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The Pharmacological Actions of Phenylethanolamine.

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Phenylethanolamine (*a*-phenyl-*b*-aminoethanol) is related chemically to tyramine, epinephrine and ephedrine. According to the recent work of Alles¹ its circulatory stimulant efficiency would be higher than that of ephedrine. In view of this and because its general pharmacological action have not been previously studied it was thought desirable to make a survey of its possibilities. The product used was synthesized as the sulphate by Gr. Gordon A. Alles of the Clinic of Dr. George Piness, Los Angeles, who generously donated a large quantity to the laboratory. The method of synthesis eliminated contamination with its position isomer (*b*-phenyl-*b*-aminoethanol). The product consisted of white glistening crystals; was freely soluble in water, and had a melting point of 239-240°C.

The toxicity of phenylethanolamine is relatively low, the minimal fatal dose intravenously in white rats is about 0.14 gm. per kilo, which is the same as that of ephedrine reported by Chen.² This tendency to low toxicity agrees with the results of Alles¹ on guinea pigs and rabbits. Doses of 1 to 5 mg. per kilo intravenously in anesthetized dogs, cats and rabbits promptly raised the blood pressure from 25 to 103%, and accelerated the pulse to 42%, the effects persisting about 10 minutes, and hence qualitatively resembling tyramine. There seemed to be less cardiac depression with phenylethanolamine than with ephedrine. During the blood pressure rise the pupils dilated, while the hind leg and intestine usually were passively dilated, but occasionally were constricted. In cats, the pressor action was not reversed by ergot, but was abolished by cocaine during sensitization to epinephrine, resembling the actions of tyramine³ and ephedrine.⁴ In rabbits, cocaine diminished but did not abolish the rise of blood pressure. Circulatory effects from gastric administration were inconclusive. Respiration in cats and rabbits showed no constant changes, but in rats there was a marked increase in rate with sublethal doses.

Concentrations of 1:25,000 to 1:2,500 applied to strips of excised rabbit and cat intestine, using the Magnus method, caused an inhibition and fall of tonus, but either inhibition or stimulation with guinea pig intestine. The nonpregnant uterus of the rabbit

and pregnant guinea pig uterus were stimulated by both the amine and epinephrine, while the nonpregnant cat uterus was stimulated by the amine but relaxed by epinephrine, thus again resembling tyramine and ephedrine. Bronchi constricted from histamine and pilocarpine were not effectively relaxed by phenylethanolamine or ephedrine, while epinephrine caused relaxation; additional tests are necessary. Administered subcutaneously and intravenously, phenylethanolamine was less effective than epinephrine, about as effective as tyramine, but more effective than ephedrine in preventing the experimental edema of paraphenylenediamine and equally as effective as epinephrine in dionine chemosis, but ineffective (also tyramine and ephedrine) against mustard oil chemosis and dermatitis. Local application of 1% concentrations in the nose of human subjects shrank congested nasal mucosae and turbinates promptly without objectionable irritation, the effects persisting 2 to 3 hours, thus resembling ephedrine.

Provisionally, the pharmacological actions of phenylethanolamine resemble those of tyramine and ephedrine more than epinephrine. Further tests are being made experimentally and clinically.

¹ Alles, G. A., *J. Pharm. Exp. Therap.*, 1927, xxxii, 121.

² Chen, K. K., *J. Pharm. Exp. Therap.*, 1926, xxvii, 61.

³ Tainter, M. L., and Chang, D. K., *J. Pharm. Exp. Therap.*, 1927, xxx, 193.

⁴ De Eds, F., and Butt, E. M., *PROC. SOC. EXP. BIOL. AND MED.*, 1927, xxiv, 800.

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Excretion, Distribution and Fate of Bismuth Under Clinical Conditions.

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The object of this study is to determine the limitations and usefulness, and, if possible, to establish better control, of bismuth therapy in syphilis by quantitative studies of the excretion of bismuth in urine and feces, its distribution in body fluids and organs, influence of various conditions on mobilization of stored bismuth, relationship of bismuth concentration and dosage to therapeutic efficiency, toxicity, etc., in human subjects, both convalescent and syphilitic. The plan includes also a study of various agents and