

TABLE III.
Growth Promoting Effect of Various Materials in Cyanide Medium.

Material tested	Apparent potency
Yeast extract (standard of reference)	1.0
Filtrate preparation	0.18
Eluate preparation	0.07
Casamino acids	0.20
Yeast extract (1 mg) + filtrate (1 mg equivalent)	2.1
Yeast extract (1 mg) + eluate (1 mg equivalent)	1.0
Yeast extract (1 mg) + casamino acids (1 mg)	2.0
Filtrate + eluate (equivalent amts of each)	1.0
Filtrate (1 mg equivalent) + casamino acids (1 mg)	0.40
Eluate (1 mg equivalent) + casamino acids (1 mg)	1.1
Filtrate + nicotinic acid (10 γ per tube)	0.27
Filtrate + folic acid (20 γ per tube)	0.22
Filtrate + nicotinic acid (10 γ) + folic acid (20 γ)	0.36

acid other than the ones tested or that its effect is a composite one due to several amino acids.

Even though nicotinic acid (or its amide) and folic acid were found to be somewhat stimulatory, neither individually nor variously combined did they behave in the same manner as did the eluate principle.

By repeated adsorption and elution from charcoal, a preparation was obtained which was approximately 8 times as active as that resulting from the initial treatment of yeast extract. A 6-fold concentration of the eluate principle was achieved by refluxing yeast extract with 95% ethyl alcohol and treating the soluble fraction once with Darco G-60.

Evidence indicating that the activity of eluate preparations does not depend on a single substance was derived by subjecting the principle to electrolysis at high voltage in the electrical transport apparatus described

by Williams and Truesdail.⁵ The active principle was not concentrated in a single cell but was distributed throughout the 4-cell system employed.

Summary. Yeast extract has been shown to reverse the inhibition of yeast growth caused by cyanide. No known compound was found which duplicated the action of yeast extract, although methionine and cysteine had some "anti-cyanide" activity. Excess pantothenic acid had a beneficial effect on growth under certain conditions.

It has been demonstrated that the action of yeast extract depends on at least 2 substances which can be separated by charcoal adsorption. Indirect evidence indicates that the activity of both filtrate and eluate principles is due to more than a single substance.

⁵ Williams, R. J., and Truesdail, J. H., *J. Am. Chem. Soc.*, 1931, **53**, 4171.

15722

Effects of Various Anesthetic Agents on the Blood Pressure of the White Rat.*

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In an investigation involving the role of the autonomic nerves in cardiovascular disorders it was found desirable to measure the

blood pressure repeatedly in rats without injury to the animals and to determine the effect of anesthetic agents on the blood pressure. A survey of the literature showed that the apparatus used was varied and that de-

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terminations of blood pressure were in many cases inconsistent. In some instances no mention was made of the anesthesia used.

The observations of Page and Reed,¹ Williams, Harrison and Grollman,² Kempf and Page,³ and Medoff and Bongiovanni⁴ are somewhat in agreement. All of their blood pressure determinations fall within a range of 100 to 140 mm Hg. Duncan, Hyman and Chambers⁵ reported blood pressure determinations from 90 to 140 in unanesthetized rats and from 70 to 120 in anesthetized animals. The studies of Telford, Swegart and Schoern⁶ are in agreement with those of the above workers, but in addition they found, in animals one year older, a blood pressure range between 84 and 95. Proskauer, Neumann and Graef⁷ reported normal blood pressure readings of 60 to 95 mm Hg. Duncan *et al.*⁵ found a decrease in blood pressure within a range of 70 to 120 in anesthetized animals and Byrom and Wilson,⁸ using ether, obtained blood pressures from 72 to 132 mm Hg.

Corcoran and Page,⁹ studying the effects of pentobarbital-sodium on the blood pressure of dogs, reported an increase in blood pressure, whereas Mylon, Winternitz and de Suto-Nagy¹⁰ found that nembutal simulates a condition like shock causing a lowering in blood pressure. Grimson, Kernodde and Hill,¹¹

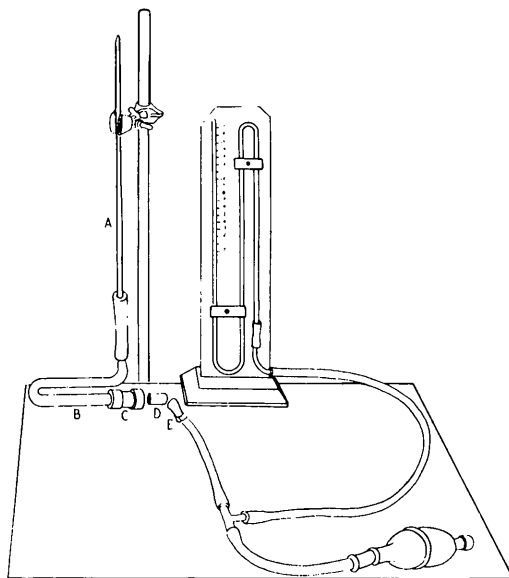


FIG. 1.

Blood pressure apparatus: A, 0.2 mm pipette; B, plethysmograph; C, gland; D, metal cuff; E, rubber pressure cuff.

studying the effects of various anesthetics on the blood pressure of dogs, obtained wholly inconsistent results.

In a study of spinal anesthesia in a large number of human cases Koster¹² found that it lowered the blood pressure which he believes due to a decrease in cardiac output.

Methods. In the present study, 40 female white rats of the Wistar Strain weighing 135 to 200 g were used. The room temperature at the time of the determinations was kept at $25 \pm 2^\circ\text{C}$. A modification of the tail plethysmograph method of Byrom and Wilson⁸ was used to determine blood pressure. It was found that the pressure cuff described by Griffith and Jeffers¹³ was most suitable. The plethysmograph consisted of a piece of bent glass tubing with a bore of 1 cm and a 0.2 mm bacteriological pipette (Fig. 1).

Unanesthetized rats were wrapped in a Turkish towel. In a short time they became quiescent and did not appear to be disturbed by the procedure. From 4 to 6 readings were

¹ Page, E. W., and Reed, R., *Am. J. Physiol.*, 1945, **143**, 122.

² Williams, J. R., Harrison, T. R., and Grollman, A., *J. Clin. Invest.*, 1939, **18**, 373.

³ Kempf, G. F., and Page, I. H., *J. Lab. and Clin. Med.*, 1942, **27**, 1192.

⁴ Medoff, H. S., and Bongiovanni, A. M., *Am. J. Physiol.*, 1945, **43**, 297.

⁵ Duncan, G. W., Hyman, C., and Chambers, E. L., *J. Lab. and Clin. Med.*, 1943, **28**, 886.

⁶ Telford, I. R., Swegart, J. E., and Schoern, C., *Am. J. Physiol.*, 1945, **143**, 214.

⁷ Proskauer, C. G., Neumann, C., and Graef, I., *Am. J. Physiol.*, 1945, **143**, 290.

⁸ Byrom, F. B., and Wilson, C. J., *J. Physiol.*, 1938, **93**, 301.

⁹ Corcoran, A. C., and Page, I. H., *Am. J. Physiol.*, 1943, **140**, 234.

¹⁰ Mylon, E., Winternitz, M. C., and de Suto-Nagy, G. J., *Am. J. Physiol.*, 1943, **139**, 313.

¹¹ Grimson, K. S., Kernodde, C. E., and Hill, H. C., *J. A. M. A.*, 1944, **126**, 218.

¹² Koster, H., *Arch. Surg.*, 1942, **45**, 596.

¹³ Griffith, J. A., and Jeffers, W. A., *The Rat in Laboratory Investigations*, 1942, J. B. Lippincott Co., Phila., p. 274.

TABLE I.
Effects of Various Anesthetic Agents on Systolic Blood Pressure of the White Rat.

	Mean, mm Hg.	Stand. dev., mm Hg.	Range, mm Hg.
Unanesthetized	124.8	7.54	102-140
Nembutal	104.1	7.78	86-115
Amytal	103.5	6.01	94-112
Ether (shallow)	117.0	4.62	110-126
Ether (deep)	104.0	4.91	95-110
Urethane	78.4	3.75	72- 84
Morphine	63.9	1.31	62- 70

made on each animal. If there was marked variation in the readings they were discarded and others were taken at a later time. The anesthetics used were given in the following dosages: pentobarbital-sodium (nembutal), 4 mg/100 g; sodium isoamylethyl barbiturate (amytal), 4 mg/100 g; ethyl carbamate (urethane), 20 mg/100 g; and morphine sulphate, 10 mg/100 g. Ether was applied by sponge. The other agents were all administered by intraperitoneal injection. In order to test the apparatus for high blood pressure some rats were made hypertensive by a high tryosine diet and others were injected with adrenalin. All the tabulations obtained from the observations were treated to a statistical analysis.

Results. The experimental data obtained are summarized in Table I. In the unanesthetized group only one rat had a blood pressure as low as 102 mm Hg and only one had a pressure as high as 140 mm Hg. The remaining animals were in a range between 113 and 132. Animals of 2 groups, one with an average weight of 140 g and the other with an average weight of 200 g showed no significant differences in their blood pressures.

Rats that had been placed on a 10% tyrosine diet for 2 weeks preceding their blood pressure determination showed a mean arterial systolic pressure of 168 mm Hg. Those injected with 0.5 cc of 1/1000 adrenalin showed a rise in the systolic pressure from the normal level to 180 mm Hg.

The pressure then increased at a slower rate until it reached a peak of 210 mm Hg after which it receded to a normal level.

When ether was used there was considerable variation in the blood pressure determinations in individual rats. There was a marked decrease in blood pressure during the application of the ether sponge or shortly after, a rise in pressure when the effects of the ether subsided. Experiments on several animals indicate that there is a direct correlation between the decrease in blood pressure and the depth of the anesthesia.

The markedly lowered pressures that were obtained with the use of morphine and urethane may be explained on the basis of the vasodilator effects of these agents. The barbiturates (nembutal and amytal), according to Roth,¹⁴ act as cardiac depressants in the white rat which may account, to some extent, for the decrease in blood pressure.

Summary. The method of Byrom and Wilson as modified for this study is well adapted for the determination of blood pressure in the rat. The mean arterial systolic pressure in the unanesthetized animal was found to be 124.8 mm Hg. The mean pressures obtained by the use of anesthetic agents were as follows: nembutal—104.1, amytal—103.5, ether (shallow)—117, ether (deep)—104, urethane—78.4, morphine—63.9 mm Hg.

¹⁴ Roth, G. B., *Arch. Intern. de Pharm. et de Therap.*, 1935, **51**, 179.