presented suggesting that the effect of Radon ointment applied to the skin of men and animals is: (1) To produce active hyperemia. (2) To increase lymph formation and lymph flow without appreciably increasing capillary permeability to colloids. (3) It is suggested that the therapeutic effect of Radon ointment may be apparent in these cases where lymph flow is diminished, perhaps due to partial block. Evidence is offered suggesting that lymph flow is diminished in a limb that has, in the past, been exposed to excessive x-ray irradiation. Also, the result of treating acute lesions thought to represent partial lymphatic block following penicillin injections is described, with results that are suggestively good although the series is too small for absolute certainty.

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Effects of Glutathione and Thioglycollic Acid on Acid-Production by *Lactobacillus arabinosus* in Presence of Atabrine.

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The action of atabrine as a competitive inhibitor of certain enzyme systems has been investigated by Wright and Sabine[1] and Haas.[2] The influence of different types of diets upon the toxicity of atabrine for various laboratory animals has been studied by several groups of workers, and a recent article by Siegel, Mushett and Emerson[3] reviews the contributions in this field.

Silverman and Evans[4] reported on the effects of spermine, spermidine, and other polyamines on the growth inhibition of *Escherichia coli* and certain soil organisms by atabrine. These organisms are capable of growth on an inorganic salts-glucose medium and atabrine bacteriostasis is relieved by spermidine. On the other hand, they observed that atabrine bacteriostasis produced in soil organisms with complex nutrient requirements is not relieved by spermidine and related polyamines.

The purpose of this paper is to present data respecting the response of the *Lactobacillus arabinosus* (an organism with relatively complex nutrient requirements) to atabrine with and without the addition of glutathione and thioglycollic acid to the medium.

Materials and Methods: A strain of *Lactobacillus arabinosus* 17-5 was used. This was supplied by Dr. Jerald G. Wooley of the Division of Physiology, National Institute of Health. The procedure for growth of stock cultures and preparation of culture for inoculation was that of the U. S. Pharmacopeia,[5] using the technics employed by the Food and Drug Administration. The basal medium and stock solutions were that of the U. S. Pharmacopeia for nicotinic acid assays[5] except that 0.25 g of bactodextrose, 0.20 g of sodium acetate and 0.5 μg of nicotinic acid were added to each tube, *i.e.*, 10 ml final volume.

A distilled water solution of C.P. atabrine dihydrochloride dihydrate (2.0×10^{-3}M) was added to the tubes in varying amounts in such a range that minimum and maximum bacteriostatic effects were demonstrated. Comparable tubes were set up which contained distilled water solutions of glutathione, Merck, or thioglycollic acid practical, Eastman, in a final concentration of 1.6×10^{-3} molar. In these experiments the pH of the medium was not altered by the addition of

[1] Wright, C. I., and Sabine, J. C., *J. Biol. Chem.*, 1944, **155**, 315.

[2] Haas, E., *J. Biol. Chem.*, 1944, **155**, 321.

[3] Siegel, H., Mushett, C. W., and Emerson, G. A., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 157.

[4] Silverman, M., and Evans, E. A., *J. Biol. Chem.*, 1944, **154**, 521.

[5] *U. S. Pharm.*, XII First Bound Supplemeent, 1943.

TABLE I.
Percent Inhibition of Acid Production by *Lactobacillus arabinosus* in the Presence of Atabrine Alone, Atabrine + Glutathione, and Atabrine + Thioglycollic Acid.

Molar concentration of atabrine in tube	% inhibition of acid production		
	Atabrine alone %	Atabrine + glutathione %	Atabrine + thioglycollic acid %
0	0	0	0
1.0×10^{-4}	24	27	6
1.2×10^{-4}	42	28	14
1.6×10^{-4}	91	50	29
2.0×10^{-4}	100	85	56
2.4×10^{-4}	98	98	90

glutathione and thioglycollic acid. The amount of bacterial growth after autoclaving, inoculation and incubation for 66 hours was measured by titrating each tube for acid production with 0.1 N NaOH. A blank was always run with all the ingredients but no inoculation; the amount of 0.1 N NaOH required for this blank was routinely subtracted from the titration values of the comparable inoculated tube. One hundred percent growth was the value obtained in the control tube which contained no atabrine and was inoculated. The percent inhibition of growth induced by atabrine was computed by comparing the acid production by titration under control conditions, when no atabrine was added, with acid production under experimental conditions when atabrine was added. When the effect of glutathione and thioglycollic acid was being tested the control tubes without atabrine contained an amount of glutathione or thioglycollic acid comparable to that put in the experimental tubes.

Results. The percent inhibition of acid production with atabrine alone, atabrine plus glutathione, and atabrine plus thioglycollic acid is shown in Table I. The data demonstrate that glutathione and thioglycollic acid are able to reverse the bacteriostatic effect of atabrine over a restricted range of concentration of the latter. For example, when the molar concentration of atabrine was 1.6×10^{-4} the percent inhibition of acid production was 91%, but with a similar concentration of atabrine plus glutathione the inhibition was 50%, and only 29% in the case of atabrine plus thioglycollic acid. In the experiments carried out it was not possible to counteract the effects of the higher molar concentrations of atabrine by increasing the amounts of glutathione and thioglycollic acid. Lower concentrations of glutathione and thioglycollic acid than 1.6×10^{-3} were effective in counteracting atabrine but the results were not consistent.

In addition to the above compounds, which counteracted the effect of atabrine, several others were tried under comparable conditions with negative results; these included: d-cystine, l-cystine, cysteine, dl-methionine, choline, nicotinic acid, riboflavin, and pyridoxine.

In the case of *E. coli* it has been shown[6,4] that shifting the pH of the medium to values below 6.0 (which permit satisfactory growth of *E. coli*) is effective in reversing the action of atabrine. This was tried in the case of *Lactobacillus arabinosus* and a comparable effect was attained.

Summary. Under the conditions of these experiments glutathione and thioglycollic acid are capable of reversing the growth inhibiting effect of atabrine on the *Lactobacillus arabinosus*. Once the concentration of atabrine for complete inhibition had been significantly exceeded, no reversal of bacteriostasis was attained by increased concentration of glutathione and thioglycollic acid. Several additional compounds were tested under comparable conditions with negative results.

[6] Browning, C. E., Gulbransen, R., and Keenaway, E. L., *J. Path. and Bact.*, 1919, **23**, 106.