these antibiotics.

Similar results were obtained with other strains of staphylococci. For instance, strain No. C proved to be less susceptible to tyrothricin and markedly more susceptible to both penicillin and streptothricin than strain No. 1725. The growth of strain No. 1725 was not inhibited in the presence of 1 U of penicillin, whereas that of strain No. 2535 was prevented by 0.1 U of this antibiotic. In contrast, tyrothricin in a concentration of 0.25 mg% prevented the growth of strain No. 1725 for 24 hours and failed to do so with strain No. 2535 in a concentration of 0.6 mg%. Of 3 selected coagulase-negative strains No. 2320 was more susceptible to the action of penicillin than Nos. 2203 and 2204.

Quantitatively, a certain strain of staphylococcus may grow in the presence of an antibiotic in concentrations from 2 to 10 times greater than that required to prevent visible growth of another strain. It is evident that according to the results of these experiments, the relative susceptibility or insusceptibility of a certain antibiotic does not necessarily parallel a similar susceptibility or insusceptibility to another antibiotic.

Discussion. The observations reported here seem to indicate that the mode of action of the antibiotics tested is not alike. As yet it is not possible to state which properties of different strains of staphylococci determine the relative susceptibility or insusceptibility to the action of these drugs. Furthermore, it is conceivable that the findings may have clinical implications, provided that the difference in susceptibility of various strains observed *in vitro* manifest themselves also *in vivo*. If this be the case, it may be advisable under certain circumstances to determine *in vitro* the relative susceptibility of microörganisms to various antibiotics as the basis for the selection of the most suitable chemotherapeutic agent.

Summary. Various strains of staphylococci differ in their relative susceptibility to the bacteriostatic action of penicillin, tyrothricin, and streptothricin *in vitro*. The relative susceptibility to one antibiotic is not necessarily paralleled by a similar susceptibility to another antibiotic. The implications of these observations are discussed.

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14869

2(Naphthyl-(1')-Methyl)-Imidazoline Hydrochloride (Privine).* I. Potency in Modifying Cocaine Hydrochloride-Induced Convulsions.

BRADFORD N. CRAVER. (Introduced by F. F. Yonkman.)

From the Department of Pharmacology, Wayne University College of Medicine, Detroit, Mich.†

The early work of Braun,[1] confirmed by Maurel,[2] Custer,[3] and others, seemed to establish that epinephrine simultaneously injected subcutaneously with cocaine exerted its protective action against cocaine-induced convulsions in a mechanical fashion by constricting the vicinal vessels and so delaying the absorption of the cocaine that a convulsive level was never attained in the blood stream. It occurred to us that advantage might be taken of this phenomenon to compare the effectiveness of different vasoconstrictors. As the first phase of an extended study of the vasoconstrictor properties of Privine we employed this method of comparing its effectiveness with that of epinephrine.

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† Now with the Department of Biochemistry, the University of Rochester School of Medicine and Dentistry, Rochester, N.Y.

1 Braun, H., *Arch. f. klin. Chir.*, 1903, **69**, 541.

2 Maurel, E., *Bul. gen. de Therap. Paris*, 1892, **122**, 201.

3 Custer, *Kokain and Infiltrations Anästhesie*, Basel, 1898, p. 34.

TABLE I.

Cocaine Convulsions in Guinea Pigs as Modified by Epinephrine or Privine.

Each animal received 1.0 cc/kg of 4% cocaine subcutaneously. Incorporated with the cocaine was the indicated concentration of vasoconstrictor. Time is expressed in min.

Vasoconstrictor	No. of animals	Avg time before first convulsion	Avg time before death	% convulsed	% dead*	% protected from convulsions
			Cocaine Control			
0	10	8 (7-11)†	16 (12-19)	100	50	0
			Epinephrine			
1:200,000	7	10 (5-20)	23 (16-37)	100	57	0
1:100,000	10	10 (3-17)	32 (1)	20	10	80
1: 50,000	10	6 (4- 8)	11 (1)	60	10	40
1: 25,000	26	13 (6-25)	15 (11-17)	54	15	46
1: 10,000	10	7 (4-12)	14 (11-19)	50	30	50
1: 5,000	5	4 (2- 5)	9 (6-15)	100	100	0
			Privine			
1:200,000	7	7 (3-10)	12 (7-18)	100	57	0
1:100,000	10	6 (3- 9)	14 (11-20)	90	60	10
1: 50,000	10	9 (6-13)	14 (11-17)	100	50	0
1: 25,000	10	7 (6-12)	17 (11-29)	80	50	20
1: 10,000	16	6 (2-14)	11 (5-17)	100	88	0
1: 1,000	10	5 (2- 9)	8 (4-16)	100	90	0
			Privine Control (without cocaine)			
1: 1,000	10				0	
1: 250	10				0	
1: 100	10		95 (59-148)		100	

* This includes animals dead within an hour. An occasional animal dying overnight has been omitted.

† The figures in parentheses represent the extreme values.

Methods. Guinea pigs in the weight range 275-325 g were employed for this study in order to minimize the effect of weight as a variable because we early established that the toxicity of cocaine was relatively greater for lighter animals. Guinea pigs in this weight range all convulsed after the subcutaneous injection of 1 cc of 4% cocaine per kg. Various concentrations of each vasoconstrictor were prepared and sufficient cocaine was added to each to make the solution 4% in respect to cocaine. The effectiveness of each concentration of the vasoconstrictor was then judged by its ability, when injected with the cocaine (1 cc of 4%), to prevent convulsions or to delay their onset. The occurrence or absence of convulsions in guinea pigs injected with 1 cc of 4% cocaine per kg was more desirable as an end-point than death for two reasons: (1) it was more economical and (2) the animals either developed convulsions within the first hour or never did. Some animals, on the other hand, died many hours after the injection, but these animals had always convulsed during the first hour. The results are summarized in Table I.

Discussion. This method gave a rough comparison of the relative effectiveness of the two drugs in causing subcutaneous capillary constriction but the limited number of animals did not seem to warrant a statistical analysis.

The most effective concentration of epinephrine, not only for diminishing the incidence of convulsions but for saving the lives of the animals, lay between 1:100,000 and 1:25,000. This finding may have some clinical significance. A 1:5,000 concentration of epinephrine definitely augmented the toxicity of the 4% cocaine. One-half of the animals injected with 4% cocaine alone had died, whereas all died, and after shorter intervals, that had received it with 1:5,000 epinephrine incorporated therein. From these results one could not, therefore, recommend a greater concentration of epinephrine than 1:25,000 for delaying the absorption of cocaine locally injected. Higher concentrations caused the synergistic action of the drugs systematically to predominate, a conclusion reached by Ross[4] and Gold.[5] They both gave intravenous injections of cocaine to cats.

[4] Ross, E., *J. Lab. and Clin. Med.*, 1923, **8**, 657.

[5] Mayer, Emil, *J. A. M. A.*, 1924, **82**, 876; Personal communication to committee.

Privine, on the basis of this method of comparing the effectiveness of vasoconstrictors, is not comparable in potency to epinephrine. Dilutions of Privine greater than 1:10,000 killed almost the same percentage of animals as did cocaine alone. Concentrations of 1:10,000 and 1:1000 killed respectively 38% and 40% more than did the cocaine alone. The assumption of a synergism between cocaine and Privine would explain this greater mortality with the higher concentrations of Privine, although it might also be explained by the assumption that a 1:1,000 concentration of Privine caused local vascular damage or depression with a resultant dilation so that the absorption of the cocaine was actually favored. Privine in the first 4 concentrations employed (see Table I) protected a total of 3 animals from convulsions, a result of debatable significance in view of the unchanged mortality rates in those 4 groups and the insignificantly changed average time before the onset of convulsions.

The injection of 1 cc of 1:250 (4 mg) Privine per kg killed none of 10 animals; 1 cc of 1:100 (10 mg) Privine per kg killed all of 10 animals. The LD_{50} for Privine, which we did not determine, would be intermediate between those 2 doses. Baylac[6] reported the same limits for epinephrine. Animals killed by Privine exhibited that acute pulmonary edema usually seen in animals killed by epinephrine.

Summary. 1. Privine, on the basis of the method employed for comparison, is a less effective vasoconstrictor than epinephrine. 2. The LD_{50} of Privine for guinea pigs is intermediate between 1 cc of 1:250 (4 mg) and 1 cc of 1:100 (10 mg) per kilogram. 3. Actively growing guinea pigs of less than 300 g are more sensitive to a given toxic dose of cocaine in g per kg than are mature or less actively growing guinea pigs of more than 300 g. 4. The toxicity, after subcutaneous injection, of a dose of cocaine in g per kg may be decreased by decreasing the concentration of the solution used for injection; this has been previously reported by other investigators.

[6] Baylac, J., *Arch. med. de Toulouse*, 1905, **11**, 245.

14870

Method for Testing *In Vitro* Resistance of Group A Hemolytic Streptococci to Sulfonamides.*

ARMINE T. WILSON. (Introduced by Homer F. Swift.)

From Epidemiology Unit 100, U. S. Naval Medical School, Bethesda, Md.

A suitable medium for testing sulfonamide susceptibility of Group A streptococci should meet certain requirements: it should promote good growth of all freshly isolated strains; it should promote growth from a uniform and measurable inoculum; and it should be practically free of substances antagonistic to sulfonamide action. Most media lack the last mentioned qualities. Furthermore, the relative capacity of different strains to multiply *in vitro* in the presence of sulfonamides is determined not only by inherent differences in their drug susceptibility but also by the size of the inoculum as well as by the character of the medium.

This paper describes a test in which the above mentioned criteria are fulfilled. It demonstrates the inhibition of streptococcal growth by various concentrations of sodium sulfadiazine in a semi-synthetic, semi-solid medium reinforced with serum.

The semi-synthetic medium was developed

* The opinions expressed in this paper are those of the author and do not necessarily represent those of the Navy Department.