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Growth and Viability of *Cryptococcus hominis* at Mouse and Rabbit Body Temperatures.

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Mice were readily infected with strains of *Cryptococcus hominis* isolated from human cases of torula meningitis, subcutaneous tumor, and generalized infection.[1] Death occurred following a regular increase in the number of viable yeasts in the mouse tissues, especially in the brain and lungs. On the other hand, rabbits resisted infection and the number of viable yeasts in the tissues decreased regularly, even when very large doses of cryptococci were given intravenously. Mice and rabbits each were found to produce only a very low grade acute cellular reaction when the yeasts were injected intraperitoneally.[2]

When the normal body temperatures* of mice were compared with those of rabbits and especially when it was noted that mice failed to produce fever with experimental cryptococcus infection, whereas the temperatures of injected rabbits readily rose to 105°-107°F (40.6-41.7°C), the writer decided to determine if the growth and viability of *C. hominis* at rabbit and mouse body temperatures was significantly different.

Six strains of group III cryptococci (Benham grouping[3]) which were isolated from human cryptococcus infections during the past 5 years were inoculated into dextrose veal infusion broth (pH 7.0) and grown at 99°F (37.3°C), 101°F (38.3°C), 103°F (39.4°C), 105°F (40.6°C), and 107°F (41.7°C). At the higher temperatures fewer organisms were produced and viable cells (determined by plating in Sabouraud's dextrose agar) decreased in number. The effect on the number of viable cells of one of the strains of *C. hominis* is shown in Table I.

At 105°F (40.6°C) viable cells had decreased in number after 3

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[1] Report in preparation.

[2] Kuhn, L. R., *Arch. Path.*, 1939, **27**, 803.

* The mean of 546 recordings of the body temperatures of normal mice was 99.1°F. The temperatures ranged from 95.5° to 101.5°, with 75% of the recordings between 98° and 100.5°. The mean of 334 recordings of the body temperatures of normal rabbits was 103.15°F. The temperatures ranged from 102.25° to 104.25° with 87% of the recordings between 102.75° and 103.5°.

[3] Benham, R. W., *J. Inf. Dis.*, 1935, **57**, 255.

TABLE I.
Effect of Temperatures Between 99°F (37.3°C) and 107°F (41.7°C) on Number of Viable Cryptococci in Broth Cultures.

Time in days after inoculation	Mean* of the number of viable yeasts per mm³ in 3 tubes incubated at each temperature				
	99°F† 37.3°C	101°F† 38.3°C	103°F† 39.4°C	105°F† 40.6°C	107°F† 41.7°C
0	570	630	583	567	593
½	1713	1173	650	280	45
1	2707	2163	723	151	13
2	4033	2767	667	42	2
3	4943	2620	458	5.6	0.04
4	5680	2253	246	0.80	0.0036
5	6263	1750	87	0.03	0‡-0.001
6	6723	643	15	0.0014	0
7	7267	224	2	0	0
8	7480	58	0.09	0	0

Each tube contained 5 cc of dextrose veal infusion broth and was inoculated from a similar 24-hour broth culture.

* The greatest variation from the mean in any one of the 3 tubes was 5% of the mean.

† The temperature of the water bath varied 0.25°F above and below the temperature given.

‡ Two tubes were sterile, the third had 1 viable yeast per cc of broth.

hours' incubation, at 107°F (41.7°C) they decreased within an hour and only 2.5% survived at the end of 24 hours.

The total number of yeast cells was also counted (hemacytometer) in tubes of dextrose veal infusion broth and Sabouraud's dextrose broth incubated at 22°, 29° and 36°C. With each strain of cryptococcus employed samples examined from 1 to 5 days after inoculation showed that the cell count was higher in the tubes incubated at 29°C than in the 22° or 36°C tubes, and higher in the 22°C than in those incubated at 36°C. The optimum temperature for these organisms appears, therefore, to be below the normal body temperature of either the mouse or the rabbit.

In attempting to account for the resistance of the rabbit to experimental cryptococcus infection, the high normal and fever temperatures of this animal must be considered. Experiments on the effect of alteration of body temperature of experimental animals on their resistance to these organisms are now in progress.