vitamin B_2 complex. Biotin is an additional factor that is connected with the maintenance of the normal pigment metabolism of the fur in rats and mice under special dietary conditions.

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Effects of Epinephrine and Amphetamine on Respiration and Blood Pressure in Different Postures.

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The cause of the overventilation of the erect posture, as indicated by lowering of the alveolar CO_2 tension, is unknown. Main[1] suggested that it might be due to the fact that the pressure in the carotid sinus is lowered about 20 mm Hg on standing,[2] which should therefore stimulate respiration. Turner[3] believed it might be due to cerebral ischemia. I decided to test the former hypothesis by raising the blood pressure of a standing subject, to see if this would remove the excess respiratory stimulation by increasing the pressure in the carotid sinus back to the normal level.

I decided to use epinephrine subcutaneously to raise the blood pressure. Two reports in the literature on the effect of epinephrine on alveolar CO_2 are somewhat at variance; Arnoldi[4] reporting a rise, and Peters,[5] a slight fall. However, the side effects of this drug, such as marked tremor, cold perspiration, feeling of apprehension, and the possible production of a lactacidemia,[6] made it advisable to control the results with some other vasopressor drug which would not produce such deleterious side effects. Amphetamine sulfate subcutaneously was selected because of its entirely different side effects: euphoria, and the complete lack of tremor and sweating.

It was soon found that the subjects, males between the ages of 20 and 30, varied greatly in their response to epinephrine; some being severely affected by 0.5 cc, and others showing very little ill effects from 0.75 cc of a 1 to 1000 solution in ampules (Parke-Davis). No ill effects were noticed in any case from amphetamine

1 Main, R., *Va. Med. Monthly*, 1937, **64**, 330.

2 Loman, J., and Myerson, A., *Am. J. Psychiat.*, 1936, **92**, 791.

3 Turner, A., *Am. J. Physiol.*, 1927, **80**, 601.

4 Arnoldi, W., *Deut. Med. Woch.*, 1924, **50**, 1397.

5 Peters, J., *Am. J. Physiol.*, 1917, **44**, 84.

6 Cori, C., *J. Biol. Chem.*, 1925, **63**, 253.

sulfate in doses up to 30 mg. Care was always taken not to make an accidental intravenous injection, and not to massage the area after injection. Not more than one injection a week was given to a subject, in order to prevent any possible adaptation. A total of 12 subjects was used, in 12 experiments with amphetamine, and 24 with epinephrine.

After eliminating a few subjects who were very sensitive to the effects of epinephrine, I found it necessary to administer from 0.5 to 0.75 cc of a 1 to 1000 solution, in order to obtain a maximal increase in systolic blood pressure of about 20 mm Hg. From 20 to 30 mg of amphetamine sulfate subcutaneously was required to produce a similar effect.

The subjects came to the laboratory within an hour after having eaten, so that hunger contractions would not intervene toward the end of the experiment to disturb the CO_2 tension.[7] They were not permitted to have coffee at the previous meal or to smoke one hour beforehand. They would lie down for at least 30 minutes before the experiment was started. The effect of the drug was tested in the supine position the entire period, or at other times was given while standing.

Alveolar CO_2 samples were usually taken every 10 minutes to cover normal variations in tension, and unconscious errors in obtaining the sample. The Haldane-Priestley method was used; the forced expiration being made at the end of a normal expiration.

Fig. 1 illustrates the typical effect of epinephrine (0.6 cc subcutaneously) on the same subject, lying and standing. With the doses of epinephrine used throughout (0.25 to 0.75 cc), there was never noted any distinct effect upon alveolar CO_2 tension, even when the blood pressure of the standing subject rose over 20 mm Hg. Apparently any possible lactacidemia produced by these doses of epinephrine is inadequate to affect the acid-base balance of the blood. Neither the distinct tremor nor the apprehension produced by the drug seemed to have any effect upon the CO_2 tension.

The effect of amphetamine sulfate was tested in the same way as with epinephrine. There was always a distinct feeling of euphoria which lasted less than 2 hours and had disappeared by the end of the experiment. No effect on alveolar CO_2 was noticed with this drug, even when it caused a distinct increase in blood pressure.

I would estimate, that from its maximum effect on blood pressure (but not duration), that 20 to 25 mg of amphetamine sulfate is equivalent to about 0.6 cc of 1/1000 epinephrine, by subcutaneous administration.

[7] Main, R., *Am. J. Physiol.*, 1937, **119**, 7.

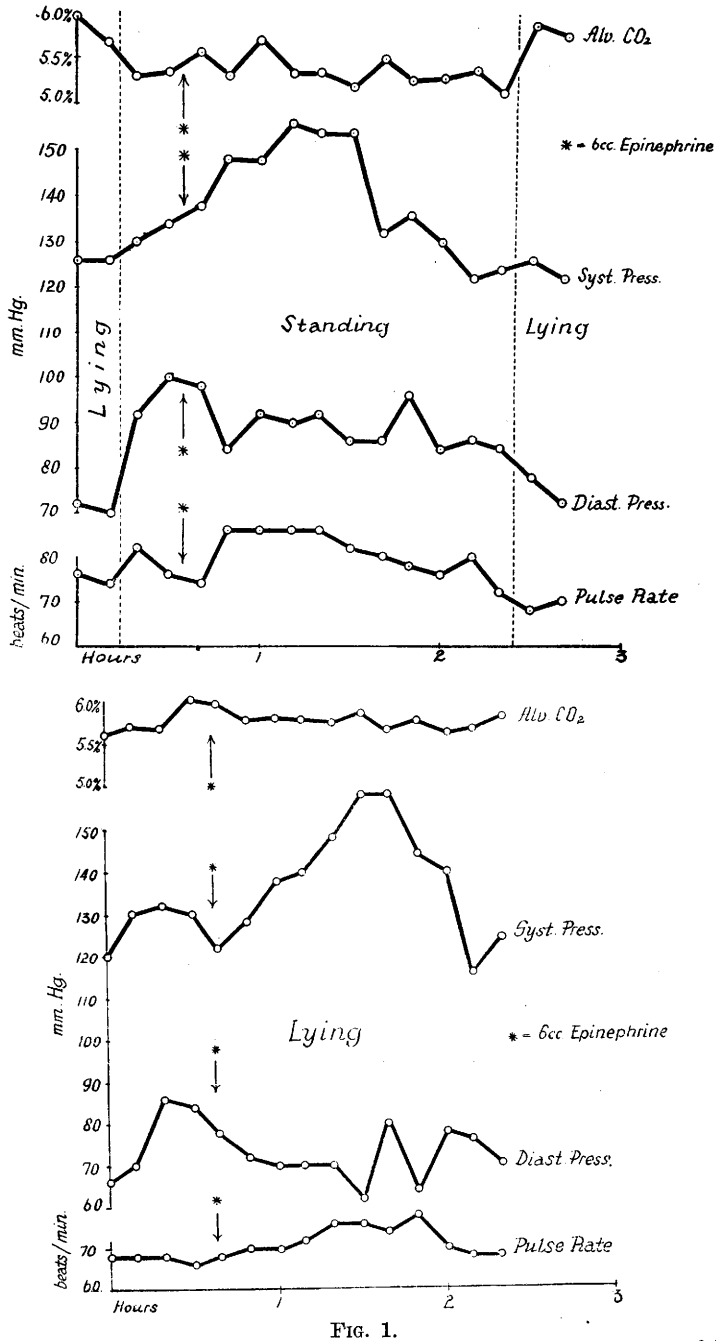

FIG. 1.

Effects of 0.6 cc epinephrine (1-1000) subcutaneously on the same subject in different postures.

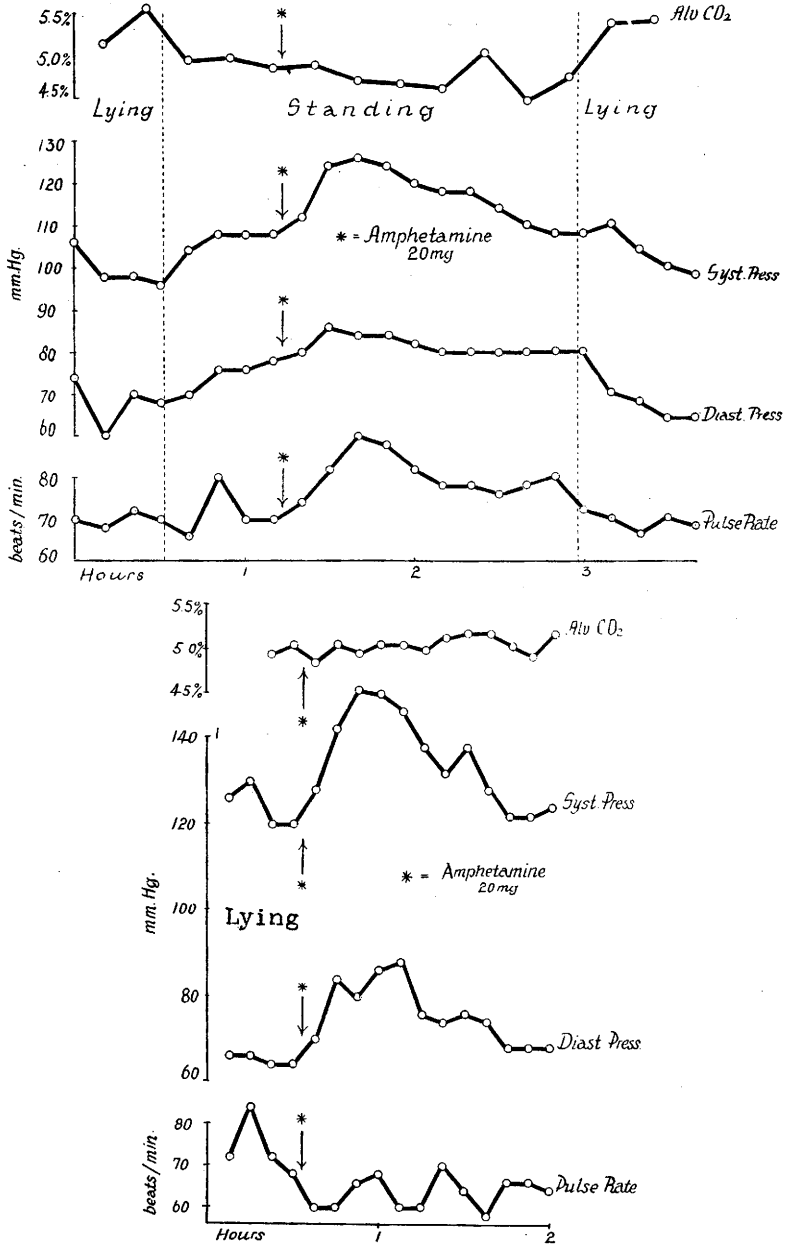

FIG. 2.

Effects of 20 mg amphetamine sulfate subcutaneously to one subject in different postures.

Fig. 2 illustrates the effect of 20 mg of amphetamine sulfate on the same subject, lying and standing. Considerable variation was

found, even in the same individual from day to day. A dose that would produce a rise of 20 mm Hg in blood pressure in one day, might produce a rise of only half as much the next week. Neither drug had a distinct effect upon the respiratory rate.

Since increasing the systemic blood pressure and thereby probably restoring the normal pressure in the carotid sinus, did not restore the alveolar CO_2 to normal, we must assume that the overventilation of standing may not be due to the drop in blood pressure in the carotid sinus and we are forced back to the remaining hypothesis, that the respiratory stimulation is due to a relative ischemia of the brain. These results would indicate that the rise in alveolar CO_2 on bending over while standing,[7] may be due not to the return to normal pressure in the carotid sinus, but rather to relief of the cerebral ischemia. It at first seemed illogical that the drop in blood pressure in the carotid sinus on standing should not cause respiratory stimulation, but it may be that the probable *increase* of pressure in the aorta on standing exactly neutralizes the *drop* in blood pressure in the carotid sinus.

Conclusion. Neither epinephrine nor amphetamine in the doses used affected the alveolar CO_2 tension of subjects when standing or lying. Consequently the lowered alveolar CO_2 of the erect posture may be due to a relative cerebral ischemia.

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Twenty-four Hour Response to Androgens in the Immature Male Rat.*

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Astwood[1] has demonstrated that estrogens cause a measurable increase in the uterine weight of the immature rat within 6 hours after administration. The weight increment which is largely due to increased hydration of the uterine tissues forms the basis for his

* Aided by a grant from Ciba Pharmaceutical Products, Inc.

1 Astwood, E. B., *Endocrinology*, 1938, **23**, 25.