pressive when compared with the results obtained under the same conditions with 4,4'-diaminodiphenylsulfone.

Effects on the blood. The only observations made on the changes in the blood of the 4 groups of animals were limited to determinations of hemoglobin.§ When the animals were killed 60 days after infection specimens of blood were obtained by cardiac puncture from 3 of the groups. The results expressed in grams of hemoglobin per 100 cc of blood are as follows: Group 1, untreated controls, 13.3; Group 2, treated with 4,4'-diaminodiphenylsulfone, 10.2; Group 3, treated with 1% of 2,4'-dichlorobenzophenone by weight in the feed, 11.2. If one assumes that the average concentration of hemoglobin for normal guinea pigs is 14 to 15 g per 100 cc of blood it is evident that neither drug reduced the amount of hemoglobin to critical levels.

Blood concentrations of the drugs. When the experiment was terminated the concentration of 4,4'-diaminodiphenylsulfone in the animals in Group 2 ranged from 1.8 to 5.7 mg per 100 cc of blood, the average being 4.1 mg. No determinations were made concerning the concentration in the blood of 2,4'-dichlorobenzophenone. We are not aware of practical methods whereby this can be accomplished.

Results of splenic cultures. Among the 10 spleens cultured for tubercle bacilli from the group of untreated controls acid-fast bacilli were obtained from 9. Seven splenic cultures were made from the group that received 4,4'-diaminodiphenylsulfone; the results were negative for 5 and positive for 2. Eight spleens were cultured from the animals in Group 4 (1% of 2,4'-dichlorobenzophenone by weight of the feed) and acid-fast bacilli were obtained from each.

Summary and conclusions. The effect of 2,4'-dichlorobenzophenone on experimental tuberculosis of guinea pigs was studied. Although 4,4'-diaminodiphenylsulfone was capable of exerting an impressive inhibitory effect, the chlorine derivative of benzophenone did not retard or influence favorably the course or character of the disease as exemplified among the animals in the untreated or control group. The following conclusions are drawn: 1. Favorable bacteriostatic results *in vitro* of chemical compounds against tubercle bacilli are not necessarily indicative of favorable results in experiments *in vivo*. 2. 4,4'-diaminodiphenylsulfone under the conditions imposed proved capable of combating a tuberculous infection rather satisfactorily. 3. The one chlorine derivative of benzophenone studied proved ineffective in altering the expected course of the disease.

§ The hemoglobin values were determined by the Cenco-Sheard-Sanford photelometer.

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Effect of Some Chemicals, Which Affect Smooth Muscle Contraction, on Ciliary Activity in *Paramecium*.

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Mast and Nadler,[1] Merton,[2] Oliphant[3] and others have shown that monovalent cation salts and hydrates induce reversal in the direction of the effective beat of the cilia in protozoa while, with few exceptions, bi- and tri-valent cation salts and hydrates do not. Similar observations have been made regarding ciliary reversal in the metazoa, and the reproductive cells of plants and animals have been observed to swim backward.

1 Mast, S. O., and Nadler, J. E., *J. Morph. and Physiol.*, 1926, **43**, 105.

2 Merton, H., *Biol. Zentralbl.*, 1935, **55**, 268.

3 Oliphant, J. F., *Physiol. Zool.*, 1942, **15**, 443.

Alverdes,[4] Worley[5] and others have also shown that in fragments of ciliated protozoa the cilia continue to beat as long as they are connected with a fragment of cytoplasm. Such ciliated fragments have also been observed to reverse direction of ciliary beat in response to environmental change and this suggests that cilia here are automatic in their activity and that alterations in ciliary behavior are of an extraneous nature. Furthermore it is now generally agreed that the fundamental phenomena of protoplasmic contractility are essentially alike for pseudopodial movement, ciliary activity and muscular contraction, and that a theory which will adequately explain one will doubtless be applicable to the others.[6-8] However the demonstration of similarity between various forms of cellular movement is by no means complete.

From these observations and assumptions it would be expected that substances which profoundly affect cellular movement in populations of smooth muscle cells would also profoundly affect ciliary activity, possibly inducing ciliary reversal. It is the object of this investigation to explore the possibility of such a similarity in behavior of ciliated and smooth muscle cells in response to chemical agents in the environment, with a view to contributing to the analysis of chemical and physical factors involved in protoplasmic contractility.

Methods. Paramecium multimicronucleatum was used because of its size and the readiness with which it lends itself to culture and experimentation. In testing the effects of chemical agents on ciliary activity paramecia were first thoroughly washed and adapted to a balanced salt solution. 2.5 cc of solution to be tested were put into a modified Columbia culture dish on the stage of a dissecting binocular microscope. One of the washed paramecia was taken up in a capillary pipette and put into the test solution. The specimen was then observed continuously until the end of the experiment and if ciliary reversal occurred its duration was measured with a stop watch. This was repeated with other specimens as often as was desired and ciliary reversal was only recorded as having occurred if the animals actually swam backward for a time readily measurable with a stop watch. No experiments were actually performed on smooth muscle cells, it being believed that the action on them of the chemicals used is sufficiently well established.

*Experimental results.** The results of an extensive series of experiments are summarized in Table I. In the first column are listed the different chemicals tested. The second column shows the range of concentrations over which the chemicals were tested. It is not practicable or particularly instructive to list each concentration investigated. In the third column is given the ciliary response to each chemical. It was observed that the behavior was not the same in all instances, even with substances inducing ciliary reversal; and the duration of the initial period of ciliary reversal, which was often followed by recovery and subsequent reversals, varied greatly in the different chemicals. It is not possible to summarize the detailed response in each solution; the third column only indicates qualitatively the nature of the ciliary response. In general, duration of ciliary reversal varied directly with the concentration of the chemical inducing it.

Discussion. The results show that those substances which induce violent contractions in smooth muscle cells regardless of innervation also induce reversal in direction of the effective beat of the cilia of *Paramecium.*

[4] Alverdes, F., *Studien Infusorien uber Flimmerbewegung Lokomotion und Reizbeantwortung,* 1922, Berlin, 123s.

[5] Worley, L. G., *J. Cell. and Comp. Physiol.,* 1934, **5**, 53.

[6] Hartmann, M., *Allgemeine Biologie,* 1933, Jena, 792s.

[7] Gray, J., *Ciliary Movement,* 1928, Cambridge, 162 pp.

[8] Gray, J., *Experimental Cytology,* 1931, Cambridge, 516 pp.

* The author is indebted to the Department of Physiology, The Lane Hospital, and Dr. E. L. Tatum for supplying most of the chemicals used in this investigation.

TABLE I.
Effect of Increase in Concentration of Various Chemicals in the Environment on Reversal in Ciliary Action in *Paramecium*.

Substance tested	Range of concentrations*	Duration of initial ciliary reversal†	pH‡
$BaCl_2$	M/250-M/500,000	1.0-2.5 min. in optimum higher concentrations	5.5-6.5
$Ba(OH)_2$	M/300-M/500,000	1.0-3.0 min.	7.5-10.5
Physostigmine sulfate	M/250-M/1,000	20-30 sec.	5.8-6.8
Physostigmine salicylate	M/100-M/1,000	25-40 "	5.9-6.5
Triturus embryo toxin	1:50 to 1:1,000	40-60 "	6.3-7.2
Novocain (procain hydrochloride)	0.5% to 0.0001%	0.5-1.5 min.	7.2-7.5
Colchicine	M/150 to M/5,000	3.0-5.0 sec.	7.0-6.5
Papaverine	1:20,000 and lower	Reversal (Hopkins)[9]	7.8[9]
Morphine sulfate	1:500 and higher	" "	
Codeine sulfate	1:500 " "	" "	

* Atropine sulfate, choline, acetyl-choline (bromide), nicotine sulfate, histamin (dihydrochloride), histidine, strychnine sulfate and nitrate, and caffein citrate were tested in concentrations from those immediately lethal to those of such dilution as would induce no or only a very weak shock reaction and in no concentration of any of them was there ciliary reversal. In histamine there were a series of avoiding reactions in which the reversal phase was less than a second. Avoiding reactions did not occur in other solutions and while behavior was not the same in all, typically, there was a marked increase in rate of forward locomotion, with sudden changes in direction of movement, lasting several minutes and often followed by subsequent shock reactions.

† Initial reversal is often followed by recovery and subsequent reversals. Range rather than averages are indicated.

‡ H-ion concentration was sometimes adjusted by addition of sodium carbonate or other substances.

This is certainly true for the barium compounds and for physostigmine; and with the probable exception of papaverine the narcotics used by Hopkins (and novocaine also), in concentrations inducing ciliary reversal, produce violent contractions of smooth muscle regardless of innervation. The action of colchicine on smooth muscle may not be sufficiently well established to warrant comparison and only preliminary studies have been made on Triturus embryo toxin (extracted from eggs of Triturus, see Tatum *et al.*),[10] however, there are indications that they too induce contraction in denervated smooth muscle. Those substances tested which relax smooth muscle or act on smooth muscle through the nervous system do not induce ciliary reversal. Histamine may be an exception and marked avoiding reactions were observed in histamine.

These results are empirical, however they do further suggest that the chemico-physical changes involved in ciliary activity and smooth muscle contraction may be fundamentally alike. It has been suggested by Mast and Nadler[11] and Oliphant[12] that ciliary reversal is associated with, among other factors, differential absorption of cations and an increase in cytoplasmic viscosity. Hopkins,[13] without having made actual measurements, attributes the action of the narcotics to volume changes through uptake or loss of water.

These experiments further suggest that protozoa may offer more satisfactory material than populations of smooth muscle cells for the analysis of chemico-physical factors involved in protoplasmic contractility. They are large, easily handled, single cells may be studied, and it is possible to obtain any desired quantity of experimental material whose genetic and environmental conditions may be satisfactorily standardized and so critically studied.

[9] Hopkins, H. S., *Am. J. Physiol.*, 1922, **61**, 551.

[10] Horsburgh, D. B., Tatum, E. L., and Hall, V. E., *J. Pharm. and Exp. Therap.*, 1940, **68**, 284.

[11] Mast, S. O., and Nadler, J. E., *loc.* cited.

[12] Oliphant, J. F., *loc.* cited.

[13] Hopkins, H. F., *loc.* cited.