THE EFFECT OF CATECHOL ON MURINE LEPROSY IN C_3H MICE

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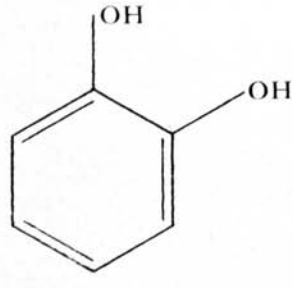
During the course of a study of surface actions of dyes on mycobacteria, it was suggested that the action of phenols might in some way be directly related to an enol-chelation involving the bacterial surface. The action of phenol in the acid-fast staining reaction leaves undetermined the question as to whether the action is directed toward the dye, or toward the material in the organism which accepts the dye. The experiment reported here attempts to show a relationship between a phenol and bacterial organisms *in vivo*, without the question of dye chemistry being involved.

Catechol, 1,2,benzenediol, or pyrocatechol, because of its ready solubility in water and absence of production of local reactions, was a convenient phenolic agent to use experimentally with murine leprosy *in vivo*.



Catechol, unlike phenol, occurs in nature in many plants and some animals. Its toxicity for mice showed an MLD at about 0.15 gm./kgm. in the strain of C_3H mice used in the experiment. At 0.20 gm./kgm. all mice were killed within a few minutes, dying of convulsive seizures. Just below the MLD all mice survive and remain symptom-free. There is a sharp endpoint. Consequently, the dosage selected was .09 gm./kgm., just under two-thirds of the dose required to kill 50 per cent of the animals. A small group of otherwise normal animals appeared to develop no tolerance to catechol, on repeated injection, and there were no deaths in the experimental animals.

EXPERIMENTAL

Sixty C_3H mice, aged 8-10 weeks, were inoculated intraperitoneally with 0.5 cc. of a 1:50 fresh suspension of a leproma of the Hawaiian strain of *M. leprae murium*. The mice were housed 5 to the cage, using mostly litter mates per cage, and were weighed at two-week intervals. They were divided into four groups of 15 each:

Group A: Untreated, controls
Group B: Treatment begun the day before inoculation
Group C: Treatment begun 30 days after inoculation
Group D: Treatment begun 60 days after inoculation

Catechol was given subcutaneously three times weekly, the dosages being increased only after a 20 per cent weight increase in any one group. The actual strengths of the solutions varied from 0.413 to 0.594 per cent, having been calculated for a 0.5 cc. inoculum of the catechol solution.

The experiment was terminated 90 days after inoculation of the animals with the murine bacillus, and autopsies were performed.

RESULTS

Except for one of the biweekly weighing periods, gain in weight was steady for all groups. It is believed that a watering deficiency over a week-end was responsible for this. No animals were lost, and all curves returned promptly to expected levels. The average gains in weight for the several groups at the end of the experiment are shown in Table 1.

TABLE 1.—*Average weight gain per mouse, in grams.*

Group	Beginning	End	Net Gain	Treament
Group A	25.8	39.9	14.1	None
Group B	25.1	31.3	6.2	90 days
Group C	21.4	32.6	11.2	60 days
Group D	22.3	35.1	12.8	30 days

At an early stage it was observed by the technicians handling the animals that catechol had a visible effect, neurophysiologically. The animals receiving catechol were much more alert, "jumpy," and sensitive to outer stimuli than before. It was as though they approached the normal status of wild mice as to activity, as compared with the extreme tameness of the controls.

All mice survived and were in good health at the end of the experiment, although a few had lost some body hair from abdominal areas. This occurred strikingly in two of the control group, and is therefore unrelated to the experimental procedure.

At autopsy no significant lesions were found in the pelvic fat, so this feature could not be used as a criterion of effect of the treatment. A few minute fibrous foci were routinely found in all groups in the lesser omental area, too small for comparison. There was no peritoneal reaction. It is speculated that this was partly the effect of the use of a finely homogenized inoculum, which was rapidly absorbed.

The livers showed murine leprosy in all groups, and all livers were excised and weighed to 10 milligrams. These weights, and other findings, are shown in Table 2.

The percentages of liver occupied by lepromas given in Table 2 were estimated from histologic sections of the individual livers. The appearance of the livers grossly corresponded to the degree of infection. There were two massively infected livers (over 50%) in the 90-day animals, one in the 60-day group, and none in the 30-day group. One control animal showed no lesions. The variations within the groups were not striking. The amount of body fat corresponded to the total weights of

the animals, there being a marked difference between the adipose controls and the 90-day animals.

TABLE 2.—*Weights of livers and of lepromas, in grams.*

Observation	Group and duration of treatment			
	A None	B 90 days	C 60 days	D 30 days
Liver weights of individual animals	2.22	2.72	2.85	3.20
	2.18	3.18	2.92	3.72
	2.52	3.20	3.52	3.36
	1.91	2.80	2.65	3.95
	2.00	3.40	2.55	3.39
	1.80	3.25	2.50	3.40
	2.19	2.65	3.30	3.09
	2.10	2.80	2.77	3.52
	1.60	4.76	2.78	3.51
	2.08	3.27	2.68	3.38
	2.42	2.89	2.80	3.99
	1.59	3.38	3.12	3.47
	2.08	3.09	2.71	3.50
	1.50	2.82	3.75	2.79
	2.71	2.81	2.85	3.15
Total	30.9	47.02	43.75	51.42
Average	2.06	3.13	2.92	3.43
Liver weight in percentage of body weight	5.16	10.01	8.95	9.77
Percentage of liver occupied by lepromas	6.1	12.2	6.6	6.0
Average weight of liver lepromas per animal (gm.)	.126	.384	1.92	.205

DISCUSSION

Evidently catechol has a significant effect on weight, beyond the expected result from the effect of murine leprosy. Even in the 90-day animals the heaviest infections would scarcely account for the limited body growth. It is possible that this is related to the overactivity of the animals.

Repeated catechol administration produces some liver enlargement, apart from the lepromas present. This was noticeable microscopically in terms of larger centrolobular areas resulting in part from some sinusoidal distention.

There was no significant difference between the groups treated for the two shorter periods. In these there was a 50 per cent increase in the amount of lepromatous tissue present, and this was nearly doubled in the 90-day treated animals to a total three times that of the controls.

Although not systematically analyzed, lesions of the spleen grossly correspond to those of the liver, and the liver lesions are presumed to be

representative of the generalized infection of the experimental animals. The histologic character of the lesions was similar in all groups.

CONCLUSION

Catechol administered to mice infected with murine leprosy enhances the development of the parasite, tripling the degree of infection in 90 days. This suggests the possibility of a direct action upon the organism, promoting its metabolism. An increased alertness of the treated mice suggested some "epinephrine" effect.

CONCLUSION

El catecol administrado a ratones infectados con lepra murina refuerza el crecimiento del parásito, triplicando en 90 días la intensidad de la infeción. Esto sugiere la posibilidad de un efecto directo sobre el microbio, fomentando su metabolismo. Un aumento de la vivacidad en los ratones tratados sugirió algún efecto "epinefrínico."

CONCLUSION

L'administration de catechol à des souris infectées avec la lèpre murine exalte le développement du parasite, triplant le degré d'infection en 90 jours. Ceci suggère la possibilité d'une action directe sur l'organisme, consistant en une accélération du métabolisme. L'agitation plus marquée des souris traitées a suggéré quelque effet "epinephrine."

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