

resistance towards the bacteriostatic activity of penicillin. 3. Small colony variants of the same strain of *Staphylococcus* produced by the exposure to BaCl_2 possessed likewise a considerable resistance to penicillin. 4. All these strains of small colony variants regard-

less of their origin acquired also a certain degree of resistance towards methyl violet. 5. The resistance of these strains of small colony variants towards penicillin cannot be considered to be a specific drug-resistance.

14193

Effect of Neosynephrin* on Gaseous Exchange of the Brain.†

H. E. HIMWICH, C. DALY, AND J. F. FAZEKAS.

From the Department of Physiology and Pharmacology, Albany Medical College, Union University, Albany, N.Y.

The effects of neosynephrin on the cerebral arterio-venous oxygen difference were studied on large dogs, narcotized with Dial,‡ 0.5 cc per kilo. The cranium was trephined above the superior longitudinal sinus, the trachea was exposed and cannulated and both femoral arteries were also exposed. The first pair of femoral arterial and cerebral venous blood samples was collected while the animals were breathing air and the second after they had come to equilibrium while respiring a gas mixture containing approximately 11% oxygen. Neosynephrin was then administered and when blood pressure had risen significantly the third pair of blood samples was collected. Blood flow of the cerebral longitudinal sinus was determined by Daly's modification of the thermostromuhr.¹ Blood pressure was recorded by means of a cannula inserted into a femoral artery. Blood samples were analyzed for oxygen and carbon dioxide contents and oxygen capacity,² for glucose,³ and for lactic acid.⁴ The oxygen tension of the blood was

estimated by using the nomogram of Bock *et al.* for humans⁵ which may also be applied to dogs.⁶ In addition, the effects of neosynephrin on the cerebral arterio-venous oxygen difference were determined on dogs breathing room air. In most experiments 2 cc of 1% neosynephrin solution were administered intramuscularly, portions of the 2 cc being injected at various sites. In a few experiments, however, 1-10,000 neosynephrin solution was injected intravenously and in these instances the amount of neosynephrin injected was much smaller than with intramuscular injection.

In Table I are presented the results of 2 out of 4 experiments on animals breathing reduced concentrations of oxygen. In all 4 experiments the blood became more alkaline as a result of the hyperpnea produced by breathing 11% oxygen and then less alkaline after injections of neosynephrin. Neosynephrin increased the concentrations of lactic acid and glucose in the blood. Blood pressure was

* We are grateful to Dr. Richard M. Johnson of the Frederick Stearns & Company for his generous supplies of Neosynephrin Hydrochloride.

† Aided by a grant from the Albion O. Bernstein Memorial Fund.

‡ We are grateful to Dr. E. Oppenheimer of the Ciba Pharmaceutical Products for his generous supplies of Dial Urethane Solution.

¹ Himwich, H. E., Bowman, K. M., Daly, C., Fazekas, J. F., Wortis, J., and Goldfarb, W., *Am. J. Physiol.*, 1941, **132**, 640.

² Van Slyke, D. D., and Neill, J. M., *J. Biol. Chem.*, 1924, **51**, 523.

³ Hagedorn, H. C., and Jensen, B. N., *Biochem. Z.*, 1923, **135**, 63.

⁴ Friedemann, T. E., Cotonio, M., and Shaffer, P. A., *J. Biol. Chem.*, 1927, **73**, 335.

⁵ Bock, A. V., Dill, D. B., Hurxthal, L. M., Lawrence, J. S., Coolidge, T. C., Dailey, M. E., and Henderson, L. J., *J. Biol. Chem.*, 1927, **73**, 749.

⁶ Dill, D. B., Edwards, H. T., Florkin, M., and Campbell, R. W., *J. Biol. Chem.*, 1932, **95**, 143.

TABLE I.
Effects of Injection of Neosynephrin on Oxygen Relationships of Dogs Respiring 11% Oxygen Under Dial.

			O ₂	O ₂	Hemo-	O ₂	pH	Sinus	Blood	Glucose,	Lactic
			content,	capacity,	globin	tension,		blood			
			vol. %	vol. %	satur., %	mm Hg		flow, cc/min	pressure, mm Hg.	mg %	acid, mg %
Dog No. 1	Room air	Art.	20.0	21.1	95	100	7.17	8.4	90	112	17
		Ven.	8.3		39	33	7.15				
		Diff.	11.7		56	67					
	11% O ₂	Art.	11.5	22.3	52	34	7.28	9.0	105	117	18
		Ven.	2.8		13	16	7.20				
		Diff.	8.7		39	18					
	11% O ₂ + Neosyn.	Art.	12.0	22.3	54	37	7.23	11.4	180	166	31
		Ven.	4.4		20	24	7.15				
		Diff.	7.6		34	13					
Dog No. 2	Room air	Art.	17.6	18.5	95	90	7.30	7.4	110	95	57
		Ven.	10.3		56	38	7.23				
		Diff.	7.3		39	52					
	11% O ₂	Art.	14.6	18.4	82	53	7.35	8.2	120	170	63
		Ven.	5.1		29	22	7.26				
		Diff.	9.5		53	31					
	11% O ₂ + Neosyn.	Art.	11.1	20.0	55	34	7.31	12.0	154	197	66
		Ven.	5.1		26	23	7.23				
		Diff.	6.0		29	11					

TABLE II.
Effect of Neosynephrin on Cerebral Arterio-Venous Oxygen Differences, Blood Sugar and Blood Pressure of Dogs Respiring Room Air.

Neosynephrin		O ₂ content, vol. %		Glucose, mg %	Blood pressure, mm Hg.
Dog No. 1	Before	Art.	22.4	100	125
		Ven.	11.3	93	
		Diff.	11.1	7	
	After	Art.	22.0	114	150
		Ven.	13.6	111	
		Diff.	8.4	3	
Dog No. 2	Before	Art.	23.8	107	100
		Ven.	13.4	103	
		Diff.	10.4	4	
	After	Art.	22.6	124	133
		Ven.	14.3	118	
		Diff.	8.3	6	

elevated following the injection of neosynephrin and accordingly blood flow through the brain accelerated.⁷ As a result of the more rapid cerebral blood flow the cerebral arterio-venous oxygen difference was diminished and the difference in tensions of the oxygen of arterial and venous blood was also decreased. Table II reveals similar results in 2 of the 8 experiments made on animals

⁷ Forbes, H. S., *Arch. Neurol. and Psychiat.*, 1940, **43**, 804.

breathing air. In each of these experiments the arterio-venous oxygen difference decreased after the injection of neosynephrin because the oxygen content of the venous blood rose. According to Courtice⁸ the pressure of oxygen in the venous blood is representative of that in the brain. It is, therefore, suggested that the effect of neosynephrin to raise the oxygen of the venous blood may produce a similar change in the brain.

⁸ Courtice, F. C., *J. Physiol.*, 1941, **100**, 198.