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NOTE ON THE RELATION BETWEEN LD50 AND AVERAGE TIME TO DEATH IN 25 STRAINS OF *H. PERTUSSIS*

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The values of the LD50 at weekly intervals for 8 weeks are shown in Table 5 (p. 254). Clearly these values vary with the time at which they were calculated. A ratio of 3 to 1 is about significant, judging from Kendrick's tests (1948), and the Table shows greater variations than this at different times. Nevertheless, whenever the LD50's are calculated they agree very well in the *order* in which they place the different strains. The coefficient of concordance, which would be unity for perfect agreement in order, is actually 0.85. Accordingly, the strains were classified into five groups of virulence as judged by the LD50 at 56 days, as follows: less than 1 million; 1 million and less than 5 million; 5 million and less than 25 million; 25 million and less than 125 million; more than 125 million.

Two questions needed answering: (a) Does the relative rapidity of killing at different doses differ significantly in different strains? (b) If so, are these variations from strain to strain correlated significantly with virulence as judged by the LD50? The answer to (a) was *Yes*, and to (b) *No*. The values of average

time of death among the dead were examined for some of their differences and ratios. Suppose these averages for doses 100, 10, 1 and 0.1 millions are denoted by x_1 , x_2 , x_3 and x_4 ; the following values and their standard errors were calculated for each strain:

$$\begin{aligned} d_1 &= x_2 - x_1, & r_2 &= d_2/l_2, \\ d_2 &= x_4 - x_1, & l_1 &= \frac{1}{2}(x_2 + x_1), \\ r_1 &= d_1/l_1, & l_2 &= \frac{1}{2}(x_4 + x_1). \end{aligned}$$

The strains showed significant differences in d_1 and d_2 and in r_1 and r_2 , but the average values of these quantities in the five virulence groups did *not* differ significantly. Further, there was no significant correlation between d_1 and d_2 , or between r_1 and r_2 . A high difference or ratio means that the strain kills *relatively* much more rapidly at the higher of the two doses compared. Table 1 shows the results in full.

Table 1

LD50 (millions)	Strains of <i>H. pertussis</i>	d_1	d_2	r_1	r_2
< 1	863	4.2	17.5	0.5915	1.2727
	L2	13.4	25.8	0.7090	1.0279
	1016	-2.5	16.4	-0.1832	0.7100
	1030	18.6	19.0	0.1273	1.1377
	1031	3.5	14.8	0.3955	1.0207
	1041	14.6	30.7	1.0355	1.3860
1 and < 5	888	2.9	13.6	0.5421	1.2710
	928	5.3	21.1	0.8760	1.5125
	962	34.5	23.2	1.0764	0.8788
	983	4.0	10.0	0.1739	0.3846
5 and < 25	894	4.0	7.0	0.6667	0.9333
	941	3.1	—	0.4960	—
	942	2.0	14.3	0.1575	0.7586
	978	15.2	-2.7	0.7876	-0.2609
	M6	21.4	17.8	1.0542	0.9622
	992	2.0	1.3	0.0952	0.0630
25 and < 125	M1	24.9	7.9	1.1555	0.6054
	M2	0	—	0	—
	907	—	16.7	—	0.4963
	910	28.4	32.1	1.0216	1.0826
	M5	—	32.0	—	0.8421
	947	-29.6	9.4	-1.8734	0.2663
	959	26.7	11.2	1.2624	0.8485
	993	-6.6	—	-0.2292	—
	L3	8.8	-7.7	0.2543	-0.2922

Evidently the strains do show differences in relative rapidity of killing at different doses, but the precise nature of the differences is not very clear.

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