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Host Adaptability of *Treponema Pallidum*.

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Since Bertarelli's discovery<sup>1</sup> that rabbits could be successfully inoculated with the *Treponema pallidum*, this animal has been widely employed in experimental syphilis. Bertarelli noted that takes became more constant after the second transfer of the organism through the rabbit and indicated the possibility of its adaptation to the new host. From then on, the majority of the published studies dealt with the variability of the incubation period, among them an excellent summary by Mulzer.<sup>2</sup> In general, most workers have confined their experimental work to the use of known strains, namely, the Truffi transferred to the rabbit in 1908, the Kuznitzki, the Mulzer, and the Nichols and Hough strains. According to Mulzer the Truffi, also known as the Kolle or Frankfurter strain, causes 100% takes after an incubation period varying from 3 to 4 weeks when injected intrascrotally or intratesticularly. Similarly, the strain of Nichols and Hough has undergone many passages through rabbits since its isolation. Bessemans and Vlaeyen<sup>3</sup> reported that corneal or scrotal scarifications were the least successful routes for the inoculation of rabbits with syphilitic material from man. However, for transplantations from rabbit to rabbit corneal and, above all, scrotal scarifications are the methods of choice. For primary isolations these authors preferred intrascrotal or intratesticular inoculations. This fact definitely indicates the readiness by which a certain tissue-resistance is overcome by a well adapted organism, and to a distinct localized immunity. Zinnser, Hopkins and McBurney also believe that localized immunity is possible and not dependent upon a generalized reaction on the part of tissues remote from the site directly involved in reaction with the invading treponemata.

The *Treponema pallidum* adapted to the rabbit does not lose its virulence for other susceptible animals or man. Uhlenbuth and

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<sup>1</sup> Bertarelli, E., *Centralbl. f. Bakt. Abt. I*, 1907, **43**, 448.

<sup>2</sup> Mulzer, P., *Handbuch der Haut. u. Geschlechtskr.*, **15**, No. 1, p. 290, Berlin, Julius Springer, 1927.

<sup>3</sup> Bessemans, A., and Vlaeyen, N., *Arch. Int. de Med. Exp.*, 1928-1929, **4**, 470.

Mulzer<sup>4</sup> have successfully inoculated monkeys, guinea pigs and goats with rabbit syphilitic material, and accidental infections of man from laboratory materials have been numerous considering the relatively few workers in this field.

All of our own (9) strains were isolated in this Institute from primary or secondary lesions of man and their incubation period (in the rabbit) varied from 26 to 84 days. In addition to these new strains we employed (4) older, standard strains, the Nichols and Hough, the Zinsser and Hopkins, obtained through the courtesy of Dr. W. Brown, the Chesney and Hanzlik strains secured through the kindness of Drs. A. M. Chesney and P. J. Hanzlik.

The incubation period of the 13 strains varied from 17 to 99 days. Bessemans and Vlaeyen reported a variation from 18 to 90 days for primary inoculations. For transplantations their periods varied from 32 to 47 days indicating a shortening of incubation periods following transfers.

We have employed a uniform technique, inoculating the animals intratesticularly with about 0.5 cc. of a suspension prepared from an aseptically excised testicle ground up with sterile sand in about 5 to 10 cc. of sterile saline. Massive doses were inoculated and careful attention was paid to avoid all possibility of aspecific infec-

TABLE I.  
Comparative Study of Incubation Period and Takes of 2 Groups (New and Old Strains) of the *Treponema pallidum*.

Strain No.	Year	No. inoculated	No. takes	Died before limit of incubation	No. survived for take	Incubation Time			Probable error †	% takes of living animals
						min.	max.	mean		
I	1929	49	23	8	41	21	60	30.91	1.07	56
II	1930	12	9	2	10	26	46	37.44	1.18	90
* III	1929	5	1	4	1	30	30	30.0	0	100*
* IV	1929	4	0	0	4	—	—	—	—	—*
V	1929	12	6	4	8	33	58	40.5	2.45	75
* VI	1930	7	1	1	5	24	24	24.0	—	20*
VII	1930	25	13	2	23	19	75	38.3	3.11	56
VIII	1930	13	6	2	11	25	78	44.0	4.79	54.5
IX	1929	69	32	25	44	23	99	40.2	1.62	72
Nichols and Hough	1913	29	23	3	26	17	43	26.13	1.10	88.4
Zinsser, Hopkins, Gilbert	1914	23	21	1	22	22	45	31.14	1.06	95.6
Chesney	1924	7	4	2	5	17	25	24.75	0.146	80.0
Hanzlik	1927	24	20	2	22	24	58	33.85	1.84	91.7

\* Not considered in series.

† Uhlenhuth, P., and Mulzer, P., quoted by P. Mulzer,<sup>2</sup> p. 265.

tions in the normal and infected animals since our problem was concerned with the cultivation of the *Treponema pallidum*. In all, 278 animals were used. The animals were kept in single cages and observed for at least 6 months.

Strains III, IV, and VI, were eliminated from our study because of the small numbers of animals used or the single takes obtained in the small series. Strain IV was extremely difficult to pass through rabbits and eventually was lost. The same is true for Strain VI. Strain VIII showed a large probable error in the group ( $\pm 4.79$ ) which in all probability is due to a late orchitis developed in one animal at the end of 78 days following inoculation, while the remainder of the series developed the disease in periods varying from 25 to 46 days.

The mean of incubation of the new strains varied from 30 to 44 days, while that of the older strains from 24.75 to 33.85 days. The mean of the maximum incubation time of the older strains almost coincided with the mean of the minimum incubation time for the younger groups. After statistical treatment both groups appeared to be homogeneous within themselves. The significance of the difference in means between the new and the older strains is seen in Table II.

TABLE II.  
Significance of Differences Between the Means of the New and Old Strains.

			Mean	Probable Error
New			37.52	$\pm 0.98$
Old			29.43	$\pm 0.83$
	D	$M_1 - M_2$	37.52 - 29.43	8.09
				$= 6.30$
	$PE_d$	$PE_{M_1}^2 + PE_{M_2}^2$	0.9604 + 0.6889	1.284
				%
				90.6
				62.9
				64.9

The ratio of difference between means and the probable errors of difference, 6.30, is more than sufficiently large to consider the difference in the means significant, and to warrant a comparison of incidence of takes between the 2 groups. An investigation of the significance of the difference between the group of old strains and the group of new ones, by the method of Fisher,<sup>5</sup> gave 4.03 as the value of which, for the number of degrees of freedom involved, is

<sup>5</sup> Fisher, R. A., *Statistical Methods for Research Workers*, 1928, p. 107. (2nd edition, Oliver and Boyd, London, Eng.)

definitely significant. This confirms the fact that the difference between the mean incubation periods of the 2 groups is real.

The incidence of takes by strains 1, 5, 7, 8, and 9 was 62.9%. Inclusion in this series of the unusually high number of takes in Group II (Table I) raises this figure to 64.9%, while the incidence of the older strains reaches 90.6%. The older strains, therefore, appear to be more consistently infectious for the rabbit than the newer strains.

*Conclusions.* A comparative study has been made between the infectivity of 2 groups of *Treponema pallidum*, 9 new and 4 older strains. The mean of incubation of the newer group varied from 30 to 44 days, while that of the older group varied from 24.75 to 33.85 days. Statistically, both groups appeared to be homogeneous in themselves and the incidence of takes for the newer strains was 64.9%, while that of the older strains 90.6%, a difference of 25.7%. These findings indicate adaptation of the organism to its new host and should be considered in all work in experimental syphilis.

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### A Species Limitation of an Enhancing Material Derived from a Mammalian Tumor.

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In an effort to differentiate the material derived from the Brown-Pearce rabbit tumor<sup>1</sup> from other enhancing materials it seemed desirable to know whether it would enhance various diseases and tumors, both in the same and in different species. To this end a series of experiments was made with a Bashford mouse carcinoma (No. 63).\* The experiments were distributed at approximately 6 weeks intervals between January, 1932, and January, 1933, each experiment consisting of 30 mice divided into 3 groups of 10. Enhancing material prepared from Brown-Pearce tumor tissue<sup>1</sup> and enhancing material prepared in an entirely similar manner from

<sup>1</sup> Casey, A. E., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 816; *J. Exp. Med.*, in preparation.

\* The experiments with the Bashford tumor were carried out in the laboratory of Dr. Jas. B. Murphy at his kind invitation. The other experiments on the enhancing material derived from the Brown-Pearce tumor were done in the laboratory of Dr. Wade H. Brown.