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TRANSLATION NO. 101

DATE: Sept 1968

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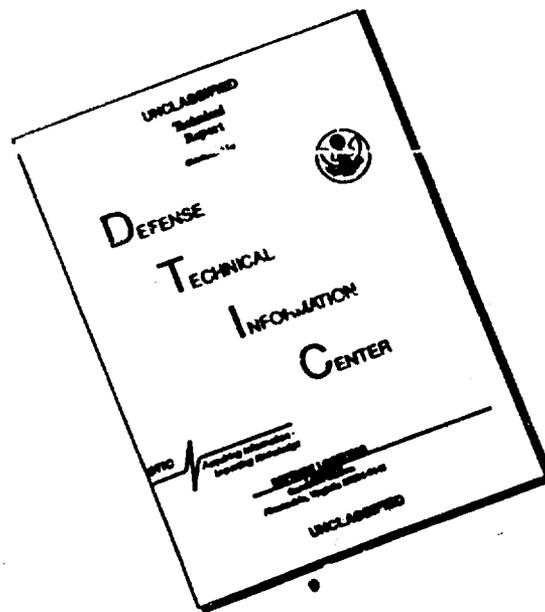
NOV 6 1968

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Zh. Mikrob. i Immunol. 1935
no. 1, 32-35

1935
041

Journal Title—Unknown

Thermo-stable small pox vaccine (Preliminary report).

A. A. Belyaev (Variolar Div. Pastuer Inst., Leningrad).

The basic and most abundant preparation used for vaccination and revaccination against smallpox is the glycerine, anti-variolar vaccine (variolar detritus). With all its positive qualities, this preparation has numerous significant deficiencies, of which the basic ones are its limited period of validity and limited, low thermostability.

As the vaccination practice indicates, the creating of the required temperature conditions for the transportation and storage of the variolar detritus, to and at vaccination points, meets with numerous, sometimes un-surmountable, obstructions. With the large territory of the Soviet Union the problem of transportation of the variolar detritus has a very important meaning.

The solution to the increase of the thermostability of the variolar detritus has agitated the scientific-research minds for some time already. As early as 1883 Reinsner tried to increase the thermostability of the variolar detritus, by application of the drying method. By this method he was able to obtain a dry preparation which would survive 5 months storage at room temperature.

From 1900 to 1920 numerous researchers—Blaksal, Zarini, Zamos, Ahdain, Fisalika, Ross, Manteifel, Degiv, Burts, Shoble and others—tried to obtain a dry, thermostable variolar detritus by means of drying under vacuum, and condensation of the vapors with sulfuric acid or caustic potash. The drying process of the above authors took place at room temperature and lasted from several hours to 2 days (43 hours). In the end they were able to obtain a preparation which survived, though

not always, storage at room temperature for 6 months. But, the preparation dissolved poorly and was very contaminated with microbes as a result of an inaccurate cleaning of the humid scales (scrapings). These inadequacies, the latter in particular, prompted a return, anew, to the glycerine detritus.

In 1927 Otten was able to obtain a dry variolar detritus by means of a 2-day drying under vacuum, with the application of P_2O_5 as the absorbent, which did not lose its virulence during storage under vacuum at 36 C. for several months, or at 56 C. for 3-4 days. In his work, irrefragably, Otten does not mention the solubility of his preparation, nor its microbic cleanliness.

Since 1929, in the Soviet Union, numerous scientists have occupied themselves with the search for a possible way of increasing the thermostability of the variolar vaccine by adding various agents to the detritus, which would slow the heat denaturation of the albumin and the acidifying processes and dampen the heat-death of the microbes. In 1929 (Morozov) an albuminous-buffer mixture was suggested as a control of the acidification, in 1930 saccharose was suggested as a conservant, in 1935 (Kadlets) it was suggested that condensed (evaporated) milk be added to the glycerine detritus as an aid to increasing the thermostability of the detritus. Studies on the thermostability of such variolar detriti indicated that the egg-albuminous and saccharide vaccines survived 10 days storage at 37 C., the lactovaccine, during storage for 3 months at 20 C., also did not decrease in virulence. It is necessary to note that an overall significant thermostability was not created by these methods.

While the method of drying variolar detritus was receiving a limited attention in the European countries, in America it was developed to a degree where it was suitable for practical application, this was by

numerous authors (Swift, Elser, Thomas, Steffen, Flosdorf, Mudd, Nox, Graves, Harvey, Adair, Sherp, Hugh, and many others).

The drying was done by means of a quick freezing of the preparation and a further drying of it under vacuum, with absorption of the vapors by chemical absorbents, or with condensers, located in temperature conditions which were lower than the preparation being dried. The entire drying process lasted from 18 hours to several days. The freezing by a majority of the authors was accomplished with solid CO₂. The obtained preparation stored well and possessed a good solubility. In the Soviet Union successful work is being conducted on the vacuum drying with the application of cold by Kalashnikov and Titov, altering the American method somewhat (Leningrad Inst. Vac. And Serums.). They were able, after numerous experiments, to prove the possibility of exchanging the solid CO₂ with a cooling mixture (ice and salt) which renders an action during drying which is as good as the application of CO₂. ¹/₂

In order to obtain a thermostable variolar detritus, I dried the scales, Scrapings), taken from a vaccinated calf, by a modified Titov and Kalashnikov method.

The drying of the variolar detritus was conducted in a specially constructed apparatus, consisting of a vacuum, single chamber, rotation oil pump (Svetlan) and two alternately engaging systems—a drying and a packaging.

The drying system consists of: 1) a condenser, designated for the absorption of the vapors and packed in a bath which maintains the temperature at minus 20 C., 2) a collector, to which are connected bottles of the material to be dried, 3) baths for the maintenance of the bottled

1. Jour. Micro. Epidem. Immunc., No. 1, 1941: S. S. Rechmenski; Lyophilization as a method of concentrating biopreparations.

material in a frozen state (the temperature of the bath varies according to the process of drying—from minus 18 to plus 45 C.), and 4) a mercury manometer for gaging the vacuum during drying.

The packaging system consists of: 1) a collector for directing the measured dry material into the ampules (after evacuation of the air the ampules are sealed directly on the collector), 2) a phosphorite, filled with P_2O_5 and serving as a drying system, 3) a Geisler tube, with a Tesle apparatus, serving as a substitute for the mercury manometer in keeping the mercury vapors from entering the ampules with the material.

The material for drying is first ground in a ball-grinder and then placed into sterile bottles. In the bottles the material is frozen in a thin layer along the sides. After the freezing the bottles are connected to the collector of the drying system.

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Drying 100-200 cm³ of material takes an average of 8 hours. At the end of the drying the preparation is measured and packaged in ampules in determined doses, containing a chemical humidity absorbent, the ampules are sealed under vacuum. Small ampules of the preparation can be used immediately in vaccinating areas. Larger ampules are suitable for distribution to bacteriological laboratories or drug units for dilution with glycerine, repackaging and a later distribution to vaccinating stations.

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For practical purposes the dry variolar detritus can be diluted in glycerine as well as in any other solvent. The solubility of the preparation is very good. The bacterial cleanliness is good. The degree of dilution of the dry variolar vaccine is determined by the titration of the original series of the preparation. The glycerine diluted dry small pox vaccine has the properties of an ordinary fresh glycerine vaccine.

Our tests of the virulence and thermostability of the dry detritus indicated that the best results were given by a preparation prepared from a lactovaccine, somewhat altered by me (Table).

As the Table indicates, after storage at 37 C. for 10 months the dry lactovaccine proved highly virulent, giving an index of infiltration of $\frac{95 \text{ mm}}{24}$ according to Grot; a 30-day action by a higher temperature (55 C.) did not cause a decrease of its virulence either.¹ At this same time an 8-month storage of the dry egg-albuminous vaccine at 37 C. stipulated a significantly great decrease of its virulence (Grot index $\frac{32 \text{ mm}}{10}$).

Because the work on the drying of the variolar detritus was only started in 1940 by me, the maximum period of validity of the vaccine has not yet been established.

The virulence of several series of dry smallpox vaccine, prepared by me, was tested by the Central Governmental Scientific-Control Institute and received a high appraisal, one series was tested on inoculation of children and gave a 100% inoculation, even by incision.

Conclusions

The obtained data lead us to ^{consider} it urgently necessary that a further development, improvement and instillation into practice of the dry variolar detritus be devoted attention. This has a great advantage, because the dry smallpox vaccine can be transported over un-limited distances and at any temperature; thanks to its compactness, an accumulation and storage can be made of it without fear of spoilage, and ,

1. Unfortunately the author did not state the initial virulence of the the preparations. This allows for a statment of the 'retainment of a sufficient virulence, but not of the 'absence of a decrease of the virulence.' Editor.

finally, the dry smallpox vaccine is a constant, non-varying preparation, very valuable in length experiments.

Table follows:::::

One illustration not duplicated. See original text.

Table 1. Results of tests of thermostability of several preparations of dry smallpox vaccine.

Preparation	Storage period (days)				Gret index (after storage)
	18 C	57 C	55 C	Gret-est	
Lactovaccine 269 No. 2	-	300	-	300	$\frac{95 \text{ mm}}{27}$
Cacaovaccine 269 No. 3	-	15	-	15	$\frac{51 \text{ mm}}{15}$
Lactovaccine 269 No. 4	45	42	-	87	$\frac{113 \text{ mm}}{35}$
Lactovaccine 269 No. 5	-	26	-	86	$\frac{132 \text{ mm}}{35}$
Detritus 269 No. 6	-	19	-	19	$\frac{73 \text{ mm}}{24}$
Egg-Albuminous vaccine 270 No. 8	19	240	-	259	$\frac{32 \text{ mm}}{10}$
Lactovaccine 271 No. 1	73	105	-	178	$\frac{125 \text{ mm}}{32}$
Detritus 271 No. 2	67	105	-	172	$\frac{57 \text{ mm}}{22}$
Lactovaccine 277 No. 10	-	-	30	30	$\frac{95 \text{ mm}}{27}$

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