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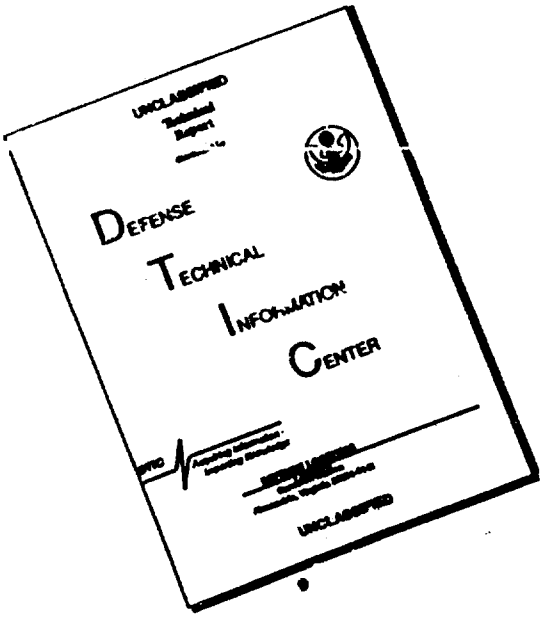

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Test on Mass Vaccination against Q-fever. Report I- Reactivity and Immunogenicity of the Q-vaccine.

R. I. Zubkova, N. I. Fedorova and N. L. Kalmekov (N. F. Gamale Institute of Epidemiology and Microbiology, AMS USSR)

In connection with the establishment of the presence of Q fever in the Soviet Union and the difficulty in creating an anti-epidemical solution, the development of a specific vaccination for this illness is acquiring a special actuality.

There are reports in foreign literature on the methods of preparation and effectiveness of a vaccine against Q fever (Bengston, 1941; Smadel, Snyder and Robbins, 1953; Meiklejohn and Lennette, 1950; Siegert, Peter, Simrock and Schweinsberg, 1953; Babudieri, 1953 and others).

Meiklejohn and Lennette, Smadel and co-workers reported on the good results of vaccination of lab workers. Inoculation with the Q vaccine caused the accumulation of antibodies in them. Clinically expressed infections among those vaccinated were not observed.

The first attempt to vaccinate agricultural animals was by Luoto, Winn and Hubner (1952). Morbidity among the inoculated animals proved 3 times lower than among the non-inoculated, and the isolatability of the rickettsia from the brain was 5 times lower.

In the USSR a vaccine against Q fever was experimentally developed and prepared in the Department of Typhus Fever and Other Rickettsioses of the Gamaley Institute AMS USSR by L. V. Vasileva and V. A. Yablonskaya (1955). The vaccine was prepared from egg cultures of the Bernet Rickettsia which had been killed with formaline and processed with ether according

to Kreg. One ml of the vaccine contained 250 million microbe bodies according to the usual bacterial standard, there 1 ml contains 1.6 milliard rickettsia.

A study of the prophylactic properties of this vaccine indicated that guinea pigs, inoculated thrice with doses of 0.25-0.5-1 ml with weekly intervals, proved fully stable after a month to 1000 infectious doses of standard rickettsia material injected subcutaneously. Good immunological indications were obtained during vaccination of 43 lab workers with this vaccine. Of the 36 inoculated, examined 30-50 days after vaccination, 34 had positive complement fixing reactions with a Q antigen in titers of 1:5-1:320 and only two gave negative results. The inoculations showed the weak reaction of the Q vaccine and fully protected those who had been inoculated against infection while working with this infectious material.

These data allow us to resort to massive vaccination against Q fever in endemical centers.

One of the regions of the Kirgizsk SSR was selected for our observations, this area had been affected by Q fever for a number of yeers a and from time to time is the victim of outbreaks which envelop a large number of people.

Before the inoculations a serological examination was conducted on the population with the complement fixing reaction with a Q antigen from the Italogrecian strain (Grita)(according to the instructions on the application of the Q vaccine, allergical reactions could be avoided if only those people with negative complement fixing reactions were brought into the endemical centre). The reaction was set by means of a lengthy fixation in the cold. First they diluted the serum only 1:5. When they obtained positive results (++++ and +++) the serums were titrated further.

Of 2310 people examined, 542 showed positive reactions (23.5%), of them 509 (93.9%) had titers from 1:5 to 1:80 and 33 (6.1%)- from 1:160 to 1:5120. These data speak of the expensive dissemination of Q fever in this locality; the titers 1:5-1:80, evidently, indicate that the infection was present quite some time ago (complement-fixing antibodies are maintained for several years after recovery from the illness), the titers 1:160-1:5120 indicate fresh infections.

1768 people whose serum proved negative in the complement fixing reaction were selected for the inoculations. These were people who were 20-50 years old and worked in similar surroundings, a majority of them had been living in the locality being studied for several years; only a small percentage were new arrivals from various points of the USSR.

Medical workers (internes, doctors assistants) were enlisted to aid in the inoculation and computation of results. Lectures and sessions were held in the workers establishments to explain the goal and meaning of the inoculations. Individual charts were initiated for each member who would be inoculated and data of the serological examination and computation of reactivity of the vaccine were noted.

The inoculations were administered strictly according to the instructions of the Council Ministry of Health USSR on the application of Q vaccine. A medical examination was conducted before the first inoculation. People who had anti-indicators were dismissed from the inoculations. We utilized a vaccine of killed Bernet rickettsia for the inoculations which was prepared by L. V. Vasileva. The vaccine was administered thrice with weekly intervals in doses of 0.25, 0.5, 1 ml under the skin in the subscapular region and only in a small number of cases in the region of the shoulders. Inoculation was conducted on a

control group (30 people), according to instructions, in the beginning for the varification of the reactivity of the said series of vaccine. After three days observation, which indicated the weak reactivity of the vaccine, the mass vaccination was conducted in the period of 20 June to 7 July 1955. Of the 1768 people chosen for the inoculations, 1128 received three injections, 49- two and 29- one. Computation of the reactivity of the vaccine was by means of questioning, and examination of the place of injection on the day following and day of the next injection.

Subjective complaints, size of hyperemia and temperature reaction were entered on the chart.

The greatest number of general, as well as local reactions were noted after the second injection; reactions after the first injection were noted in 39.1%, after the second- in 62.6%, after the third- in 51.3% (Table 1).

Temperature reactions were observed after the first inoculation in 4.4%, after the second- in 7.1%, after the third- in 6.7%. Of these, severe reactions (higher than 38.5%) were noted only in a small number of those inoculated: after first inoculation- 0.4%, after second-0.2%, after third-0.1%.

Symptoms of general inability and/or headaches were noted also more expressedly after the second and third inoculations. Muscular pains were noted more often after the first inoculation. Allergical appearences (feeling of tenseness in the chest, short-windedness, tachycardia, dissyness) in the first hours after the inoculations were-not noted.

During computation of the local reaction we observed the greatest hyperemia also after the second inoculation. Hyperemia after the first inoculation was noted in 26%, after the second-in 47.7%, after the third-in 40.1%. Significant hyperemia (bigger than 6 cm) was noted in a small

percentage of the cases, mainly in the women who had been inoculated in the region of the shoulders.

Infiltrates at the place of inoculation, slowly resolving but not painfull, were observed quite often: after first inoculation- 27.2%, after second- 31.4%, after third- 20.4%.

Thus, our observations indicated the weak reactivity of the Q vaccine. The tests of mass vaccination had a weaker reaction than after inoculation of the lab workers, even though the vaccine in both cases was of one series. This, evidently, is because the lab workers were vaccinated in the region of the forearm, in our tests the vaccine was introduced into the subscapular region where, as is known, the reaction is less pronounced upon injection and there is less pain.

In further work we attempted to decide whether or not the inoculations could be conducted without serological examinations. With this in mind, we inoculated 19 people thrice; these people had positive complement fixing reactions in low titers (1:5-1:20). We did not observe any severe local or general reactions in any cases as a result of these inoculations. A temperature reaction of 38.5 C was noted in two people after the first and second inoculations. Hyperemia at the place of injection of the vaccine, measuring to 6 cm, was noted in 11 people.

These observations are basis for the conduction of more expansive tests without preliminary serological selections.

In the vaccination tests of the lab workers (Vasileva and Yablonskaya, 1955), it was indicated that inoculations with the Q vaccine caused an active accumulation of antibodies in those people. The highest titer on the complement fixing reaction was noted 6 months after the vaccination(average 1:45), while the average titer 36 days after was 1:28.

According to the data of Meiklejohn and Lennette (1950) the durativity of immunization in those inoculated is 4–5 months; after this period the authors recommend revaccination.

To varify the above statement we conducted serological examinations on a group of 294 people 5 months after vaccination which had been in three injections. A positive reaction of complement fixing was noted in 73%. The titers of reaction fluctuated from 1:5 to 1:640, the average titer was 1:70. More often (85.6%) the serums were encountered with titers from 1:5-1:80, and 1:160-1:640 in only 14.4%. (See Table 2).

Thus, our observations established the good immunological effectiveness of the applied vaccine and the durative maintanence of high vaccinal titers in a majority of the cases. These data allow us to deviate from the recommendations of Meiklejohn and Lennette who suggested revaccination after 4–5 months. It seems that the authors, in their tests, utilized a vaccine of a lower quality, because in the period stated, they witnessed a lowering of the titer of antibodies in thoseinoculated.

Conclusions

1. Serological studies of the population of one of the regions of Kirgiz SSR indicated that 23.5% of the inhabitants had been ill with Q Fever.

2. In the test on the mass vaccination of 1128 people it was established that the Q vaccine has a weak reaction. Severe temperature reactions (higher than 38.5) were noted in 0.3%, hyperemia at the place of injection of the vaccine was bigger than 6 cm in 0.3%.

3. A study of the serum of those vaccinated, 5 months after inoculation, indicated the good immunological effectiveness of the Q vaccine: positive complement fixing reactions were noted in 73%, average titer- 1:70.

Table 1. Reactivity of the Q-vaccine in Humans.

Injection.	Number inoculated	Reaction was		General reaction							Local reaction				
				Temperature							Hyperemia				
		Neg	Pos	Total	To 37.5 C	To 38.5 C	Above 38.5 C	Headaches	Myalgia	Inability	Total	To 3 cm	3-6 cm	Above 6 cm	Infiltrate
First	1206	734	472	53	41	7	5	217	69	206	314	258	51	5	338
%		60.8	39.1	4.4	3.4	0.5	0.4	17.9	5.7	17	26	21.3	4.2	0.4	27.2
Second	1177	440	737	84	60	21	3	433	56	261	563	477	83	3	370
%		37.3	62.5	7.1	5.1	1.7	0.2	36.7	4.7	22.1	47.7	40.5	7	0.2	31.4
Third	1128	549	579	76	59	15	2	365	34	228	453	391	62	-	231
%		48.6	51.3	6.7	5.2	1.3	0.1	32.3	3	20.2	40.1	34.6	5.5	-	20.4

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Table 2. Results of serological examinations of population 5 months after vaccination.

Indicator	Quant serums	of them Neg	Pos	Titer on complement fixing reaction 1:5	1:10	1:20	1:40	1:80	1:160	1:320	1:640
Number	294	79	215	12	29	34	58	51	20	8	3
%	100	27	73	5.7	13.5	15.8	27.0	23.6	9.3	3.7	1.4
				85.6 %					14 %		