Linkage between S and sickling could not be found. The blood groups MN and S afforded evidence for linkage thus fitting into the very considerable evidence on this point for Caucasians.

1. Snyder, L. H., Russell, H., Graham, E. B., *Science,* 1947, v106, 347.
2. Snyder, L. H., Clarke, H., Moore, C. V., *Ohio J. Sci.,* 1949, v49, 32.
3. Snyder, L. H., *Hereditas, Suppl.* 1949, 446.
4. Race, R. R., Sanger, R., Lawler, S. D., Bertinshaw, D., *Heredity,* 1949, v3, 205.
5. Sanger, R., Race, R. R., *Nature,* 1947, v160, 505.
6. Levine, P., Kuhmichel, A. B., Wigod, M., and Koch, E., PROC. SOC. EXP. BIOL. AND MED., 1951, v78, 218.
7. Neel, J. V., and Hanig, M., *Genetics,* 1951, v36, 84.
8. Finney, B. A., *Ann. Eugenics,* 1940, v10, 171.
9. Fisher, R. A., *Ann. Eugenics,* 1935, v6, 187; v6, 339.
10. Neel, J. V., *Science,* 1949, v110, 64.

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Effect of Dihydroergotamine on Epinephrine Response in the Hind-Limb of Dogs.* (19663)

LEWIS D. FINK AND TED A. LOOMIS.

From the Department of Pharmacology, School of Medicine, University of Washington, Seattle.

The vasoconstrictor action of exogenous epinephrine can be blocked readily with the various ergot alkaloids(1). Conclusions based primarily on changes in the systemic blood pressure indicate that these alkaloids will not block the vasodilator response of epinephrine. On the other hand the ergot alkaloids will block the inhibitory action of epinephrine on isolated intestinal strips(2-4). There may be no similarity between the mechanism of inhibition of the intestine by epinephrine and the vasodilator response on the vascular system. Nickerson(1) objects to the use of the intestine to investigate the effect of ergot compounds on the inhibitory action of epinephrine because of the presence of intramuscular parasympathetic ganglia in this tissue and the potentiation of the cholinergic response with some of the ergot alkaloids. The experiments reported here were designed to determine the influence of ergot alkaloids on the response of the vascular system of the hind-limb of dogs to intra-arterially injected epinephrine.

Method and material. Dogs of either sex and weighing between 12 and 23 kg were anesthetized with 25 mg/ kg of thiopental and 40 mg/kg of chloralose. Through a mid-line abdominal incision, all branches of the lower 5 to 8 cm of the abdominal aorta and inferior vena cava, except the common iliac artery and vein for the experimental leg, were ligated. Blood flow from the experimental hind-leg was measured with a bubble flowmeter inserted into the common iliac vein. The blood was returned to the inferior vena cava by way of the opposite common iliac vein. The temperature in the flowmeter was maintained at 37°C by means of a water jacket. Blood pressure was recorded from the common iliac artery of the opposite leg and the heart rate was recorded with the electrocardiograph. The intra-arterial injections were made through a cannula inserted into the middle sacral artery. Intravenous heparin was given periodically throughout the experiment. Fresh solutions of synthetic l-epinephrine,† dihydroergotamine methanesulfonate and Hydregine (CCK-179) were prepared in a 0.9% sodium chloride solution. All intra-arterial injections were of a 2 ml volume and were given over a one minute period.

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† Synthetic l-epinephrine kindly supplied by Stansbury Chemical Co., Seattle; the dihydroergotamine and Hydregine supplied by Mr. Harry Althouse, Sandoz Chemical Co.

TABLE I. Summary of Changes in Blood Flow Response of Hind-Limb of Dogs to Epinephrine Injected Intra-arterially at Various Time Intervals During a 3-Hr Experimental Period. First injection considered the control response.

Epinephrine, γ/kg I.A.	Constriction No reduction	Dilation Partial reduction	Dilation No reduction
1	+	+	
	+	+	
	+	+	
	+		+
3	+	+	
	+	+	

Partial reduction = 25% to 75% decrease in epinephrine response from control.
No reduction = 25% or less decrease in epinephrine response from control.

Results. The procedure and calculation of the results for the experiments were as follows: Approximately 30 to 45 minutes after the bubble flowmeter was incorporated into the system, control blood flow responses were obtained to the intra-arterial injections of one and/or 3 γ per kilo of epinephrine. These quantities of epinephrine produced little or no change in the systemic blood pressure and heart rate. The epinephrine injections were repeated at least twice between ½ to 2½ hours after the intra-arterial injection of 20 γ per kilo of dihydroergotamine. For each epinephrine injection there was calculated the maximal per cent changes in blood flow from the control pre-injection rate. In order to compare the experimental data, this method of calculating the results was used because the pre-injection flow rates would vary throughout the experimental period. The maximal per cent changes in blood flow with each epinephrine injection following the dihydroergotamine were calculated in the same manner and then compared with the control epinephrine responses.

Table I shows that in the absence of dihydroergotamine repeated intra-arterial injections of epinephrine result in no reduction in the vasoconstrictor response and a partial reduction in the vasodilator response. Table II shows that dihydroergotamine completely blocked the vasoconstrictor action of epinephrine but failed to completely block the vasodilator action of epinephrine in the majority of experiments. In 2 additional experiments, Hydregine (CCK-179) in a dose equal to that used for dihydroergotamine resulted in complete blockade of epinephrine vasoconstrictor action but only partial blockade of the vasodilator action.

In the experiments with dihydroergotamine, this substance produced a transient increase in blood flow during the injection, otherwise it had no effect on flow rates.

Discussion. Some of the experiments showed that dihydroergotamine produced a partial decrease in the vasodilating response to epinephrine. This effect of dihydroergotamine could be due to factors other than its direct action on the vasodilator epinephrine mechanism. A decrease in the vasodilator action of epinephrine could be due indirectly to the blocking of the vasoconstrictor effect of epinephrine thereby modifying the concentration and the duration that the epinephrine would remain in contact with the receptor mechanism in the leg vessels. This could explain the fact that the larger dose of epinephrine resulted in a definite systemic effect on heart rate and blood pressure after dihydroergotamine and little or no systemic effect before dihydroergotamine.

Another factor responsible for the decreased vasodilator response of epinephrine could be due to a progressive decrease in the response of the vascular system to repeated injections of epinephrine during the experiment. The present experiments showed no change in the normal vasoconstrictor response of intra-arterial injected epinephrine and a partial reduction of the vasodilator response. The partial blockade of the epinephrine vasodilator response following dihydroergotamine in some of the experiments could be due to the progressive decrease of the normal vasodilator response of repeated injections of epinephrine.

In some of the experiments with dihydroergotamine, there was an increased vasodilator action of epinephrine which subsequently returned toward normal at the end of the experiment. The initial increase in the vasodilator action could be due to the blocking of the vasoconstrictor mechanism thereby unmasking the vasodilator response. The subsequent decrease in the vasodilator response could represent a definite effect of dihydro-

TABLE II. Summary of Effect of Dihydroergotamine on Blood Flow Response to Epinephrine Injected Intra-arterially in Hind-Limb of Dogs. Epinephrine injected between ½ and 2½ hr after intra-arterial injection of 20 γ/kg of dihydroergotamine.

Epinephrine, γ/kg I.A.	Constriction Complete block	Dilation Complete block	Dilation Partial block	Dilation No change	Dilation Iner. response
1	+		+		
	+				+
	+	+			
	+		+		
	+	+			
	+				+
	+			+	
3	+				+
	+		+		
	+				+
	+		+		
	+				+

Complete block = >75%
Partial " = 25% to 75%
No change = 25% or less
} decrease in epinephrine response after dihydroergotamine.

ergotamine on the epinephrine dilator mechanism or a recovery of the vasoconstrictor action.

Conclusions. In blood flow experiments in the hind-limb of dogs, dihydroergotamine completely blocks the vasoconstrictor action of epinephrine but fails to uniformly block the vasodilator action of epinephrine.

1. Nickerson, M., *Pharmacol. Rev.*, 1949, v1, 27.
2. Rothlin, E., *Bull. de l'Acad. Suisse des Sc. Med.*, 1946, v2, 1.
3. Thienes, C. H., PROC. SOC. EXP. BIOL. AND MED., 1929, v26, 501.
4. Nanda, T. C., *J. Pharmacol.*, 1931, v42, 9.

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Effect of Dietary Molybdenum Upon Chicks and Poults.* (19664)

F. H. KRATZER.
From the Division of Poultry Husbandry, University of California, Davis.

When cattle and sheep graze on pastures in which the molybdenum exceeds approximately 10 p.p.m., toxic symptoms may appear which include diarrhea, anemia, weight loss and a change in the color of the hair or wool(1,2). Rats and rabbits can tolerate molybdenum better than ruminants although 500 p.p.m. caused a definite growth retardation and 5000 p.p.m. resulted in the death of all of the rats in one experiment(3-6). Copper is capable of counteracting the symptoms of molybdenum toxicity in both ruminants and rats. The present studies were undertaken to determine the effects of feeding various levels of molybdenum and copper to chicks and poults.

Experimental. Exp. 1, 2 and 3 were conducted with S. C. White Leghorn male chicks while Bronze poults were used in Exp. 4, 5 and 6. Practical chick and poult starting rations were used as basal rations to which various levels of sodium molybdate dihydrate and copper sulfate were added. The basal rations contained 1.5, 1.5, 1.3, 4.0, 6.0, and 1.5 p.p.m. molybdenum in the successive trials. The copper in the basal ration was determined only in Exp. 2, 3, 5 and 6 in which it was found to be 9.9, 8.2, 20.0 and 10.0 p.p.m., respectively. The birds were housed in electrically heated batteries with wire floors and were supplied feed and water *ad libitum*. The birds were weighed at frequent intervals. There were 7, 13, 10, 6, 7 and 10 one-week-