

TABLE II.  
Action of Sulfathiazole, Sulfapyridine and Sulfamethylthiazole *in vivo*.

Strain	No. of mice in each group	ST	SP	SMT	Control
MK NH	30	22*	3	22	0
Co. NH	40	17	4	14	3
469 H	30	15	2	9	2
687 H	30	21	3	15	1
631 H	20	20	6	18	2
Total	150	95	18	78	8
% of survivors whose organs gave positive cultures		14%	18%	25%	12.5%

H—Hemolytic strain. NH—Non-hemolytic strain.

\* Figures indicate number of survivors over 31-day period.

*Staphylococcus aureus* recovered from the mice treated with each of the 3 drugs.

*Summary.* In *in vitro* experiments with *Staphylococcus aureus* sulfamethylthiazole has shown greater bacteriostatic activity than sulfathiazole; the activity of the latter was in turn greater than that of sulfapyridine. In *in vivo* experiments with the same organism sulfapyridine has had little, if any, activity. Both sulfathiazole and sulfamethylthiazole have protected mice and the former drug has been slightly but consistently more active than the latter.

## 11266

### Mechanism of the Blood Pressure Response to Anoxia During Hypoglycemia.

A. VAN HARREVELD AND W. L. MCRARY.

*From the William G. Kerckhoff Laboratories of the Biological Sciences, California Institute of Technology, Pasadena, California.*

Gellhorn, Ingraham and Moldavsky<sup>1</sup> found that breathing a mixture of 6.2% oxygen in nitrogen caused a marked rise in blood pressure in dogs which had been made hypoglycemic by the injection of insulin. Intravenous injection of glucose made this blood pressure

<sup>1</sup> Gellhorn, E., Ingraham, R. C., and Moldavsky, L., *J. Neurophysiol.*, 1938, 1, 301.

response disappear. Since, according to Ingraham and Gellhorn,<sup>2</sup> this rise in blood pressure is not due to a discharge of adrenalin, the authors first mentioned assumed that this phenomenon is caused by a "tremendous excitation of the sympathetic centers." Lambert and Gellhorn<sup>3</sup> reported (contrary to Heymans, Nowak and Samaan<sup>4</sup>) that the rise in blood pressure caused by the inhalation of a gas mixture low in oxygen is not due to a direct stimulation of the medullary centers but to a stimulation of the chemoreceptors in the carotid sinus and in the thorax, causing through a reflex the rise in blood pressure. Therefore, Gellhorn, Ingraham and Moldavsky think it probable that the responsiveness of the medullary centers to these impulses is increased by hypoglycemia.\*

The same phenomena have been observed in man by Kraines and Gellhorn<sup>5</sup> under similar conditions, and Gellhorn<sup>6</sup> has used the above assumptions to explain the therapeutic effect of insulin shock in cases of schizophrenia.

When trying to explain the large rise in blood pressure from anoxia during hypoglycemia it should be kept in mind that the blood pressure is the resultant of a large number of often opposite reactions. Heymans and Bouckaert<sup>7</sup> emphasized that the excitability of the central nervous system (c.n.s.) is an important factor in determining the result of anoxia on the blood pressure.

To investigate the influence of the excitability of the c.n.s. on the blood pressure response to anoxia, this reaction was studied at various levels of narcosis. The blood pressure was recorded with a mercury manometer connected with one of the carotid arteries. The dye "fastusol BBA" served as an anticoagulant.<sup>8</sup> In very superficial narcosis the blood pressure response of dogs, cats and rabbits to breathing nitrogen or a gas mixture of 4.7% oxygen in nitrogen for 1 to 2 minutes (either spontaneously or by artificial respiration) was inconsistent; sometimes a small rise resulted, but in other experiments an appreciable fall of the blood pressure was observed. In all experiments deepening of narcosis (chloralose or nembutal) increased

<sup>2</sup> Ingraham, R. C., and Gellhorn, E., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 315.

<sup>3</sup> Lambert, E., and Gellhorn, E., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 427.

<sup>4</sup> Heymans, C., Nowak, S. J. G., and Samaan, A., *Compt. Rend. Soc. Biol.*, 1934, **117**, 248.

\* Assuming that the response of the chemoreceptors to anoxia is the same in the hypoglycemic and in the normal state.

<sup>5</sup> Kraines, S. H., and Gellhorn, E., *Am. J. Psychiatry*, 1939, **95**, 1067.

<sup>6</sup> Gellhorn, E., *Arch. Neurol. Psychiat.*, Chicago, 1938, **40**, 125.

<sup>7</sup> Heymans, C., and Bouckaert, J. J., *Ergebn. Physiol.*, 1939, **41**, 28.

<sup>8</sup> Modell, W., *Science*, 1939, **89**, 349.

the rise in blood pressure as a response to anoxia, or changed the fall of the pressure during anoxia into a rise. As narcosis became deeper the blood pressure level often fell, so that the blood pressure rise as a response to anoxia, though larger, often failed to reach as great a height as a similar rise during light narcosis. In Fig. 1 are shown 3 responses to anoxia in an experiment which does not have this disadvantage. A cat of about 3 kg body weight was given artificial respiration and at 10-minute intervals the animal was caused to breathe nitrogen instead of air for a period of 1 minute. The response in very light narcosis (100 mg chloralose) was a very marked fall of the blood pressure accompanied by a decrease of the heart rate (A). Three previous periods of anoxia in this state of narcosis had given almost identical curves. After injecting another 100 mg of chloralose the blood pressure response (B) consisted of a rise followed by a fall. In curve A also, a suggestion of this initial rise can be seen. After the injection of another 100 mg of chloralose the initial rise was still larger and the following fall in blood pressure had diminished materially (C). The blood pressure was practically the same at these 3 levels of narcosis. These experiments suggest that a moderate depression of the functions of the c.n.s. favors a blood pressure rise as a response to anoxia. It is likely that this is caused by a suppression by the narcosis of reactions counteracting a marked rise in blood pressure, either caused directly by the anoxia or indirectly by a slight rise in blood pressure (*e. g.*, the carotid sinus pressure reflex). It has to be assumed that these latter reactions are depressed more markedly by the narcosis than are the reactions causing the rise in blood pressure.

It is well known that hypoglycemia causes a depression of the functions of the c.n.s., which can in severe conditions lead to coma. Less severe hypoglycemia also depresses the functions of the c.n.s. as has been shown by Wiedeking<sup>9</sup> for cortical functions. It is therefore quite possible that the combined effects of hypoglycemia and narcosis caused, in the experiments of Gellhorn, Ingraham and Moldavsky, a depression of the c.n.s. to such a degree that anoxia brought about a marked rise in blood pressure because the reactions counteracting this rise were depressed. To examine this conception the effect of hypoglycemia on one of the reactions counteracting a marked rise in blood pressure was investigated, namely the depressor reflex in the rabbit. Two to 3 hours after the intravenous injection of 10 to 15 units of insulin per kg body weight in the fasting animal, the depressor nerve was isolated and the carotid artery arranged for

---

<sup>9</sup> Wiedeking, J., *Z. ges. Neurol.*, 1937, **150**, 417.

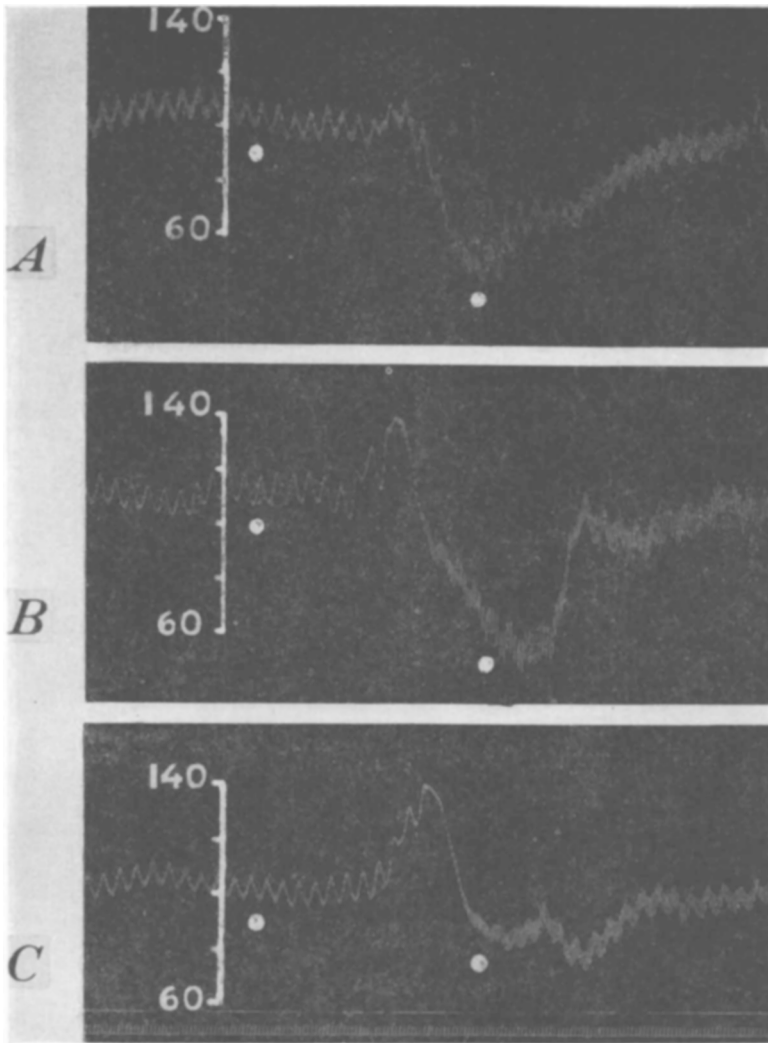


FIG. 1.

Three blood pressure responses to anoxia (nitrogen for 1 minute) at 3 levels of narcosis in a cat of 3 kg bodyweight. The white dots indicate the beginning and end of introducing nitrogen into the apparatus for artificial respiration. "A" after administering 100 mg of chloralose, "B" after a total of 200 mg, and "C" of 300 mg of chloralose. Time intervals, 1 second.

blood pressure recording. The animals usually were in a hypoglycemic coma and showed occasional convulsions. Chloralose or nembutal was used as narcotic. The blood sugar was determined before and after the intravenous injection of 3 to 5 gr glucose. The depressor nerve was stimulated faradically with maximal stimuli.

TABLE I.  
Blood pressure level and fall in blood pressure during 10 sec stimulation of the depressor nerve

Exp.	Before glucose		After glucose				Blood sugar in mg/100 cc	
	B.p. level	B.p. fall	10 min		20 min		Before glucose	After glucose
			B.p. level	B.p. fall	B.p. level	B.p. fall		
1	80	21	86	28	88	34	30	197
2	76	0	80	4	46	4	—	—
3	64	16	68	26	60	28	41	249
4	72	9	74	14	76	26	30	215
5	58	0	56	11	60	16	48	225
6	—	3	—	4	—	6	—	—
7	76	3	80	13	80	14	—	—
8	88	3	84	11	88	12	30	152

Before injecting glucose the depressor nerve was stimulated repeatedly; no large fluctuations of the responses were observed. In all the cases presented in Table I the fall in blood pressure during 10 sec of depressor stimulation was larger after administering glucose than during hypoglycemia. It takes about 20 minutes for this effect of the glucose injection to fully develop. In some cases (2 and 5) the stimulus did not cause any reaction during hypoglycemia; after injection of glucose, however, the same stimulus caused an appreciable fall. It can be concluded that this reflex, like many other reactions of the c.n.s., can be depressed by hypoglycemia.

On repeating Gellhorn, Ingraham and Moldavsky's experiment on the rabbit we found in part of the cases no marked blood pressure rise caused by anoxia, though the blood sugar level was found to be quite low. It is possible that this is characteristic for the rabbit, since Gellhorn, Ingraham and Moldavsky, working on the dog, did not report this inconstancy. It must be assumed that in these cases the combined effect of hypoglycemia and narcosis did not depress markedly the reactions counteracting a blood pressure rise. In agreement with this the depressing effect of hypoglycemia on the depressor reflex was found only in part of the experiments, in the others the injection of glucose in the hypoglycemic animal caused no change in this reflex.

This explanation of the marked rise in blood pressure as a response to anoxia during hypoglycemia, as a depression of the functions of the c.n.s. is quite in keeping with the usual depressing effect of hypoglycemia on the c.n.s.

*Conclusion.* The large blood pressure rise due to anoxia, observed during hypoglycemia, may be caused by a severe depression by the combined effect of narcosis and hypoglycemia of those reactions which counteract a marked rise in blood pressure, the reactions causing this rise in blood pressure being less severely depressed.