blood for the different examinations. A few of the malarial infected birds were kept in the chamber and no smears were made. The fact that these ducks survived for a longer time when given oxygen would lend support to the opinion that anemic anoxia is a significant factor in the mechanism of death in the acute forms of malaria. The results of this study would indicate that the acute forms of this disease should be treated with a plasmodicial drug and also blood transfusions and oxygen should be given to combat the anoxemia.

Summary. It has been shown that ducks injected with *P. lophurae* survive for a longer time when placed in a chamber with 75 to 90% oxygen than the controls kept in batteries in the animal room. These observations support the opinion that anoxia is a significant factor in the mechanism of death in the acute forms of malaria.

15536

Inability of Penicillin to Neutralize Dick and Schick Toxins.

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The effect of penicillin upon the toxins of various bacteria is not as yet definitely established. Neter[1] showed that penicillin did not modify the action of tetanus toxin on mice. On the other hand, Boor and Miller[2,3] demonstrated that endotoxins obtained from meningococci and gonococci caused the death of fewer mice when the mice also received injections of penicillin. Meads and his associates,[4] as well as we,[5] have observed shortening of the course of scarlet fever in most of the patients who were treated with penicillin. The fever and toxicity diminished as soon as adequate doses of penicillin were given. As a result of these clinical observations we became interested in determining whether penicillin would neutralize the erythrogenic toxin of the hemolytic streptococcus. The experiments were later extended to include the toxin of the diphtheria bacillus. The results of these investigations are reported in the present paper.

Methods and Materials. One-tenth cubic centimeter of sodium penicillin in concentrations ranging from 10 to 1000 units per cc of isotonic salt solution were mixed with 0.9 cc of standard Dick or Schick toxins. In some instances the mixtures were injected immediately and in others they were first incubated for 4 or for 24 hours. The 2 controls used with each test were: (a) the same concentration of penicillin as that in the test dose, and (b) the standard toxins, diluted in salt solution to 90% of their usual strengths. Whenever the test mixtures were incubated prior to injection, the control materials were incubated for the same period of time. The skin reactions to Dick toxin were read 24 hours after intracutaneous injection and the Schick tests after 48 hours. The degree of erythema, edema and induration was used as criteria for judging the results.

Results. Dick Tests. Altogether 67 tests with mixtures of penicillin and Dick toxin were done on 63 subjects. The results are shown in Table I. The control tests containing penicillin in salt solution gave nega-

[1] Neter, Erwin, *J. Infect. Dis.*, 1945, **76**, 20.

[2] Boor, A. K., and Miller, C. P., *Science*, 1945, **102**, 427.

[3] Miller, C. P., and Boor, A. K., PROC. SOC. EXP. BIOL. AND MED., 1946, **61**, 18.

[4] Meads, M., Flipse, M. E., Barnes, M. W., and Finland, M., *J. A. M. A.*, 1945, **129**, 785.

[5] Hirsh, H. L., Dowling, H. F., and Sweet, L. K., *Ann. Int. Med.*, 1946, **25**, 78.

TABLE I.
Effect of Penicillin upon Erythrogenic Toxin of *Streptococcus hemolyticus* as Determined by Dick Tests.

Conc. of penicillin in the test mixtures (units per cc)	Period of incubation (hr)	No. of tests	Results of control injection (0.9 cc Dick toxin and 0.1 cc salt solution)		Results of test injection (0.9 cc Dick toxin and 0.1 cc penicillin solution)	
			Negative	Positive	Negative	Positive
10	0	6	2	4	3	3
100	0	21	11	10	14	7
1000	0	18	3	15	3	15
100	4	3	2	1	2	1
1000	24	19	10	9	10	9
Total		67	28	39	32	35

TABLE II.
Effect of Penicillin upon Toxin of *C. diphtheriæ* as Determined by Schick Tests.

Conc. of penicillin in the test mixtures (units per cc)	Period of incubation (hr)	No. of tests	Results of control injection (0.9 cc Schick toxin and 0.1 cc salt solution)		Results of test injection (0.9 cc Schick toxin and 0.1 cc penicillin solution)	
			Negative	Positive	Negative	Positive
100	0	2	0	2	0	2
1000	0	2	0	2	0	2
10000	0	2	0	2	0	2
100	24	2	0	2	0	2
1000	24	2	0	2	0	2
10000	24	2	0	2	0	2
Total		12	0	12	0	12

tive results. Negative skin tests were observed with the Dick toxin control in 28 instances, while positive reactions were found in 39. When the combination of penicillin and Dick toxin was used, 32 were negative, and 35 were positive. The slight differences in the reactions observed are not considered significant. Incubation of the mixtures of penicillin and erythrogenic toxin did not modify the results.

Schick Tests. Twelve tests were performed on 6 subjects. The control tests with penicillin in salt solution were negative. As shown in Table II, all of the tests were positive regardless of whether the Schick toxin was mixed with isotonic salt solution or with penicillin, and regardless of whether the Schick toxin-penicillin mixtures were incubated or not.

Other Experiments with the Erythrogenic Toxin. Other methods were used to determine whether penicillin had any effect upon Dick toxin. In an experiment designed to ascertain whether penicillin would act similarly to antitoxin in the Schultz-Carlton reaction, 0.1 cc of a solution of penicillin containing 1000 units per cc was injected intracutaneously into an erythematous area of 3 patients with a florid scarlet fever rash. Blanching in this area did not occur before blanching of the general rash.

Ten patients receiving penicillin for an unrelated disease were found to be Dick positive. After they had received penicillin for one week and while penicillin was still being administered, a Dick test was again given. The test remained positive in each instance.

Summary and Conclusions. 1. When mixtures of penicillin and Dick toxin were injected intracutaneously into normal subjects along with parallel mixtures of Dick toxin and isotonic salt solution, no significant difference was observed in the number of positive Dick tests in the 2 series. Incubation of the mixtures, previous to testing, did not influence the outcome.

2. Similar results were obtained with Schick toxin.

3. Penicillin injected into an area of rash of patients with scarlet fever did not cause blanching.

4. Dick positive patients receiving penicillin for an unrelated disease did not become Dick negative after a week of penicillin therapy.

5. It is concluded that penicillin has no neutralizing effect upon Dick or Schick toxin.

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15537

Hypertonic Sodium Chloride Solution as Serum Diluent in Agglutination Tests with *Rickettsia burneti.**

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In the course of agglutination tests employing as antigen a killed suspension of the Balkan Grippe strain of *Rickettsia burneti*,[1] it was found that a prozone effect occurred with considerable frequency. In addition, the fine granular quality of the aggregates some-

TABLE I.
Effect of Varying Concentrations of Sodium Chloride, as a Diluent for Sera, on Agglutination of a Suspension of *Rickettsia burneti.*

Convalescent serum	Conc. of diluent % NaCl	Dilution of serum 1:4	1:8	1:16	1:32	1:64	1:128	1:256	Diluent control
1	0.85	4	4	4	2	1	0	0	0
	2.5	4	4	4	4	2	±	0	0
	5.0	4	4	4	4	2	1	0	0
	7.5	4	4	4	2	1	0	0	0
	10.0	4	4	3	2	0	0	0	0
	12.5	4	4	3	2	0	0	0	0
	15.0	4	4	3	1	0	0	0	0
2	0.85	4	4	4	2	2	±	0	0
	2.5	4	4	4	4	2	1	0	0
	5.0	4	4	4	4	2	1	0	0
	7.5	4	4	4	2	1	0	0	0
	10.0	4	4	3	2	0	0	0	0
	12.5	4	4	3	2	0	0	0	0
	15.0	4	4	2	1	0	0	0	0
3	0.85	4	4	4	4	3	±	0	0
	2.5	4	4	4	4	4	2	0	0
	5.0	4	4	4	4	3	2	0	0

0—No agglutination.
±, 1, 2, 3—Increasing degrees of agglutination.
4—Complete agglutination.

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[1] Commission on Acute Respiratory Diseases, *Am. J. Hyg.*, 1946, **44**, 110-122.