The variations of the blood pressure and the pulse were striking. There was usually a fall of the systolic and the diastolic blood pressure levels and of the pulse following the injection of soluble amytal. Attention is directed to the response in Case 10. In every case 10 mg. of benzedrine sulfate restored the blood pressure to approximately the pre-narcosis level, although the pulse tended to remain slow or become slower. In Case I marked hypertension was produced with extreme rapidity. In other cases, 20 to 30 mg. of benzedrine sulfate raised the systolic level 50 to 100 points with a 20 to 40 increase in the diastolic level. Extremely high levels were maintained for only a short time, after which a gradual fall occurred to pre-narcosis levels which were reached in every case under 7 hours. In most instances the pulse became slower as the blood pressure rose. It must be pointed out that the blood pressure and the pulse variations in the test period are a response to both benzedrine sulfate and soluble amytal.

Although benzedrine sulfate seemed to exert an antagonistic action to soluble amytal, the narcosis produced by 0.5 gm. (7½ grains) intravenously in some of the patients studied was not as deep as we desired. The needle-prick accompanying the benzedrine sulfate injection produced a momentary response in some patients and must therefore be considered a source of error.

Benzedrine sulfate merits further investigation as a therapeutic aid in barbital intoxications.

We wish to express appreciation to the Smith, Kline and French Laboratories for supplying benzedrine sulfate, and the Eli Lilly Research Laboratories for soluble amytal used in this study.

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Anaphylactic Shock Prevented by Ketenizing Serum.*

M. JOHN BOYD AND JOSEPH T. TAMURA. (Introduced by S. Tashiro.)

From the Departments of Biochemistry and Bacteriology, College of Medicine, University of Cincinnati.

Our investigations[1] concerning the action of ketene ($CH_2 = CO$) on the endotoxin-producing bacteria (*B. dysenteriæ* Shiga) proved

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[1] Tamura, J. T., and Boyd, M. J., *Science*, 1936, **83**, 61.

that ketene detoxified the bacteria without altering the antigenic properties of the organisms. Subsequent research (unpublished) on such toxins as diphtheria, tetanus, and ricin, has established the fact that ketene is an effective detoxifying agent. The mechanism of the detoxification involves the chemical reaction between ketene and the primary amino groups of the toxin, with the formation of an acetylated toxin.

Recently, Goldie and Sandoz[2] have studied the influence of ketene on the antigenic and the anaphylactogenic (shock producing) properties of diphtheria antitoxin. They conclude that ketene-treated diphtheria antitoxin is modified to some extent by a change in its chemical structure. The anaphylactogenic power of the antiserum undergoes nearly complete attenuation while the major part of its antitoxic properties remains unaltered.

Anti-Brucella horse serum and young healthy guinea pigs were used in our investigations. All the animals were sensitized to antiserum diluted 1:10, each one receiving 0.5 cc. subcutaneously. To each 10 cc. lot of the original antiserum to be ketenized, 0.5 gm. of $NaHCO_3$ was added to buffer the acetic acid which is formed during the process. A few drops of caprylic alcohol were introduced to prevent foaming. Ketene gas was passed through the antiserum for various lengths of time at the rate of about one bubble per second (diam. of inlet tube, 4 mm.). At the end of the ketenizing process the pH of the antiserum was determined by the glass electrode method and it was found to be between 6.7 and 6.3 for antiserum treated 35 and 40 minutes respectively. Sufficient $NaHCO_3$ was added immediately, usually 0.1 gm. to adjust the pH to 7.0. The control antiserum was made by adding the same amount of $NaHCO_3$ to the original antiserum and adjusting the pH to 7.0 by addition of acetic acid. Both the control and the ketenized antisera were treated with the bicarbonate for approximately the same length of time. Since a slight precipitation of protein occurred during the ketenizing process the protein content of each lot of precipitate-free antiserum was determined by kjeldahl.

Two weeks after sensitizing the guinea pigs to the original antiserum, a shocking dose of ketenized antiserum was injected intracardially into one group of the animals and the control antiserum given likewise to another group. The results of this experiment are given in Table I.

Eleven animals showed very mild signs of shock or no anaphylac-

[2] Goldie, H., and Sandoz, G., *Comptes Rendus des Séances de la Société de Biologie*, 1937, **126**, 291.

TABLE I.
Results in Guinea Pigs Previously Sensitized to Anti-Brucella Horse Serum and Later Injected Intracardially with Original and Ketenized Antiserums.

Serum	No. of Guinea Pigs	Amount of shocking dose injected		Results
		cc.	mg. protein	
Control	1	.5	38.5	Shocked. Died in 3 min.
	2	.5	38.5	" " " 2.5 "
	3	.5	38.5	" " " 4 "
	4	.4	26.6	" " " 2 "
	5	.3	19.9	" " " 3.5 "
	6	.2	13.9	" " " 2 "
	7	.2	13.9	" " " 3.5 "
Ketenized 15 min.	1	.5	38.5	" " " 3 "
" 30 "	1	.5	38.5	" " " 5.5 "
	2	.5	38.5	" " " 12.5 "
	3	.5	38.5	Shock delayed. Recovered
	4	.5	38.5	Syndrome in lesser degree. Recovered.
" 35 "	1	.4	28.0	Very mild dyspnea for few minutes. Recovered.
	2	.5	32.5	Very mild dyspnea for few minutes. Recovered.
	3	.5	32.5	No anaphylactic syndrome
	4	.5	32.5	" " "
	5	.5	35.0	" " "
	6	.6	42.0	" " "
" 40 "	1	.5	33.7	Mild dyspnea—scratching nose
	2	.5	33.7	No anaphylactic syndrome
	3	.5	33.7	" " "
	4	.75	50.2	" " "
	5	1.0	67.0	Mild dyspnea—scratching nose

tic syndrome when injected with antiserum that had been treated with ketene for 35 minutes or more, containing from 28 mg. to 67 mg. of protein per dose. Seven control animals died within 2 to 4 minutes with the usual severe shock when injected with the control serum containing 13.9 mg. or more of protein per dose.

TABLE II.
Agglutinating Power of the Antiserums, Before and After Ketenization.

Serum	1:10	1:20	1:40	1:80	1:160	1:320	1:640	1:1280	1:2560
Original	4+	4+	4+	4+	4+	4+	4+	4+	—
Ketenized 15 min.	4+	4+	4+	4+	4+	4+	4+	4+	—
Ketenized 30 min.	4+	4+	4+	4+	4+	4+	4+	3+	—
Ketenized 35 min.	4+	4+	4+	4+	4+	4+	4+	2+	—
Ketenized 40 min.	4+	4+	4+	4+	4+	4+	4+	2+	—

The antibody content of the serums used in this investigation was determined by titration of the agglutinin titer against *Brucella abortus* suspensions.

The results of the test given in Table II show that the major part of the agglutinins were still intact after ketenization.

Conclusion. The treatment of anti-Brucella horse serum with ketene for 35 minutes or more prevents anaphylactic shock in animals sensitized to the original antiserum. Such a serum still retains the major part of its agglutinating antibody.

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Pathogenesis of Hemorrhagic-Necrotic Skin Lesions in Intradermal Infection of Rabbits with Pneumococci.*

ERNEST WITEBSKY AND ERWIN NETER.

From the Bacteriological Department, Buffalo General Hospital, and the Department of Pathology and Bacteriology, University of Buffalo School of Medicine.

The hemorrhagic necrotic changes occurring in certain endermal infections of rabbits closely resemble those described by Shwartzman. This induced us to examine various species of pathogenic microörganisms as to their capacity to produce the lesion in question. Previously reported experiments[1-4] revealed 3 different types of reactions represented by the following bacteria:

(1) *H. influenzæ,* when injected into the skin over the abdomen produces a localized swelling and infiltration. There is no trace of hemorrhagic necrosis to be observed. When, 24 hours after the intracutaneous injection of *H. influenzæ,* a suspension of *H. influenzæ* is given intravenously, the site of the dermal infection may be transformed into a bluish hemorrhagic lesion within a few hours. Not only living and heat-killed influenza bacilli but also agar-washing filtrates of *B. typhosus, B. coli,* or meningococcus may induce the same change. On the other hand, those filtrates may be activated by the intravenous injection of *H. influenzæ.* (2) Some

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1 Witebsky, E., and Salm, H., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 351.

2 Witebsky, E., and Salm, H., *J. Exp. Med.*, 1937, **65**, 43.

3 Witebsky, E., Neter, E., and Salm, H., Second International Congress for Microbiology, London, Report of Proceedings, 1936, 414.

4 Witebsky, E., and Neter, E., *Arch. Path.*, 1937, **24**, 271.