with sodium pantothenate. Our observations are summarized in Table I.

All rats that received vitamin B_6 improved, but 9 of them had a recurrence within an average of 15 days. Of the other 2, one has been receiving vitamin B_6 for 12, the other for 30 days. Of the rats that received a pantothenic acid salt, 2 were cured. One of these was normal at death and the other had a mild recurrence of the dermatitis at the last observation. Some of the others improved but as yet none has made a complete recovery. When both vitamins were supplied simultaneously the animals recovered within a week and made considerable gains in weight. Three other rats, which failed to recover on vitamin B_6 alone and were on the point of death, responded in a similar manner when a pantothenic acid salt was also supplied. One animal died after the dermatitis had disappeared, from a secondary infection in both eyes.

The eyes of the animals which do not respond to vitamin B_6 alone are affected more severely than those of the animals which do not respond to pantothenic acid salts alone. The lids adhere and are soon covered by a large scab. If pantothenic acid is supplied in addition to vitamin B_6 at this stage the scab falls off, leaving a spectacled appearance which disappears without any additional treatment as the hair grows back in the denuded areas. Up to the present the other lesions characteristic of this type of dermatitis, if either vitamin B_6 or a pantothenate is supplied singly, are indistinguishable.

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Potencies of Vitamin K_1 and of 2-Methyl-1, 4-Naphthoquinone.

SIDNEY A. THAYER, R. W. MCKEE, S. B. BINKLEY AND EDWARD A. DOISY.*

From the Department of Biochemistry, St. Louis University School of Medicine, St. Louis.

In a previous investigation[1] we have confirmed the report of the marked antihemorrhagic activity of 2-methyl-1,4-naphthoquinone.[2] A careful comparison of the potencies of this compound and of pure vitamin K_1 by our 18-hour procedure[3] showed that the latter is

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approximately one-half as active as the former. In view of this observation and the report that by the 6-hour procedure vitamin K_1 is only 1/30 as potent as 2-methyl-1,4-naphthoquinone,[4] it seems desirable to publish the results that we have obtained in a comparison of the potencies of the two compounds by the 6-hour observation period.

Experimental. In our experiments. we have used for the evalua-

TABLE I.
Bioassay of Vitamin K_1 and 2-Methyl-1,4-Naphthoquinone.

Exp. No.	Compound	Dosage μg	Chicks used,* No.	Response: Clotting time <10 min %	Response: Clotting time Mean; S.E. min	Response: Prothrombin time, Mean; S.E. sec
1	Vitamin K_1†	0.50	9	11	71.0 ± 24.2	
		1.00	10	30	23.0 ± 4.6	
	2-Methyl‡	0.50	14	50	13.1 ± 2.6	
	Controls	none	8	0	>180.	
2	Vitamin K_1	2.00	10	90	7.3 ± 1.5	
		4.00	9	100	4.5 ± 0.46	
	2-Methyl	0.50	9	67	17.2 ± 4.5	
		1.00	9	100	5.3 ± 0.90	
	Controls	none	9	0	>180.	
3	Vitamin K_1	1.50	14	86	6.0 ± 1.8	
	2-Methyl	0.50	10	50	12.1 ± 2.1	
	Controls	none	10	0	110.	
4	Vitamin K_1	2.00	19	100	4.5 ± 0.46	
	2-Methyl	1.00	20	100	5.2 ± 0.83	
	Controls	none	10	0	100.	
5	Vitamin K_1	1.00	20	75	8.0 ± 0.8	46.6 ± 2.4
	2-Methyl	0.25	15	40	25.6 ± 8.2	76.6 ± 4.3
		0.50	30	70	12.0 ± 2.7	47.0 ± 3.0
	Controls	none	10	0	325.	93.3
6	Vitamin K_1	2.00	15	100	5.8 ± 0.5	28.7 ± 1.2
	2-Methyl	1.00	15	100	5.5 ± 0.4	33.7 ± 0.8
	Controls	none	5	0	361.	99.0

*Chicks used in Exp. 4 were 15 days of age; all others 21.
†Natural vitamin K_1 was used in these experiments.
‡Used in this table as an abbreviation for 2-methyl-1,4-naphthoquinone.

[1] Thayer, S. A., Binkley, S. B., MacCorquodale, D. W., Doisy, E. A., Emmett, A. D., Brown, R. A., and Bird, O. D., *J. Am. Chem. Soc.*, 1939, **61**, 2563.

[2] Ansbacher, S., and Fernholz, E., *J. Am. Chem. Soc.*, 1939, **61**, 1924.

[3] Thayer, S. A., McKee, R. W., Binkley, S. B., MacCorquodale, D. W., and Doisy, E. A., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 194.

[4] Ansbacher, S., Fernholz, E., and MacPhillany, H. B., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 655; Ansbacher, S., Fernholz, E., and Dolliver, M. A., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 652.

tion of the response of the chicks: (1) the percentage of chicks showing a clotting time of less than 10 minutes;[3] (2) the mean clotting time; (3) the mean prothrombin time.[5] Following Ansbacher's suggestion, a solution of the compound in cod liver oil was administered and the blood drawn 6 hours later for the evaluation of the reaction. Each assay included the response of the same lot of deficient chicks to the administration of one or 2 dosages of each compound and the mean clotting time of a control group. The data are summarized in the table.

In Experiments 1, 2, 3 and 4 the volume of cod liver oil used for administration of the compounds was 0.10 cc; in Experiments 5 and 6 only 0.05 cc was used. From other reports and the data of this paper it appears likely that in experiments in which the response is restricted to a period of 6 hours or less the volume of oil used may play a rôle in the absorption of vitamin K_1 and therefore in the apparent potency. We believe that the first 4 experiments of the table (0.10 cc oil used) indicate clearly that vitamin K_1 is approximately one-third as potent as 2-methyl-1,4-naphthoquinone, whereas the more complete data of Experiments 5 and 6 in which only 0.05 cc of solvent was used show that the vitamin is at least one-half as active.

Since the relative inactivity of vitamin K_1 with respect to 2-methyl-1,4-naphthoquinone and a purified extract of alfalfa is one of the important points in the claim that an antihemorrhagic compound more active than vitamin K_1 is present in alfalfa the discrepancy between Ansbacher's data and our observations should be examined. In his recent report Ansbacher[4] gives for the minimal effective dose of 2-methyl-1,4-naphthoquinone 0.5 μg and for vitamin K_1 15 μg. The table in this paper shows that in the 4 experiments in which 0.50 μg of 2-methyl-1,4-naphthoquinone was administered the percentages of the groups showing clotting times of less than 10 minutes were 50, 67, 50 and 90; with 1.0 μg the response was always 100%. Consequently, it appears that the agreement with Ansbacher's data in the case of this compound is entirely satisfactory and that the discrepancy is due to the difference in the results obtained with vitamin K_1. In our experiments the response to quantities of from 1 to 2 μg ranged from 30 to 100%. The highest ratio of potencies of the two compounds (Exp. 2) was about 3:1; the lowest (Exp. 5) less than 2:1.

Since the purity of the vitamin K_1 used in these experiments is an

[5] Almquist, H. J., and Klose, A. A., *Biochem. J.*, 1939, **33**, 1055.

important point, we wish to state that it was prepared by hydrolysis of the pure diacetyl dihydrovitamin K_1. The vitamin K_1 was purified by recrystallization at —70°C.

Analysis: Found C 82.39%; H 10.37%
Calculated C 82.62%; H 10.26%

$E^{1\%}_{1\ cm}$ of a hexane solution at λ 249 mμ = 448

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Effect of Leukotaxine on Cellular Permeability and on Cleavage Development.

VALY MENKIN

*From the Department of Pathology, Harvard University Medical School, and the Marine Biological Laboratory, Woods Hole, Mass.**

Previous studies have demonstrated the presence of a nitrogenous substance in inflammatory exudates capable *per se* of increasing capillary permeability and of inducing rapid diapedesis of polymorphonuclear leukocytes. This substance has been named leukotaxine.[1-3] Its isolation has offered a reasonable explanation for two of the basic mechanisms in the development of the inflammatory reaction. Furthermore, this substance has been shown to possess none of the manifest physiological properties of histamine, thus rendering it difficult to accept the view that the latter plays a primary rôle in increasing capillary permeability at the site of injury.[4-5] Kaiser has recently reached in regard to histamine an essentially similar conclusion, *i. e.*, at least as far as a long-standing inflammatory reaction is concerned.[6]

The present series of experiments have been undertaken in an endeavor to determine whether leukotaxine exerts any direct effect

* Aided by grants from the Milton Fund of Harvard University, from the International Cancer Foundation, and the Dazian Fund for Medical Research.

1 Menkin, V., *J. Exp. Med.*, 1936, **64**, 485.

2 Menkin, V., *J. Exp. Med.*, 1938, **67**, 129.

3 Menkin, V., *J. Exp. Med.*, 1938, **67**, 145.

4 Menkin, V., *Physiol. Rev.*, 1938, **18**, 366; *Dynamics of inflammation*, 1940, Macmillan Co., New York.

5 Menkin, V., and Kadish, M. A., *Am. J. Physiol.*, 1938, **124**, 524; Menkin, V., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 103.

6 Kaiser, P., *Schweiz. Z. f. allg. Path. u. Bakteriol.*, 1939, **2**, 1.