is extracted from the pellicles of a particular strain of *B. subtilis,* is of unknown chemical composition.[6] Eumycin is prepared by acid precipitation of the medium.[7] The chemical relationship between bacillin and subtenolin has not been ascertained since data pertaining to the chemical nature of bacillin is not available for comparison.[8]

Subtenolin has a low molecular weight. Its chemical and physical properties indicate that it contains a resonating double bond, phenolic groups, a very active enolic group, and an aromatic aldehyde radical. This antibiotic gives typical color reactions such as the Molisch and enol reaction. These tests, and the indicator test shown in Table I, may be used in its identification. Although the antibiotic has not been obtained in a pure state, its chemical and antibiotic properties, particularly its stability in aqueous solution or when dry, make it an interesting object for further studies.

[6] Dimick, K. P., Alderton, G., Lewis, J. C., Lightbody, H. D., and Fevold, H. L., *Arch. Biochem.,* 1947, **15**, 1.

[7] Johnson, E. A., and Burdon, K. L., *J. Bact.,* 1946, **51**, 591.

[8] Woodruff, H. B., and Foster, J. W., *J. Bact.,* 1946, **51**, 371.

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Respiratory Arrest in Rabbits Exposed to Hypoxia after Dibenamine.*

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The observations here reported were made as part of a systematic elucidation of the effect of alteration of function of the autonomic nervous system on the response of the intact animal to hypoxia.

Rabbits underwent early and sudden respiratory arrest on exposure to hypoxia after receiving Dibenamine (N, N-dibenzyl-β-chloroethylamine) in ethyl alcohol and propylene glycol aa by vein. Control animals underwent such arrest very rarely even under more prolonged similar exposure to hypoxia.

Procedure. Normal rabbits (weight 1.5 to 4 kg) under intravenous pentothal anesthesia were subjected to tracheotomy. Procaine hydrochloride 2% was infiltrated through the margins of the incision and skin closure around the cannula was made with skin clips.

The rabbits were restrained in the supine, head low position on a table offering a slope of 15° from the horizontal in order to aid the venous return. After recovery (minimum 30 min.) from the general anesthesia the inspiratory ventilation volume on room air was measured by spirometer. This was made possible by an hydraulic flutter valve‡ interposed between the tracheal cannula and the spirometer. The dead space of the system was 3 to 5 cc. This compares favorably with the dead space of the eliminated respiratory tract above the cannula in the rabbit.

Measurements were then continued as the animal was abruptly shifted to an atmosphere of 5% oxygen in helium for a period of 5 minutes. After one or a series of such control

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‡ A modification of the type pictured on page 206, Jackson, D. E., *Experimental Pharmacology and Materia Medica,* 2nd Edition, 1939. C. V. Mosby Co., St. Louis, Mo.

TABLE I.
Occurrence of Respiratory Arrest on Exposure to *Circa* 5% O_2 for 5 Minutes.

Treatment	No. of rabbits showing no arrest	No. of rabbits showing arrest
Normal	49	2
Dibenamine in Propylene Glycol and Ethyl Alcohol āā 12-24 mg/kg*	2	20
Dibenamine in 50% Alcohol 12-24 mg/kg	1	4
Dibenamine in 50% Propylene Glycol 12-24 mg/kg	1	5
Propylene Glycol 50% 2 cc	6	0
Alcohol 50% average 0.5 cc	6	0
Propylene Glycol and Absolute Alcohol āā average 0.5 cc	6	0

* By Chi square test the probability of chance distribution of 29 positive in 33 as opposed to 2 positive in 49 is less than 1 in 10,000.

observations on the effect of hypoxia. Dibenamine (at a concentration of 50 mg cc in the chosen medium)§ was administered in marginal vein of ear in calculated dose over a period of one minute. Usually the primary dosage of Dibenamine was 12 mg kg.

After a variable delay the ventilation volume on room air was measured and the animal was again presented with the hypoxic atmosphere for 5 minutes. If respiratory arrest occurred artificial ventilation was established after 1 to 2 minutes of apnea, by means of human expired air through the tracheal cannula. Successive periods of hypoxia were rarely at intervals less than 20 minutes.

Gas mixtures were made in large rubber bag of some 1500 liter capacity and analyzed for oxygen content repeatedly through the day's experiments. Maximum variation of different days' mixtures was 4.0-5.5% oxygen (mean 5% ±0.5).

Observations. Table I records the incidence of respiratory arrest in rabbits exposed to hypoxia for 5-minute periods after various medications.

Normal Controls. The 2 cases of respiratory arrest in 49 normals showed arrest only once each in several trials. Time required for arrest to occur was 230 and 240 seconds respectively. It was repeatedly shown that 5-minute periods of hypoxia did not predispose to respiratory arrest in later 5-minute periods of exposure (11 animals up to 9 trials each over periods up to 6 hours).

Dibenamine: Incidence. In the total series of 38 animals given Dibenamine 5 died within 10 minutes of the intravenous injection of 12 mg kg. Twenty-three animals showed arrest during hypoxia after the first 12 mg of the drug. Six animals required a second dose at the end of an hour or more before arrest would result from hypoxia. The remaining 4 animals never showed respiratory arrest.

The pattern of respiratory arrest after Dibenamine was bizarre. The rise of ventilation volume at the beginning of the period of hypoxia (average 59% rise) differed little from that of the control hypoxic condition (average 72% rise). However, after an average exposure of 158 seconds (in 44 trials, range 30 to 300 seconds) the respiration became more labored, followed abruptly by an apparently tonic contraction of the diaphragm, accompanied by twitching movements of the abdomen. Simultaneously the tidal volume fell to zero and the tonic contraction faded out. Thereafter no respiratory movements appeared in most animals though one or two gave a feeble gasp reflex.

Duration of susceptibility to respiratory arrest. In animals tested serially to determine the time course of susceptibility to respiratory arrest on exposure to hypoxia, arrest could be elicited at the earliest in most animals between 20 and 40 minutes (mean 33 minutes) after the administration of the drug. Susceptibility endured throughout the period of test (up to 4 hours) in a number of animals. In others the ability to compensate for hypoxia returned, after as little as

§ Media used included Propylene glycol and absolute alcohol āā most commonly, Propylene glycol and water āā or absolute alcohol and water āā on other occasions.

48 minutes following administration of Dibenamine.

Controls receiving solvents without Dibenamine. See Table I.

Discussion. That the susceptibility to respiratory arrest is not dependent on some residual effect of the pentothal was demonstrated by the occurrence of respiratory arrest in cats under the same conditions except that cyclopropane was utilized during the preparatory period. The pilot experiments in the cat also showed that the susceptibility to arrest is not species specific in the rabbit alone.

That the helium was not an active factor in the elicitation of respiratory arrest was shown in animals tested on nitrogen and oxygen (5%). Five minutes on this mixture never caused arrest in several trials in each of 11 animals tested before Dibenamine. It was at least as potent in producing respiratory arrest after Dibenamine.

That the phenomenon observed was a true respiratory arrest was shown by the demise of 8 animals allowed to go untreated in the apnea which occurred during hypoxia after Dibenamine. No animal ever recovered spontaneously from this state of arrest. On resuscitation spontaneous respiration was reestablished promptly after a minute or more of artificial ventilation with human expired air.

As to the mechanism of action of Dibenamine in inducing respiratory arrest during hypoxia little evidence is available. Pilot experiments have shown that bilateral vagotomy, with its removal of inhibitory sensory discharge does not prevent the occurrence of arrest on hypoxia after Dibenamine (3 animals). Three experiments suggested that Dibenamine does reverse the normal pressor response to hypoxia in rabbits as in other species. However, the fall of blood pressure is inconstant and respiratory arrest has been noted unaccompanied by a depressor response. Acapnia seems an unlikely cause of the apnea, since the hyperventilation normally seen in hypoxia of this grade is at least as great as that after Dibenamine. Finally, a direct depressant action of Dibenamine on the respiratory center seems unlikely, since the center still responds to the carotid body under hypoxia by inducing hyperventilation.

Summary. Rabbits given Dibenamine 12 to 24 mg/kg in propylene glycol or ethyl alcohol by vein show sudden respiratory arrest within 3 minutes of exposure to hypoxia (circa 5% O_2 in helium).

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Results of Heterophile Antibody Agglutination and Kahn Tests in Patients with Viral Hepatitis.*

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Attempts to develop a *specific* immunologic test for viral hepatitis have been unsuccessful, up to the present, although positive results have been described in certain serologic reactions in this disease.[1,2,3] Eaton *et al.*[2] reported that 34% of a group of pa-

* This work was conducted under the auspices of the Commission on Virus and Rickettsial Diseases, Army Epidemiological Board, Office of the Surgeon General, U. S. Army, Washington, D.C.

1 Sawyer, W. A., Meyer, K. F., Eaton, M. D., Bauer, J. H., Putnam, P., and Schwentker, F. F., *Am. J. Hyg.*, 1944, **39**, 337; Am. J. Hyg., 1944, **40**, 35.