

If, on the other hand, it is assumed that seven months after vaccination the immunity of all three classes has declined to a negligible point, then during the natural outbreak of disease the incidence of attack would be approximately equal on all three groups, and later, at the time of testing, there would be approximately equal immunity among the groups, i.e., variations in the attack-rate in these three groups would only be those encountered in a normal distribution.

TABLE V.
IMMUNITY TESTS.

TYPE (1).

	<i>Attacked.</i>	<i>Immune.</i>	<i>Total.</i>
Observed	2.0 ...	27.0 ...	29.0
Expected	4.2 ...	24.8 ...	29.0
χ^2/m ...	1.15 ...	0.2 ...	

TYPE (2).

	<i>Attacked.</i>	<i>Immune.</i>	<i>Total.</i>
Observed	11.0 ...	13.0 ...	24.0
Expected	3.74 ...	20.26 ...	24.0
χ^2/m ...	14.1 ...	2.5 ...	

TYPE (3).

	<i>Attacked.</i>	<i>Immune.</i>	<i>Total.</i>
Observed	1.0 ...	36.0 ...	37.0
Expected	5.75 ...	31.25 ...	37.0
χ^2/m ...	3.1 ...	0.7 ...	
$\chi^2 = 21.75, n = 2.$			

In Table V the distribution of immunity in these three groups is examined by the method used in Table IV. The only difference here is that there are two degrees of freedom, that is to say, that it is necessary to calculate two quantities before the remainder may be averaged by addition and subtraction from the available totals. Pearson's tables inform us that with this value of for two degrees of freedom, the proportion (p) is .00002. The odds therefore against such a distribution occurring fortuitously, i.e., as a result of the natural incidence of rinderpest among animals equally susceptible, are 50,000 to 1. We can conclude then that the immunity is not a naturally acquired one, and that the experiment has not been interfered with by the outbreak of rinderpest. One other statistical problem remains to be answered, and this relates to the question whether or not the results of this sampling will hold for the remaining animals of each class. The attached report by Mr. Walter deals with this problem. Further samples will be drawn from these batches of vaccinated animals when two years have elapsed from the period of vaccination, and the results of test inoculations will be reported in due course.

These observations afford us information concerning another very important point, viz., the reinforcement of immunity in immune or partially immune animals. Conclusion 16 (page 41) of the attached paper states: "There is evidence that the inoculation of virulent

blood reinforces the immunity of an immune or partially immune animal only when it produces a reaction in the inoculated animal. This finding casts some doubt upon the value of repeated hyper-immunization with virulent blood." That is a conclusion drawn from experiments some of which are recorded in the paper. An observation recorded by Walker in the Annual Report for 1927 (published 1928), page 121, is in full agreement with this conclusion. Four animals, numbers 1970, 1999, 2007 and 2025, were inoculated twice at a total dose-rate of 60 c.c. per 100 kilos, with toluolized vaccine prepared by Mr. Walker. Eight days later these animals were inoculated with 2 c.c. of virulent blood representing some 2,500 *m.i.ds.* of virus. One animal, number 2025, reacted to the test inoculation of virulent blood, and animals 1970, 1999 and 2007 did not react. A subsequent retest of immunity three months later provoked reactions in two of the animals, numbers 1970 and 1999, which did not react to the first inoculation. Number 2007 apparently did not react to either test, while number 2025 which reacted to the first test did not react to the second. This experimental result is in complete agreement with the conclusion quoted above, and we make take it as a fact then that an animal that is partially immune and does not react to the injection of a moderate dose of virulent blood will not benefit from that injection by any increase in immunity; or to express it in another way, that an animal which is temporarily in a refractory state cannot be immunized by a moderately large dose of virulent blood. Experience teaches that such refractory periods do occur in normal susceptible animals, and further there can be no doubt whatever that an ordinary double-inoculation carried out during this period entirely fails to confer any lasting immunity.

The position with regard to vaccination is entirely different. On farm (B) 231 animals were vaccinated with the completely inactivated vaccine type (2) on the 9th January, 1928; seven days later 169 of these animals were reinoculated with an infective vaccine precisely similar to that which had already produced 108 reactions out of 127 of the animals classed as type (1). Of 169 animals receiving this vaccine as a second inoculation, four only showed transient temperature reactions on or about the sixth day; there were no symptoms of rinderpest. The remainder were in a refractory state as a result of the previous inoculation of completely inactivated vaccine. Now if one refers to the result of sampling this batch of animals which are designated type (3) in Table III, and of the 62 animals that had received only the first inactivated vaccine, type (2), it is quite evident that the second vaccination has reinforced the immunity of these animals, although in 97 per cent. of them it produced no reaction whatever. Herein therefore lies one of the great advantages of vaccination over ordinary double-inoculation that its immunizing action will be exerted on all animals inoculated and that it will not miss any animals that may be temporarily in a condition refractory to the inoculation of virus. The animals of type (3) are just as immune as those of type (1), although only 2.8 per cent. of the former reacted to the infective vaccination as against 85 per cent. of the latter. Further, this finding offers considerable support to conclusion 15 of the accompanying paper which implies that a maximum immunity may be conferred by vaccine without the production of any reactions.

The immunization of calves is affected by the same factor. Calves may be—and in a double-inoculated country almost invariably are—temporarily in a refractory condition due to the passive transference of anti-bodies in the milk of an immune mother. The passive immunity no doubt deteriorates as lactation advances and finally disappears within a few weeks after weaning. Double-inoculation of unweaned calves has always been considered unsatisfactory, and the rinderpest immune brand is not given to animals inoculated before weaning since a large proportion of them fails to react to double-inoculation, and again becomes susceptible after weaning has taken place. Croveri (1919), and Rabagliati (1928), have both pointed out the dangers inherent in this position, and Rabagliati has recently carried out experiments with a view to determining the efficacy of double-inoculation one month or more after weaning. Of 98 calves, all of which had been weaned for periods in excess of one month, Rabagliati was able to immunize 94 by the double-inoculation method. When tested on their immunity from 3 to 7 months after inoculation, four of the calves developed rinderpest, and one died as a result of the test inoculation of virulent blood, but there is no record of the occurrence of temperature reactions unassociated with symptoms of rinderpest in any of the calves. In the light of the present writer's experience a number of such reactions may have occurred. Rabagliati's figures for this particular experiment can with fairness be compared with the figures included in Table III. The animals inoculated in the Kenya experiment were from eight to twelve months old and the majority of them were weaned specially for the inoculation, many of them in fact within a few days of vaccination. Of the 90 animals tested three only developed rinderpest and in each case the attack was so mild that there was never any question that mortality might occur. All three cases of rinderpest occurred in the one class, type (2), which had been inoculated with a single dose of the weakest type of antigen, and the period elapsing between the vaccination and testing varied from twelve to more than sixteen months. The double-inoculation experiment therefore has advantages in both the age of the calves and the period between immunization and testing. The results, however, are without doubt in favour of the vaccination. When one takes into consideration this capacity of the vaccine to immunize refractory animals it is not unreasonable to hope that good results can be obtained from the vaccination of unweaned calves, and experiments to prove this point are now in hand.

DISCUSSION.

The advantages of a suitable rinderpest vaccine as indicated by the experiments are many, and there do not appear to be any corresponding disadvantages. A successful vaccine can be made that will immunize animals for periods in excess of fifteen months without the production of rinderpest, and with not more than about 3 per cent. of slight temperature reactions. During most of the writer's experiments at the laboratory susceptible animals were maintained in contact with vaccinated animals during the period following vaccination, and in no case was infection transmitted naturally by animals showing a febrile reaction as a result of inoculation with a partially-attenuated vaccine, although the blood of such reacting animals is infective. One may conclude therefore that the 3 per cent. of reactions expected in vaccinations of type (3) do not imply any risk

of spreading rinderpest by contact; further there is evidence that a completely-inactivated vaccine prepared in a weak concentration of formalin (1 in 1,500) will confer an immunity as great as that given by a lightly-infective type of vaccine prepared at a concentration of formalin 1 in 2,000. Confirmatory experiments on this point are now in progress. Vaccines prepared in formaldehyde do not transmit piroplasmosis, anaplasmosis, trypanosomiasis, or other blood-borne diseases to susceptible animals. The importance of this feature to a country where dipping has been only partially successful cannot be over-estimated.

Vaccination can be undertaken by the owner, and the rate at which it can be applied to large blocks of country far exceeds that at which double-inoculation can be carried out. Since no reactions are to be expected there is no reason to confine treatment of animals to those seasons of the year when they are in good condition. Although the figures given here constitute perhaps the first attempt to obtain reliable information as to the duration of the immunity conferred by vaccination, research in several countries is advancing rapidly, and within the next year or so we are likely to be in a position to apply vaccination to the problem of eradicating rinderpest in certain countries where it is at present enzootic.

With reference to the possible spread of rinderpest by game, experience suggests that in the absence of susceptible cattle game are not capable of keeping the disease alive for periods of more than a few months, and that in the presence of an entirely immune domestic animal population, rinderpest in game must rapidly die out. The introduction of rinderpest can be prevented by a comparatively short period of quarantine, and by the vaccination of all imported animals with distinctive branding. It might be necessary in the event of rinderpest being eradicated from a country to maintain a deep belt of vaccinated animals on any dangerous frontiers.

Efforts are being made to arrange for the application of this method to a fairly large area of country containing a large proportion of susceptible animals. All cattle within the area will be vaccinated with two doses of completely-inactivated vaccine. No double-inoculations will be carried out within the area and all animals imported will be immediately subjected to vaccination. Calves will be vaccinated soon after birth, and re-vaccinated at later date if it is found necessary. The immunity of the animals within the area will be renewed when experimental observations point to the necessity. If it is possible to maintain such an area free from rinderpest without game restrictions, and in the presence of double-inoculations and natural outbreaks of rinderpest on its borders, then undoubtedly the method must be applicable to the treatment of larger areas.

STATISTICAL NOTE BY A. WALTER, STATISTICIAN TO THE
CONFERENCE OF EAST AFRICAN GOVERNORS.

I have investigated the figures sent to me by Mr. Daubney, and find that for the first table the value of χ^2 given corresponds to a value of $p = .00001$. So that the odds are about 1 in 100,000 being due to chance.

In the case of the immunity tests in Table V where $\chi^2 = 21.75$, the value of $p = .00002$, the chances here being about 1 in 50,000.

It is useful to have this measure of the odds against these results, although they are so markedly significant in themselves that the actual measure is hardly necessary.

With reference to the third point, i.e., the probability that the results of testing samples will hold good for the remainder of the population, I have taken the animals of type (3), Table III, of which 132 untested animals still remain, and have calculated the probability curve on the basis of the hypergeometrical series. The probability ordinates together with the area are shown in the following table.

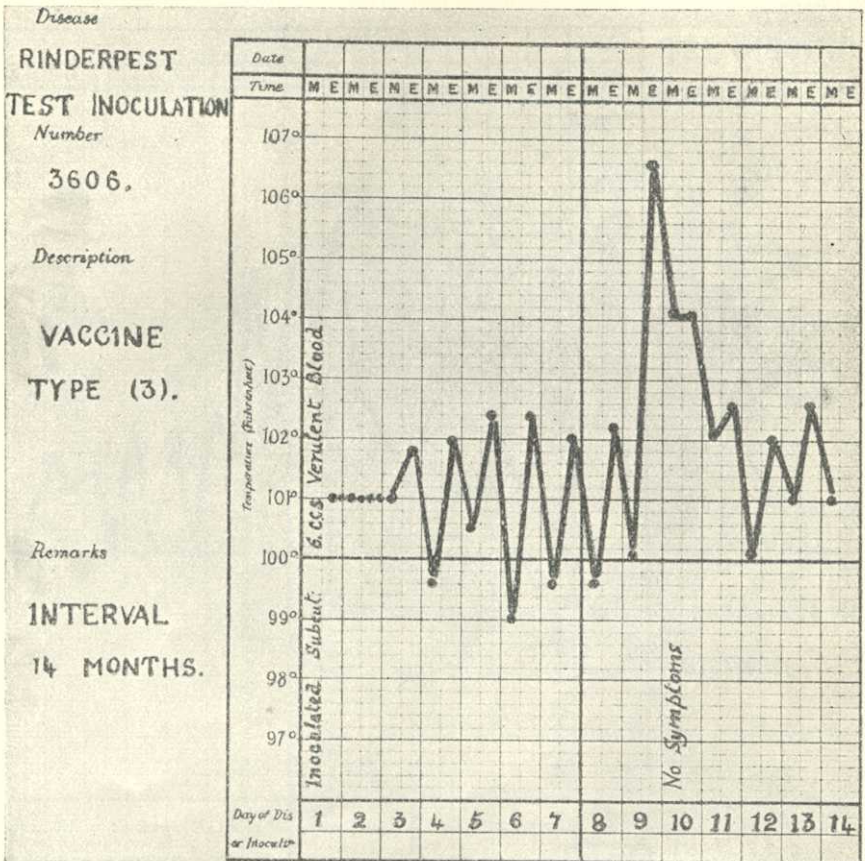
It will be observed that the highest probability occurs for 129 successes. 95 per cent. of the area falls between 113 and 132 so that if the whole of the remaining populations of 132 animals in this lot were examined it is probable that a very high percentage would be found immune.

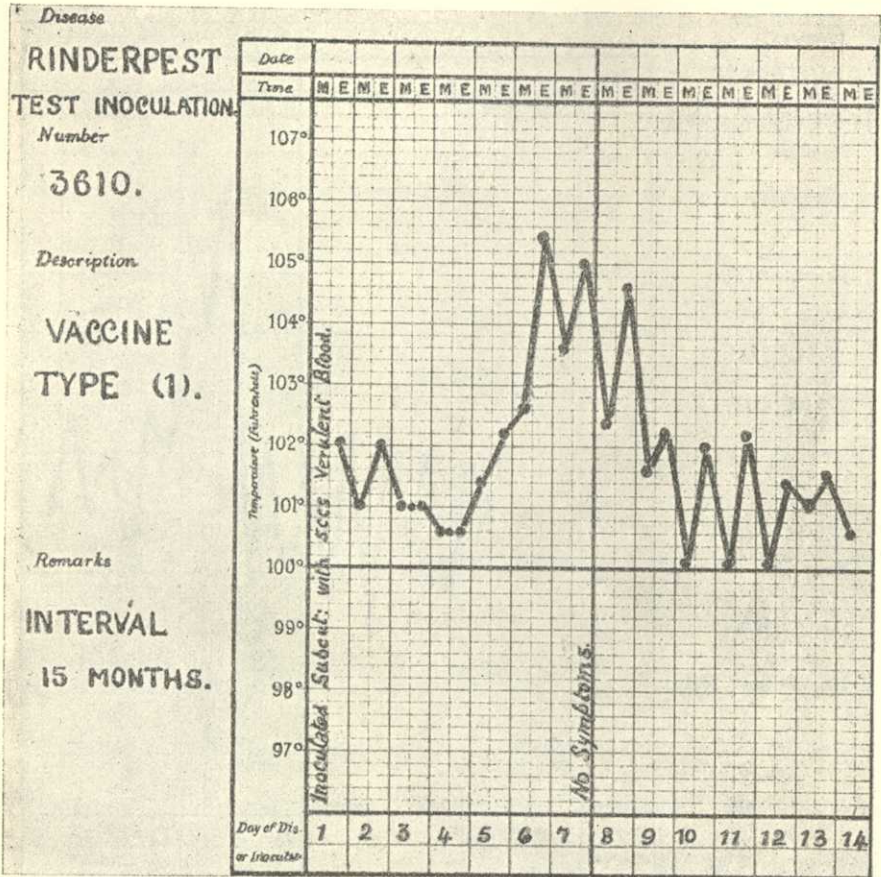
TABLE OF THE TERMS OF THE HYPERGEOMETRIC SERIES DERIVED FROM MR. DAUBNEY'S VACCINE IMMUNITY TESTS.

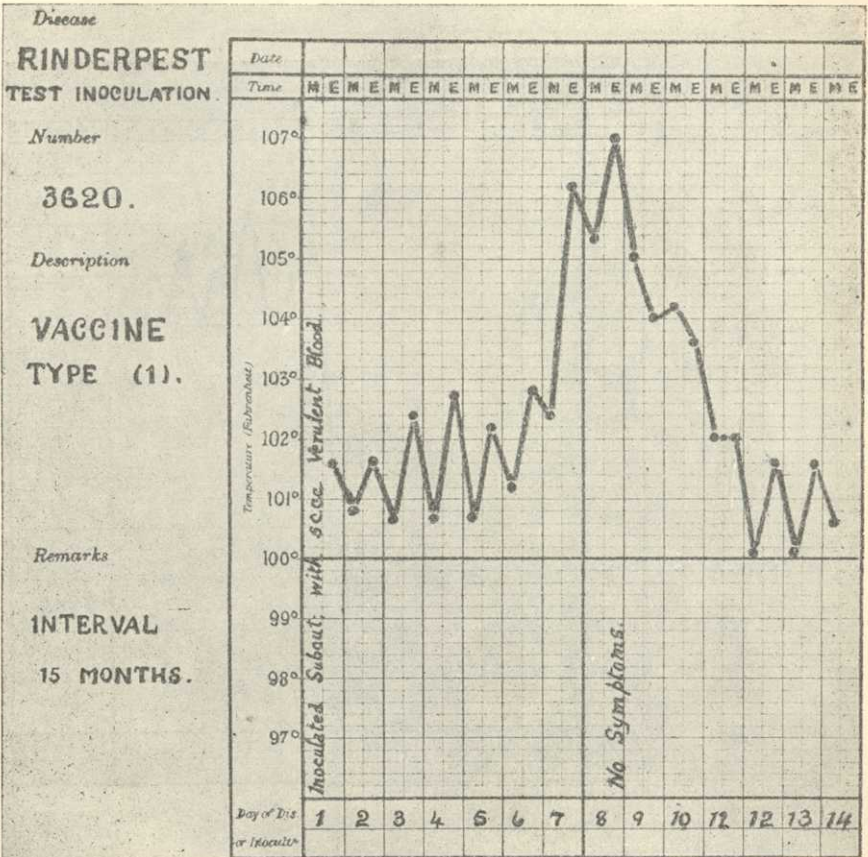
<i>Successes Less than</i>	<i>Probability Ordinates.</i>	<i>Area.</i>
100	.01037	.01037
100	.00028	.01065
101	.00037	.01102
102	.00048	.01150
103	.00063	.01213
104	.00082	.01295
105	.00106	.01401
106	.00137	.01538
107	.00177	.01715
108	.00227	.01942
109	.00290	.02232
110	.00369	.02601
111	.00467	.03068
112	.00589	.03657
113	.00740	.04397
114	.00924	.05321
115	.01150	.06471
116	.01423	.07894
117	.01752	.09646
118	.02143	.11789
119	.02605	.14394
120	.03145	.17539
121	.03767	.21306
122	.04472	.25778
123	.05258	.31036
124	.06104	.37140
125	.06988	.44128
126	.07861	.51989
127	.08648	.60637
128	.09234	.69871
129	.09492	.79363
130	.09049	.88412
131	.06694	.95106
132	.04894	1.00000

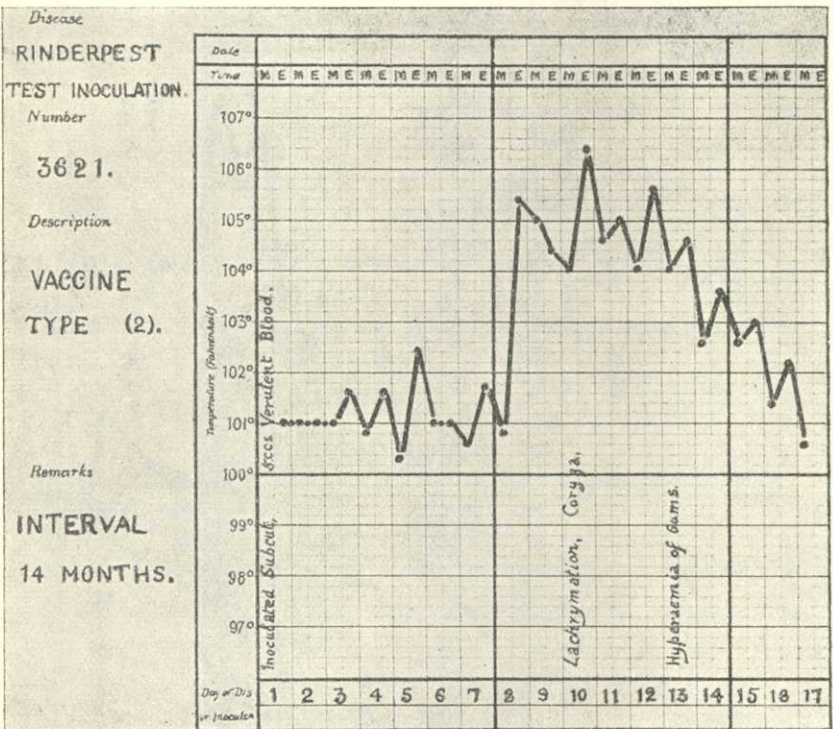
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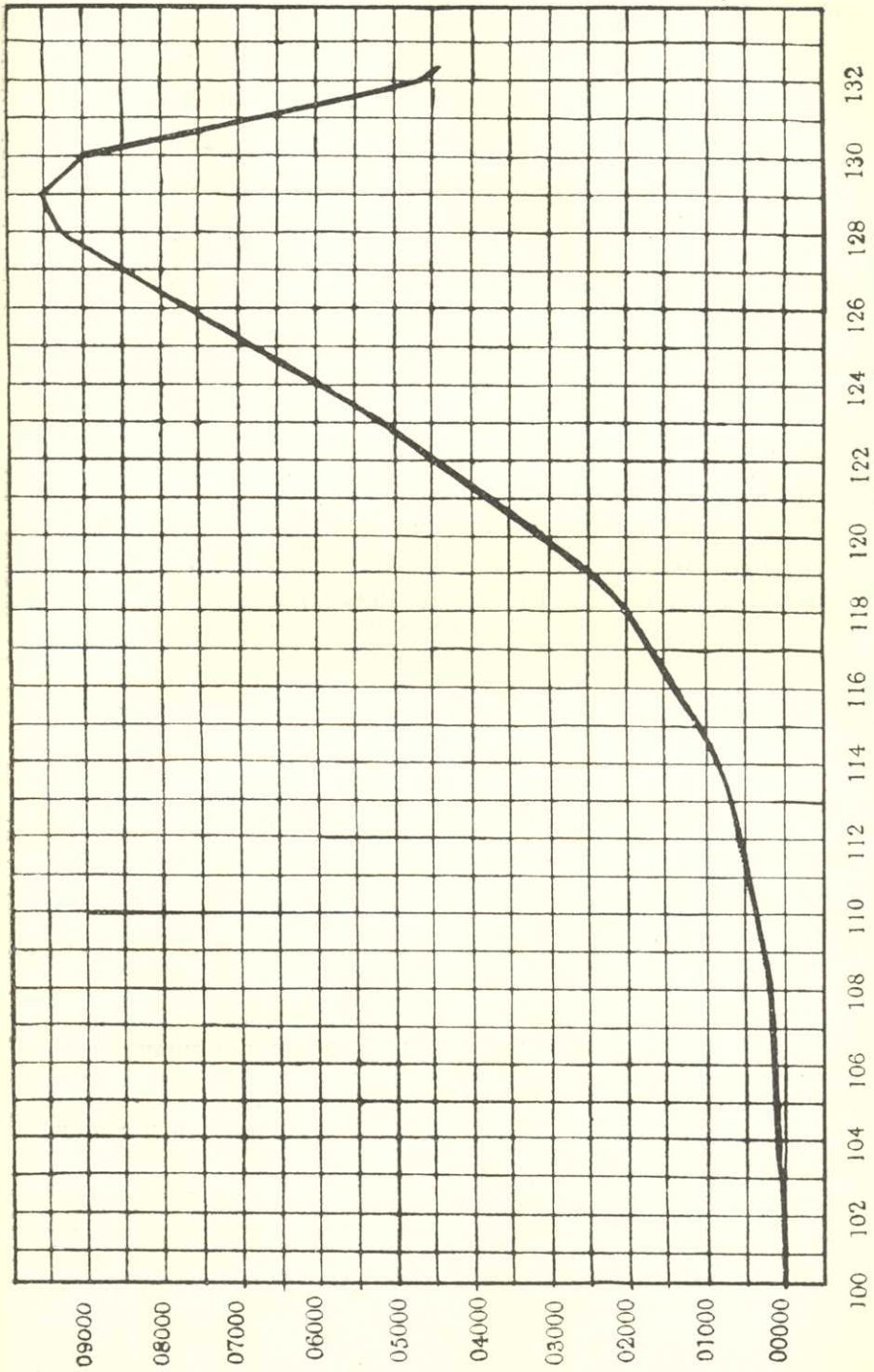
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CURVE ILLUSTRATING THE HYPERGEOMETRICAL SERIES DERIVED FROM MR. DAUBNEY'S IMMUNITY TEST.