filtrate and plasma, had a markedly accelerating coagulating effect, similar to sulfanilamide.

No explanation is put forward to account for the influence which the sulfonamides have upon staphylocoagulase activity. It should be emphasized that the presence of significant traces of calcium in the sulfonamide solution was ruled out.

Summary. 1. Sulfathiazole and, to a slightly lesser extent, sulfanilamide accelerated the clotting action in citrated plasma of staphylocoagulase contained in a sterile broth filtrate. Sulfadiazine markedly inhibited the coagulating effect, while sulfapyridine had only slight inhibitory activity. 2. Para-aminobenzoic acid operated like sulfanilamide and accelerated the coagulating action. 3. Broth filtrates with staphylocoagulase did not cause coagulation of every sample of normal, citrated human plasma. The degree of coagulation also varied.

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Influence of Tissue on Bacteriostatic Effect of Paranitrobenzoic Acid.*

JOSEPH T. KING AND MARIAN SEGAL KAPLAN.

From the Department of Physiology, University of Minnesota.

King and Henschel[1] reported that paranitrobenzoic acid exerted a bacteriostatic action against Type II pneumococcus in tissue culture clots which compared favorably with that of sulfathiazol in the same medium. Earlier the same authors[2] reported that " . . . . the characteristic effects of sulfanilamide on beta hemolytic streptococci are markedly inhibited by the products of tissue-breakdown."

In this paper we report the results of a study on the inhibition of the bacteriostatic effect of the sodium salt of paranitrobenzoic acid by the products of tissue-breakdown. The details of the tissue culture technic used have been described in the above papers.

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1 King, J. T., and Henschel, A. F., PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 400.

2 *Ibid.*, 1939, **41**, 208.

Pneumococci, Type II, were cultured in rabbit serum extract of 8-day chick embryos; incubation 3-5 hours at 37.5°C. The culture was then rapidly diluted through Tyrode solution into the serum extract to make a dilution of 10^{-8}.

The suspension was well mixed and divided into two equal portions to one of which sufficient sodium paranitrobenzoate was added to make 15 mg % in the final culture; to the other portion an equal volume of saline was added. The drug and saline were sterilized by Berkefeld filtration. pH of both drug solution and saline was adjusted to 7.6 before using.

To determine the degree of bacteriostasis 6 cultures were planted from the suspension without drug and 6 from the suspension containing the drug. Each culture consisted of 3 drops of suspension and one drop of heparinized rabbit plasma.

To determine the degree of bacteriostasis in the presence of disintegrating tissue, a similar set was then planted, each culture containing a sterile fragment of chick heart from a 17-19-day embryo. The fragments which were matched for size and shape measured 1.5-2.0 mm in diameter.

Cultures were incubated as lying-drop preparations for approximately 15 hours at 37.5°C in a special incubator previously described.[3] Measurement of the diameter of the colonies was made at 60 × (114 eyepiece units = 1 mm).

The results are given in Table I.

It may be noted that addition of even a small tissue fragment to the drug-free control medium accelerates the growth rate. The difference is large when few colonies are present and may be rather slight when the colony count is high.

In this concentration the drug exercised a consistent inhibitory effect both in the presence and absence of tissue but in all experiments the effectiveness of the drug was markedly reduced by a small tissue fragment.

TABLE I.

Colonies per cc	Cell free		With tissue		Inhibition %	
	Control	PNO_2	Control	PNO_2	Cell free	With tissue
424	56.8*	21.7	66.7	57.3	61.8	14.1
592	79.4	23.8	94.4	69.8	70.0	26.0
2812	38.0	18.8	43.9	32.7	50.5	25.4
45	117.7	41.6	213.5	140.8	64.7	34.1
454	54.7	30.5	74.2	57.8	44.3	22.1
696	48.0	25.8	70.7	56.7	46.2	19.8

*Eyepiece units.

3 King, J. T., *Arch. f. Exp. Zellforsch.*, 1937, **20**, 208.

The mechanism of action of the sulfa compounds and probable explanations for their inhibition by various factors are thoroughly discussed in recent papers by Long,[4] by Kohn and Harris,[5] and by Harris and Kohn.[6] Presumably the same reasoning may be applied to paranitrobenzoic acid.

Conclusion. The bacteriostatic effect of paranitrobenzoate on the pneumococcus is markedly reduced by the products of disintegrating tissue.

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Penetration of Sulfonamides Through Intact Skin by Iontophoresis and other Means of Local Application.

WILLIAM G. CLARK, ERNEST A. STRAKOSCH AND CLARICE NORDLUM.

From the Department of Zoology and the Division of Dermatology and Syphilology, University of Minnesota, and the Department of Dermatology and Syphilology, Minneapolis General Hospital.

This report presents some preliminary studies in which penetration by topical application of various sulfonamides has been measured by tissue analysis. It was thought that iontophoresis (electrolytic ion transport) might be an effective means of forcing the anion of sulfonamide salts into the skin. Penetration by iontophoresis was, therefore, compared with that from wet dressings and from an ointment, in the rat, rabbit, and human. The effect of circulation and the depth of penetration were estimated.

Methods. The experimental animals were anesthetized with nembutal and the hair removed with clippers. In the iontophoresis experiments, Canton flannel (6 oz grade) was wetted with the test solution and applied to the skin. Metal gauze electrodes were firmly applied over the flannel as the negative pole. The positive electrode was applied to one of the extremities, and currents of 1-2 milliamperes at 110-125 volts D.C. were applied.

Penetration from wet dressings (gauze or flannel) without current passage, was similarly studied in comparable areas on the same animal or on different animals.

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[4] Long, P. H., *Sigma Xi Quarterly*, 1941, **29**, 149.

[5] Kohn, H. I., and Harris, J. S., *J. Pharm. and Exp. Therap.*, 1941, **73**, 343.

[6] Harris, J. S., and Kohn, H. I., *J. Pharm. and Exp. Therap.*, 1941, **73**, 383.