION WITH DRY DUST VACCINES AND TOXOIDS

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## AEROSOL IMMUNIZATION WITH DRY DUST VACCINES AND TOXOIDS

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### Communication VIII. A Study of the Method of Aerosol Immunization with Dust Plague Vaccines During Mass Immunization

The successful test of the method of aerosol vaccination on limited groups of people in 1961 permitted going on to broader observations on people with the permission and on the recommendation of the Serumal-Vaccinal Committee of the Ministry of Health USSR. In this work we posed the task of testing the worked-out method of mass aerosol immunization of people by the dust plague vaccine in practical conditions as well as to verify and define more precisely the data previously obtained which attested to the harmlessness and weak reaction of this method of vaccination.

As in all previous investigations a dry dust plague vaccine from the EB strain was used. The original biological activity of the test series of dust vaccine was within the limits of 50-100 billion live microbes per gram. Aerosol immunization was carried out in a normal room with a volume of 112 cubic meters (7.5 x 6 x 2.7) which was cleared only of excess furniture. During the four immunization sequences, the length of each of them being 15 minutes, there were up to 190 persons in the room (in a standing position) at the same time.

7

The vaccine was sprayed with a special instrument, PAV-60, which is a proportioning feeder attached to a household fan operating on electric current. The spraying was done continuously over the entire period of immunization. The batch of vaccine sprayed in the room per immunization sequence was 10-12 grams. The preparation for the sequence (setting up and equipping the instrument, opening the vaccine ampoule) took 10 minutes.

The concentration of the vaccine aerosol and the doses of live microbes of the vaccine strain inspired by each of those immunised were determined by taking samples of the aerosol from the room in absorption instruments of the bubbling type with subsequent screening of the absorption liquid from the instruments onto a solid culture medium and counting the grown colonies. In addition, the weight content of the dust vaccine in the absorption liquid was determined by a chemical method. Calculation of the biological (number of live microbes per liter of aerosol) and the weight concentration was done by calculating the amount of air sucked through the absorption instrument per unit of time. The inhaled dose was determined as the product of the magnitude of concentration, exposition, and minute volume of pulmonary ventilation of a person. [See Note]

(Note: The minute volume of pulmonary ventilation was taken as 10 liters per minute for the average person.)

The quantity of microbes of the EB vaccine strain inspired by each of the vaccinated persons, calculated by determining the weight concentration, was 150-200 million.

In an experiment on monkeys even smaller doses of dust vaccine with two aerosol immunizations produced resistance in 50 percent of the animals on subsequent aerosol contamination. [See Note]

(Note: Experiments on monkeys were performed by N. F. Nepogodin, A. A. Korneyev, and V. I. Vetoshkin.)

In the four sequences of aerosol immunization by dust plague vaccines, 543 persons were vaccinated. Before immunization all persons were subject to medical examination accompanied by a clinical analysis of blood and urine and an X-ray examination of the thoracic organs. Healthy persons of the male sex aged 18-25 years were permitted for immunization.

Immediately following the vaccinations medical observation of the health of those vaccinated was begun and continued for half a year. For seven days after vaccination there were daily check-ups and temperatures of all were taken; persons with complaints on the state of their health were subjected to detailed clinical examination to determine the diagnosis. Aside from daily temperature taking, on the 1st-2nd, 3rd-4th

and 7th-8th days after immunisation, 157 persons were given X-rays (thoracic organs) and hematological examinations (total number of leukocytes, sedimentation reaction) and in each period an average of 50 persons were examined.

As a result of the observations of the vaccinated persons, it was established that the clinically expressed post-vaccinal reaction to the aerosol immunisation of the dust plague vaccine in the applied dosage was practically absent. In not a single vaccinated person was there a temperature reaction or any sort of other changes in the condition of health. All those vaccinated continued to perform their duties. No changes were revealed upon X-ray examination of the thoracic organs. Nevertheless there was some reaction to the aerosol immunisation, but it was revealed in subclinical form and discovered only upon laboratory investigation.

The clinical analysis of the blood done on 157 persons showed that in 91.1 percent of those examined, there were marked changes expressed in an increase of leukocytes. Results of the investigation of hemograms of those subject to the aerosol immunisation by the dust plague vaccine are presented in the table in which it is seen that in the first and second days after aerosol immunisation, changes were registered on 96.3 percent of those examined. An increase with the greatest consistency was noted in the number of leukocytes (87 percent), reaching 500-5,000 cells or more, in comparison with the original level. In 50 percent this increase exceeded the upper limit of the physiological norm and was determined as leukocytosis. The average number of leukocytes computed for this group was 8,536. Changes in the sedimentation reaction in the vaccinated persons was inconsistent and insignificant (fluctuations of plus or minus 1-3 mm/hour), its average index measured 5 mm/hour, and instances of an increase in the physiological norm under the influence of the immunisation were practically absent (one out of 52).

Within three to four days after the aerosol immunization, changes in the blood were observed in 84.6 percent of those examined. In 36 percent there was, as before, an increased content of leukocytes; however, in 40 percent of those vaccinated there was a marked decline. The degree of increase was less significant; leukocytosis was observed in only 13.5 percent of them. Changes in sedimentation reaction in this period were also insignificant and inconsistent; however, there was some tendency toward slowing down.

Examinations conducted seven to eight days after the aerosol immunisation showed that in the blood of those vaccinated some changes were noted which by their nature corresponded to those described above. An increased number of leukocytes was observed in 78.4 percent of those vaccinated and in 47.1 percent of them leukocytosis was observed. It should be pointed out that the increase was more expressed than in the previous periods

of examination; the average content of leukocytes in the blood in this period was 9,745. Changes in sedimentation reaction were, as before, weakly expressed and inconsistent, and a certain tendency toward slowing down was noted.

Thus, under the influence of aerosol immunisation of dust plague vaccine, against a background of complete absence of clinically expressed reactions in the majority of those vaccinated, there was a distinct increase in the number of leukocytes in the earlier periods after immunization. The results obtained testify to the development in the overwhelming majority of those vaccinated of a stereotype general reaction which emerged in subclinical form. Unfortunately, changes in the blood were studied by us only up the seventh and eighth day after the aerosol immunization and it was not possible to study the formula of the white blood. The absence of these data makes difficult a thorough analysis and also does not permit establishing a closer link in the changes of the hemograms with the general immunological reconstruction of the organism.

Because of the absence of reliable tests, in this work we did not evaluate the immunological effectiveness of aerosol immunisation of the dust plague vaccine. The testing of new methods designed to study the immunological effectiveness of plague vaccine (a pestin test, modified reaction of fixation of the complement, and others) as well as more detailed hematological investigations are a task of further research.

For purposes of a comparative evaluation of the reaction of the aerosol immunization method with dust plague vaccine, the results of subcutaneous and epidermic vaccinations with live EB vaccine carried out at the same time as the aerosol immunization and on entirely comparable groups were studied by us. Subcutaneous vaccination by dry live EB vaccine (in the standard dosage) was given to 100 healthy people of the male sex aged 18-25 years. General post-vaccinal reaction was noted for all those vaccinated; it was heavy in 66 of them (higher than  $38.5^{\circ}$ ), average for 26 ( $37.6-38.5^{\circ}$ ), and in 8 of them it was light ( $37.1-37.5^{\circ}$ ). Local inflammatory reaction in the form of tumescence, hyperemia, and pain, which in a part of the cases were accompanied by regional lymphadenitis, was noted in 98 of the men.

Some 5,600 healthy young (18-25 years of age) men were vaccinated by the epidermic method. Immunization was conducted in accordance with existing instructions on epidermic application of live EB plague vaccine. No heavy post-vaccinal reactions of those given epidermic vaccinations were noted. However, 120 men (2.1 percent) were observed as having medium reactions and 96 men (1.7 percent) had light reactions. In addition, 96 percent of those vaccinated had a local reaction which were in the form of inflammatory changes where the vaccine was injected as

well as in the form of regional lymphadenitis. Local reactions disappeared or diminished considerably (scabs fell off, hyperplasia of the lymph nodes diminished) only after 7-8 days after the epidermic vaccination.

The comparison of the data obtained testifies that the reaction of the method of aerosol immunization of dust plague vaccine is considerably less than the reaction of the subcutaneous and epidermic methods of immunization against plague.

RESULTS OF INVESTIGATIONS OF HEMOGRAMS OF PEOPLE SUBJECTED TO AEROSOL  
IMMUNIZATION OF THE DUST PLAGUE VACCINE

Period of Investigation	Number Investigated	Number of Leukocytes*										Erythrocyte Sedimentation Reaction **	Total No. of Persons with Changes			
		Changes After Immunization				Absolute Magnitudes										
		Decrease	No change	Increase		4000-4999	5000-9000	9001-15000	15000-20000	Leukocytes (more than 9000)	Average					
				501-5000	over 5000									Total		
															Up to 10 mm	More than 10 mm
Before Immunization	157	-	-	-	-	20	119	18	-	18 (11.5%)	7,000	-	-	-	52 (96.3%)	
1-2 days	54	5 (9.3%)	2 (3.7%)	39 (72%)	47 (87%)	-	27	26	1	27 (50%)	8,536	19	20	15	1	44 (81.6%)
3 days	52	21 (40%)	12 (23.5%)	17 (33%)	19 (36.5%)	1	15	6	1	7 (13.5%)	7,665	24	12	14	-	47 (92.1%)
7-8 Days	51	7 (13.7%)	4 (7.9%)	27 (53%)	40 (78.1%)	-	27	18	6	24 (47.1%)	9,715	16	15	20	2	

Note: \* 5000 leukocytes per cubic millimeter was taken as the lower limit of the norm and 9000 as the upper limit.

\*\* The upper limit of the sedimentation reaction for men was taken as 10 mm/hour.

### Summary

Aerosol immunization of 543 healthy young men (18-25 years) using the dust plague vaccine in a dose of 150-200 million live microbes of the EB strain was conducted. After immunization follow-up examination were given, including X-rays of thoracic organs and hematological examinations, to 157 men. Clinically expressed post-vaccinal reactions were almost nil. There was no temperature reaction, no changes in general health, and no changes in the thoracic organs. Clinical analysis of the blood, however, showed marked increases in leukocytes, particularly in the first few days after immunization. In a large number of cases there was leukocytosis. Changes in the sedimentation rate were insignificant. Changes in the blood were not studied after 7-8 days following the immunization and no thorough analysis of the white blood was made; neither was the immunological effectiveness of aerosol immunization with the dust plague vaccine evaluated. The aerosol immunization method proved to be simple to conduct and the reaction to this method was considerably milder than reactions to the subcutaneous and epidermic methods of vaccination with the dust plague vaccine.

### CONCLUSIONS

1. Aerosol immunization of people with dust plague vaccine in doses of 150-200 million live microbes of the EB vaccine strain, appears to have practically no reaction; it does, however, cause typical reactions in the blood.
2. The aerosol method of immunization, conducted under practical conditions on sufficiently large groups of people, has proved to be extremely uncomplicated, permitting rapid mass immunization.

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