PRELIMINARY AND SHORT REPORT

FAILURE OF STILBAMIDINE TO ARREST EXPERIMENTAL BLASTOMYCOSIS IN MICE*

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Attempts at treatment of North American blastomycosis have been rather unsatisfactory in the past and the introduction of such potent drugs as propamidine and stilbamidine offered promise. In this connection, we have encountered no experimental work except Heilman's paper (3) on the effects of stilbamidine in blastomycosis in mice. Our own work was concluded prior to the publication of this paper.

MATERIAL AND METHODS

White mice of the same breed and of an average weight of 20 grams were inoculated intravenously with ground mycelial phase of *Blastomyces dermatitidis*. Care was taken to shake the inoculum suspended in saline frequently in order to prevent sediment formation. Twenty-one mice were injected and subsequently separated into 2 groups. With 10 animals serving as controls, eleven mice were given stilbamidine (2 milligrams per kilogram body weight) 8 days after inoculation. The drug was administered each day in a single subcutaneous injection. The dosage was selected as proportionate to that recommended for man. All animals died spontaneously except the last control mouse which was killed after 61 days. Stilbamidine was used immediately after mixing and the solution was kept from any undue exposure to light.

RESULTS

Gross inspection and histologic examination of the lungs revealed blastomycotic foci in all instances. The lesions were classified as "spot-like", "moderate" and "massive" involvement and the results are represented in Table 1. The disease was not arrested in any instance up to a maximum of 17 days of treatment and the extent of the lung lesion was obviously related to time between inoculation and death, rather than length of treatment.

DISCUSSION

The treatment of chronic infectious diseases can be evaluated clinically only by a large series of observations. Since blastomycosis is a rather uncommon disease, it seems obvious that the evaluation of controlled experimental treatment in animals will be more conclusive in determining the efficacy of one or another agent. From our experience, we have concluded that no beneficial effect may be anticipated using a single daily dose of 2 milligrams per kilogram body weight of stilbamidine in mice. The very much larger dose Heilman (2) used seems to benefit the animals, but the objection to such dosage is apparent. In the animals which showed improvement, 2.5 to 12.5 times the level considered safe in human beings was used. Potential toxicity of the drug cannot be lightly considered since Cohen (1) has observed 2 cases of hepatic necrosis after stilbamidine therapy in men. We have experienced an identical case and know from Dr. M. L. Furcolow about at least one more such lethal accident.

Snapper (6) has stated that stilbamidine is too toxic to be used in man and places his faith in 2-hydroxy-stilbamidine. It seems advisable to warn the profession to use stilbamidine with the greatest caution. Trigeminal lesions seem to occur with great frequency and at least 4 cases of lethal necrosis of the liver can be attributed to the drug.

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Received for publication December 29, 1952.

The temporary clearing of skin lesions in blastomycosis as reported by Schoenbach (4, 5) has been observed with many therapeutic regimens and indeed may even occur spontaneously. A follow up study of years will be necessary before the benefits of stilbamidine treatment can be proven.

TABLE 1

Results of treatment of mice inoculated with mycelial phase of blastomyces dermatitidis

DAYS AFTER INOCULATION	ANIMALS DEAD ACCORDING TO DAY				
	Treated animals			Controls	
	Number	Days of Treatment	Character of lesion	Number	Character of lesion
12	1	4	Not examined*		
13	3	5	Spot-like		
14				1	Not examined*
15	2	7	Spot-like		
16				1	Moderately severe
18				1	Not examined*
20				1	Moderately severe
20				1	Extensive
22				3	Extensive
23				1	Extensive
26	1	17	Extensive		
28	1	17	Extensive		
30	1	17	Moderately severe		
32	1	17	Extensive		
36	1	17	Extensive		
61				1	Moderately severe

* Eaten by mice in same cage.

SUMMARY

Two milligrams per kilogram body weight of stilbamidine given in a single daily subcutaneous injections to mice did not inhibit the development of severe lethal pulmonary blastomycosis in mice.

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