tration of yeast. 2. The present study shows that nicotinic acid, a substance which has been shown to be curative for the mucous membrane lesions of pellagra, likewise produces a decrease of porphyrinuria in pellagrins. 3. In addition, the present study shows that the porphyrinuria associated with a number of diseases other than pellagra likewise is promptly decreased following the administration of either yeast or nicotinic acid.

## 9784 P

## Intravenous Benzedrine Sulfate as an Antagonist to Intravenous Soluble Amytal.

EDWARD C. REIFENSTEIN, JR., AND EUGENE DAVIDOFF. (Introduced by M. S. Dooley.)

*From the Syracuse Psychopathic Hospital and the Department of Psychiatry, Syracuse University College of Medicine.*

During our previous investigations of the stimulating action of benzedrine sulfate on the central nervous system[1, 2, 3] the possibility suggested itself of employing this drug to counteract the narcosis produced by barbiturates. Alles[4] observed that benzedrine intravenously had considerable effect in waking animals from barbital anesthesia. In man, Myerson, *et al.*,[5] reported that benzedrine sulfate subcutaneously did not affect the depth, although it definitely shortened the duration of soluble amytal narcosis; and stated that hypertension produced by benzedrine sulfate subcutaneously could be reduced by soluble amytal intravenously, and also that hypotension produced by soluble amytal intravenously could be elevated by benzedrine sulfate subcutaneously. In rats, rabbits and guinea pigs unprotected by barbiturates the minimum lethal dose subcutaneously or intravenously has been reported by all observers[4, 6, 7] to be at least 25 mg. per kg. body weight. On the basis of these determinations it was felt that the dosage herein employed was entirely safe.

In the present study we decided to employ both soluble amytal and

[1] Davidoff, E., *Psychiat. Quart.*, 1936, **10**, 652.

[2] Davidoff, E., and Reifenstein, E. C., Jr., *J. A. M. A.*, May 22, 1937, **108**, 1770.

[3] Davidoff, E., and Reifenstein, E. C., Jr., *J. Lab. and Clin. Med.*, to be published.

[4] Alles, G. A., *J. Pharm. and Exp. Therap.*, 1933, **47**, 339.

[5] Myerson, A., Loman, J., and Dameshek, W., *Am. J. M. Sci.*, 1936, **192**, 560.

[6] Hartung, W. H., and Munch, J. C., *J. Am. Chem. Soc.*, 1931, **53**, 1875.

[7] Ehrich, W. E., and Krumbhaar, F. B., *Ann. Int. Med.*, 1937, **10**, 1874.

benzedrine sulfate intravenously. Ten patients without apparent physical disease were selected. Each was subjected to a control period as follows: the usual blood pressure and pulse levels were determined; then soluble amytal, 0.5 gm. (7½ grains), was given intravenously; the narcosis thus induced was allowed to terminate spontaneously; the duration of the narcosis was noted; and the blood pressure and pulse levels were again determined at the moment of awakening. Several days later the same patients were subjected to the following test period: the initial blood pressure and pulse levels were determined; soluble amytal, 0.5 gm. (7½ grains) was given intravenously; after a period of narcosis varying from 15 to 45 minutes the clinical state of the narcosis and the blood pressure variation were observed; thereafter benzedrine sulfate 10 mg. intravenously was repeated at intervals of approximately 15 minutes until the state of narcosis disappeared, and until the systolic blood pressure exceeded 150 mm. of mercury; the length of time and the amount of benzedrine sulfate necessary to overcome the soluble amytal narcosis was recorded; finally, the blood pressure and pulse variations were observed until the original levels obtained.

The results are summarized in Tables I and II. Both the depth and the duration of the soluble amytal narcosis were affected, as in every case the narcosis was completely counteracted by 20 or 30 mg. of benzedrine sulfate intravenously, and in 5 instances by only 10 mg. Every patient awakened following the initial injection of 10 mg. of benzedrine sulfate, but some remained drowsy until the third injection was completed. Almost all the patients became talkative, some were euphoric, others began to weep bitterly, and a few were restless, tremulous and complained of headache. Every patient was up and about within an hour of the first benzedrine injection.

TABLE I.
Effect of Intravenous Benzedrine Sulfate on Soluble Amytal Narcosis: Duration of Narcosis and of Blood Pressure Variations.

| | Aver. Duration, Min. | Range of Duration, Min. |
|---|---|---|
| Control Period | 257 | 155-366 |
| Prior to Benzedrine Sulfate Injection | 35 | 17-52 |
| After Benzedrine Sulfate Injection (as indicated by drowsiness) | | |
| (a) 6 Cases (10 mg.) | 4 | 2-5 |
| (b) 4 Cases (20-30 mg.) | 37 | 28-47 |
| Period of Blood Pressure Rise (Initial Benzedrine Sulfate injection to maximum level) | 66 | 5-125 |
| Period of Blood Pressure Fall (Final Benzedrine Sulfate injection to original level) | 215 | 85-417 |

TABLE II.
Effect of Intravenous Benzedrine Sulfate on Soluble Amytal Narcosis: Blood Pressure and Pulse Alterations

| | Prior to Soluble Amytal Narcosis | | Prior to Benzedrine Sulfate Injection | | After Benzedrine Sulfate Injections | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 10 mg. | | 20 mg. | | 30 mg. | |
| Case No. | B.P.† | P.‡ | B.P. | P. | B.P. | P. | B.P. | P. | B.P. | P. |
| 1. (F.A.) | 150/70 | 78 | 110/60 | 80 | 200/100 | 60 | 198/98 | 66 | — | — |
| 2. (W.V.)§ | 100/62 | 86 | 108/68 | 68 | 112/66 | 70 | 142/88 | 88 | 152/88 | 74 |
| 3. (F.J.) | 148/80 | 100 | 112/74 | 96 | 136/90 | 80 | 148/84 | 72 | 160/80 | 100 |
| 4. (R.R.) | 100/68 | 86 | 96/60 | 76 | 120/70 | 64 | 150/80 | 60 | 164/82 | 54 |
| 5. (M.M.) | 122/64 | 80 | 98/60 | 80 | 132/88 | 70 | 146/90 | 58 | 186/94 | 54 |
| 6. (S.S.) | 124/70 | 70 | 102/60 | 64 | 116/80 | 64 | 166/92 | 80 | — | — |
| 7. (J.P.) | 142/76 | 90 | 115/85 | 96 | 154/100 | 98 | 180/100 | 60 | 218/106 | 68 |
| 8. (H.R.)§ | 140/82 | 96 | 105/70 | 84 | 145/105 | 76 | 150/100 | 68 | 174/100 | 60 |
| 9. (H.A.) | 108/72 | 68 | 95/62 | 100 | 110/80 | 78 | 130/90 | 60 | 152/94 | 58 |
| 10. (L.P.) | 120/75 | 132 | 50/0 | * | 140/90 | 88 | 140/100 | 90 | 150/90 | 100 |

*Patient in collapse, pulse too rapid to be counted; Benzedrine Sulfate 10 mg. injected intravenously at once, with immediate response of patient.

†Blood Pressure. ‡Pulse. §After 40 mg.: Case 2—162/86, 68; Case 8—182/102, 70.

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.