

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 re-established 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% O₂ 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 re-

sults 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 Schwenker, F. F., *Am. J. Hyg.*, 1944, **39**, 337; *Am. J. Hyg.*, 1944, **40**, 35.

tients in the acute phase of hepatitis developed an heterophile antibody which agglutinates sheep erythrocytes in a titer of 1:40 or greater. The titer of this antibody rarely rises above 1:160, and may be differentiated from that appearing in patients with infectious mononucleosis by its absorbability on boiled guinea pig kidney and human liver.

It has also been reported that a certain number of patients with viral hepatitis develop transient falsely positive tests for syphilis,⁴ and as many as 20% of one group of patients were reported to have falsely positive Kahn and Wassermann tests during the course of acute hepatitis.⁵

Such a substantial percentage of positive serologic tests, occurring during the course of hepatitis, might constitute a problem in diagnosis. Certain similarities between hepatitis and infectious mononucleosis, such as the presence of cervical lymphadenopathy and lymphocytosis as well as the frequent occurrence of evidence of hepatic dysfunction in the latter disease, make differential diagnosis more difficult.

During recent years, experiments conducted under the auspices of the Army Epidemiological Board on the transmission of infectious hepatitis to volunteers have made it possible to study certain serologic reactions in these patients. In addition, a recent opportunity to survey the serologic response of a large number of patients with hepatitis in an American Army hospital has provided certain data. It is the purpose of this paper to report on the results of the heterophile antibody agglutination, Kahn, and cold agglutinin tests in these two groups of patients.

Method and Materials. Subjects. The patients are divided into 2 groups. *Group I:* 30 previously healthy male volunteers, ranging in age from 19 to 29 years, contracted

infectious hepatitis experimentally, following inoculation or ingestion of material known to contain infectious hepatitis virus. The strain of virus used in these experiments has been previously described.⁶ *Group II:* 478 subjects were patients in an Army hospital in Germany from June 1947 to February 1948. They had contracted acute hepatitis during the performance of duty. It is quite probable that many of these cases were examples of homologous serum jaundice, but in view of the fact that there are no means at present for differentiating infectious hepatitis from serum hepatitis clinically, the cases have all been classified as viral hepatitis. The diagnosis of hepatitis was made in both groups on the basis of characteristic symptoms and signs, accompanied by consistent deflection of appropriate tests of hepatic function. All patients in this report had clinical jaundice.

In Group I, the heterophile antibody agglutination, Kahn, and cold agglutinin tests were determined before experimental inoculation. All were negative. These subjects were tested again during the 2nd, 3rd and 4th weeks of disease, and sera with positive reactions were retested at weekly intervals until negative.

In Group II, these tests were performed in various stages of infectious hepatitis, ranging from the 1st to the 30th week. Numerous serial determinations were made, and the majority of tests were done during the first 8 weeks of disease. Sera with positive reactions were retested at weekly intervals until negative.

Results. Heterophile antibody agglutination tests. Technique of test. The tests were carried out according to the method of Stuart.⁷ Sera with a titer of 1:56 were absorbed on boiled guinea pig kidney and retested.

The results of the determinations in 508 patients represented in Groups I and II are

² Eaton, M. D., Murphy, W. D., and Hanford, V. L., *J. Exp. Med.*, 1944, **79**, 539.

³ Olitski, L., and Bernkopf, H., *J. Infect. Dis.*, 1945, **77**, 60.

⁴ Waelsch, J. H., *Brit. Med. J.*, 1946, March 9, 353.

⁵ Kuzell, W. C., and Puccinelli, V., *Bull. U. S. Army Med. Dept.*, 1944, **80** (Sept.), 3.

⁶ Havens, W. P., Jr., Ward, R., Drill, V. A., and Paul, J. R., *Proc. Soc. Exp. Biol. and Med.*, 1944, **57**, 206.

⁷ Stuart, C. A., *Infectious Mononucleosis (in) Diagnostic Procedures and Reagents*, 2nd Ed., New York, Am. Pub. Health Assn., 1945, p. 449.

TABLE I.

Results of Heterophile Antibody Agglutination Tests in 508 Patients with Viral Hepatitis.

Week of disease	No. of patients	
	Tested	Positive* 1:56
1	11	0
2	116	1
3	167	2
4	192	4
5	158	3
6	153	0
7	132	1
8-12	372	3
13-17	75	1
18-30	37	1

* After absorption on boiled guinea pig kidney, titer was 1:7 or negative. The first positive test for each patient is recorded. Subsequent serial determinations of positive tests are not included in this table.

TABLE II.

Results of Kahn Tests in 388 Known Non-luetic Patients with Viral Hepatitis.

Week of disease	No. of patients			Week tests became negative
	Tested	Positive*	Doubtful*	
1	70	3	1	2nd, 3rd 14th
2	175	2	4	3rd, 5th, 7th
3	237	0	3	4th, 6th, 7th
4	247	0	1	5th
5	212	1	0	14th
6	195	0	1	7th
7	153	0	0	
8-12	290	0	0	
13-17	58	0	0	
18-30	8	0	0	

* All tests reported as positive or doubtful had less than 10 Kahn units. The first positive test for each patient is recorded. Subsequent serial determinations of positive tests are not included in this table.

recorded in Table I. The volunteers in Group I, who were all known to have negative tests before experimental inoculation with hepatitis virus, failed to develop positive reactions during the 2nd, 3rd or 4th week after onset of disease. In Group II, none of the patients had titers of heterophile antibody above 1:14 at the 2-hour reading, although 41 patients had titers of 1:28 at the 12-hour reading. Sixteen patients had positive tests at the 12-hour reading with titers of 1:56 which were reduced to 1:7 or negative following absorption on boiled guinea pig kidney.

Kahn tests. Technique of test. The

TABLE III.

Results of Cold Agglutinin Tests in 323 Patients with Viral Hepatitis.

Week of disease	No. of patients		Week test became negative
	Tested	Positive* 1:32	
1	37	0	
2	81	0	
3	106	0	
4	108	0	
5	79	0	
6	79	0	
7	60	1	8th
8	45	1	9th
9-12	111	0	
13-16	40	0	
17-23	16	0	

*Tests reverted to negative after standing 3 hours at room temperature. The first positive test for each patient is recorded. Subsequent serial determinations of positive tests are not included in this table.

standard and quantitative Kahn tests were carried out according to methods recommended by the U. S. Army.⁸

The results of testing 388 patients in Groups I and II are recorded in Table II. One of the volunteers in Group I developed a positive Kahn test in the 2nd week of disease which became negative in the 7th week. It is of interest to note that this patient had a superimposed bacteremia with *S. cholerae suis*.⁹ In Group II, 358 patients, who were known not to have syphilis, were tested. Six patients developed positive Kahn tests, and 10 had doubtfully positive tests. These tests became negative between the 3rd and 14th week of disease in all patients.

Cold agglutinin tests. Technique of tests. The tests were carried out according to the method recommended by Bray.¹⁰

The results of testing 323 patients in Groups I and II are recorded in Table III.

⁸ Turner, T. B., and Rein, C. R., Sero-diagnosis of Syphilis, Chap. XII, (in) Simmons and Gentzkow's *Laboratory Methods of the United States Army*, 5th Ed., Philadelphia, Lea and Febiger, 1944, p. 124.

⁹ Havens, W. P., Jr., and Wenner, H. A., *J. Clin. Invest.*, 1946, **25**, 45.

¹⁰ Bray, W. E., *Synopsis of Clinical Laboratory Methods*, 3rd Ed., 1944, St. Louis, C. V. Mosby Company, p. 163.

The volunteers in Group I, who were all known to have negative tests before experimental inoculation with hepatitis virus, failed to develop positive reactions during the 2nd, 3rd or 4th week after onset of disease. In Group II, 2 patients had positive tests with a titer of 1:32, which reverted to negative after standing at room temperature for 3 hours.

Summary. Heterophile antibody agglutination, Kahn, and cold agglutinin tests were performed in 2 groups of patients with viral hepatitis. Sixteen out of 508 patients (3%) developed positive heterophile antibody tests with titers of 1:56 which were

reduced to 1:7 or negative by absorption on boiled guinea pig kidney. A rise and/or fall in titer of antibody was demonstrable in serial weekly determinations. Out of 388 patients who were known not to have syphilis, 6 (1.5%) developed positive Kahn tests, and 10 others (2.5%) had doubtful tests. Two out of 323 patients had cold agglutinins present in a titer of 1:32.

The relatively small number of positive heterophile antibody agglutination and Kahn tests is in contrast to reports of others^{2,5} who have found a considerably higher percentage of positive tests.

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Factors Influencing the Growth of Integumentary Pigment in Fishes. I. The Role of Light.*†

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It is a common observation that light is associated with changes in body pigmentation such as "tanning." Numerous clinical observations¹⁻⁵ indicate that certain types of pigmentation deficiencies in man may be corrected by light treatment. In lower mammals Bissonnette and others have demonstrated that pigmentation may be influenced by il-

lumination while experimental evidence has accumulated indicating the importance of light in producing integumentary pigmentation in lower vertebrates. Cunningham⁶⁻⁸ working with flatfishes; Herbst and Ascher⁹ using salamander larvae; Vilter¹⁰ studying axolotls; Sumner and Wells;¹¹ Sumner and Doudoroff;¹² Odiorne;¹³ Sumner;¹⁴⁻¹⁶ Os-

* This work was aided in part by a Bache Fund grant administered by Professor G. H. Parker and in part by equipment provided by the Elizabeth Thompson Science Fund.

† Contribution No. 427 of the Woods Hole Oceanographic Institution whose research facilities were generously provided for this investigation.

‡ Now located at Syracuse University.

¹ Montgomery, D., *J. Cut. and Urin. Dis.*, 1904, **22**, 17.

² Buschke, A., *Med. Klinik*, 1907, **33**, 983.

³ Buschke, A., and Mulzer, P., *Berl. Klin. Wchnschr.*, 1907, **44**, 1575.

⁴ Moser, *Med. Klinik*, 1907, **45**, 1363.

⁵ With, C., *Brit. J. Dermat.*, 1920, **32**, 145.

⁶ Cunningham, J. T., *Zool. Anzeiger*, 1891, **14**, 27.

⁷ Cunningham, J. T., *J. Marine Biol. Assn. United Kingdom*, 1893, **3**, 111.

⁸ Cunningham, J. T., *J. Marine Biol. Assn.*, 1895, **4**, 53.

⁹ Herbst, C., and Ascher, F., *Roux Arch. Entw. Mech. Organ*, 1927, **112**, 1.

¹⁰ Vilter, V., *C. R. Soc. Biol.*, 1931, **108**, 774.

¹¹ Sumner, F. B., and Wells, N. E., *J. Exp. Zool.*, 1933, **64**, 377.

¹² Sumner, F. B., and Doudoroff, P., *Pro. Nat. Acad. Sci.*, 1937, **23**, 211.

¹³ Odiorne, J. M., *J. Exp. Zool.*, 1937, **76**, 441.

¹⁴ Sumner, F. B., *Am. Naturalist*, 1939, **123**, 219.