TABLE II.
Effect of Analgetic Agents on Oxygen Uptake of Brain After at Least 90% Decrease* in Respiration on Endogenous Substrates.

	Average mm³ O_2 uptake per hr per mg wet weight of tissue			
	1st hr		2nd hr	
	No drug.	No added substrate	With drug.	No added substrate
Morphine 0.01M		.167		.019
Methadon 0.01M		.133		.029
Nu-1779 0.01M		.102		.042
Nu-1196 0.01M		.074		.011
Control		.161		.073

* Drug was added after 2½ - 3 hr of shaking in Warburg flasks. No substrate was added.

The effects produced by the drugs are compared at equi-molar concentrations with methadon (at 0.01M) on glucose as a reference substrate. This concentration of methadon was found experimentally to produce a significant inhibition of the oxygen consumption of brain respiring on glucose.[4]

Conclusion. Our experiments indicate that significant inhibitions of the oxygen consumption of brain slices may be obtained using the new analgetic agents Nu-1196 and Nu-1779 when this tissue respires on glucose, lactate, pyruvate, α- and β-glycerophosphate (52% α), citrate, and possibly succinate. It must be pointed out, however, that inhibitions due to drug with citrate as a substrate are to be considered quite dubious since the normal increase in O_2 consumption by this substrate alone is so small. Doubtful inhibitions were produced when brain slices respired on glutamate and oxalacetate. Nu-1196 and Nu-1779 showed insignificant effects at concentrations less than 0.01M.

As in the case of demerol, methadon, and morphine reported by Elliott *et al.*,[4] the concentrations of the new agents Nu-1196 and Nu-1779 required to produce significant inhibitions were vastly larger than that required in the production of *in vivo* effects.

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Reduction in the Number of Adult *Trichinella spiralis* in Rats After Treatment with Naphthoquinones.*

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The effect of naphthoquinones on the metabolism of *Schistosoma mansoni* has been studied recently.[1] 2-methyl-1,4-naphthoquinone inhibits the rate of glycolysis of *S. mansoni in vitro*. Administration of this compound with subcurative doses of "Fuadin" to mice infected with *S. mansoni* causes a marked decrease in the rate of glycolysis of the worms. Other naphthoquinones varied as to the degree of their anti-glycolytic activity *in vitro* as well as *in vivo*. The inhibitory effect on glycolysis manifested by these naphthoquinones is decreased markedly when the worms are incubated in dialysed blood serum instead of a protein-free salt solution. This suggests that interaction of the naphthoquinones with serum proteins would reduce any intrinsic activity of these compounds

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1 Bueding, E., Peters, L., and Waite, J. F., PROC. SOC. EXP. BIOL. AND MED., 1947, **64**, 111.

TABLE I.
Number of Adult Trichinae Recovered from Rats After Treatment with a Single Oral Dose of 200 mg of Various 1,4-quinones.

Compound	No. of rats used		Avg No. of worms recovered	
	Treated	Untreated	Treated	Untreated
2-Methyl-1,4-naphthoquinone	5	2	49	250
" "	5	2	217	689
" "	5	2	76	461
" "	10	3	39	411
" "	10	3	88	615
2-Hydroxy-3-N-piperidinomethyl-1,4-naphthoquinone	2	2	100	518
2-Hydroxy-3-N-piperidinomethyl-1,4-naphthoquinone	5	2	68	507
2-Hydroxy-3-N(2-methylpiperidino)-methyl-1,4-naphthoquinone	2	2	483	467
3-Hydroxy-2-isoamyl-naphthoquinone	2	2	412	510
3-Hydroxy-2-methyl-octyl-1,4-naphthoquinone	2	2	361	366
2,3-Dichloro-1,4-naphthoquinone	2		508	
Tolu-p-quinone	2	2*	581	604*
Beta-carbomethoxyethyl-(2-methyl-3-n-thiobutyl-1,4-naphthoquinonyl-6)-ketone	2		388	
2-Methyl-3-thioethyl-6-butyryl-1,4-naphthoquinone	2		444	
3-N-Thioamyl-2-chloro-1,4-naphthoquinone	2	2*	319	420*
2,5-ditertiary-butyl-1,4-hydroquinone	2		480	

* The same two rats served as controls for the accompanying three drugs tested.

against parasites living in a habitat with a high protein content. Of interest, therefore, is the study not only of their therapeutic utility, but also of the effect of naphthoquinones on the metabolism of intestinal worms, since these live in a medium relatively low in protein. The following is a report of the results obtained after treating rats with naphthoquinones during the intestinal stage of infection with *Trichinella spiralis*.

Rats weighing from 200 to 300 g were fed by stomach tube with 1100 to 1500 infective trichinae larvae each. The larvae were obtained from trichinous rat meat digested in a pepsin-hydrochloric acid mixture. Twenty-four hours later the rats were given a single dose of 200 mg† of the compound to be tested.‡ The drug was suspended in mucilage of tragacanth and then fed through a stomach tube. On the fifth day after infection the rats were killed and the number of adult trichinae present in small and large intestine were recovered and counted. Untreated rats were killed together with the treated ones to serve as controls.

Of the 11 compounds tested only two (2-methyl-1,4-naphthoquinone and 2-hydroxy - 3 - piperidinomethyl - 1,4-naphthoquinone) caused a diminution in the number of intestinal trichinae (Table I). The average number of worms recovered in the animals treated with these two compounds was significantly less than in the untreated ones. The chi-square test was calculated for each drug and the values of P were beyond the 1% level of significance.

It is of interest that the reduction in the number of worms was caused by only two of the naphthoquinones tested. Since all the compounds are closely related, the effect is apparently determined by highly specific groups attached to the naphthoquinone nu-

† For some of the compounds, 200 mg was the maximum tolerated dose for rats.

‡ The compounds used were supplied generously by Dr. Louis F. Fieser, Department of Chemistry, Harvard University, and by the Abbott Laboratories, North Chicago, Ill.

cleus. Several of the compounds that had no effect on adult *T. spiralis* are more effective inhibitors of glycolysis of *S. mansoni* than 2-methyl-1,4-naphthoquinone.[2] On the other hand, the anti-glycolytic activity of 2-hydroxy - 3 - piperidinomethyl - 1,4-naphthoquinone against glycolysis of schistosomes was a hundred times lower than that of 2-methyl-1,4-naphthoquinone.[1] Apparently, two different mechanisms are involved in the effect of naphthoquinones against adult trichinae and on glycolysis of schistosomes, since compounds that possess high anti-glycolytic activity did not reduce the number of trichinellae and the reverse was true for the 2-hydroxy-3-piperidinomethyl derivative.

No indication was obtained as to whether 2-methyl-1,4-naphthoquinone inhibits any specific metabolic reaction of adult trichinellae. The metabolism at the adult stage of this parasite differs markedly from that of the larvae. Unlike the latter,[3] adult trichinellae have an extremely low rate of oxygen uptake and do not contain any significant amount of glycogen. Furthermore, it was found that the adult worms do not utilize glucose present in the medium and do not produce any significant amounts of lactic acid or other acids when incubated in a salt medium containing glucose.

Summary. The oral administration of 2-methyl-1,4-naphthoquinone and 2-hydroxy-3 - piperidinomethyl - 1,4-naphthoquinone to rats infected with *Trichinella spiralis* produced a significant reduction in the number of intestinal adult trichinellae. Nine other structurally related naphthoquinones had no such effect.

[2] Bueding, E., and Peters, L., unpublished observations.

[3] Stannard, J. W., McCoy, O. R., and Latchford, W. B., *Am. J. Hyg.*, 1938, **27**, 666.

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Activity of Pantothenol as Pantothenic Acid in Promoting Chick Growth.*

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The activity of pantothenol as pantothenic acid in various species has been recently reviewed.[1] It is of interest that this compound interferes with the utilization of pantothenic acid by certain microorganisms[2] whereas in rats[3] and human beings[4,5] it is converted into pantothenic acid and appears to be as active as pantothenic acid itself in these two species. From the results presented in this paper, it is concluded that on an equivalent basis, molecule for molecule, pantothenol is 86% as active as pantothenic acid in promoting chick growth.

Nine groups of white leghorn cockerels one week of age were fed the low pantothenic acid diet previously described.[6] After 4 days of depletion, graded doses of calcium pantothenate ranging from 16 to 160 μg per chick per day were administered to 6 of the groups by pipette placed directly in the crop. The remaining 3 groups received pantothenol in the same manner at 40, 65, and 100 μg per

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[1] Anonymous, *Nutrition Rev.*, 1948, **6**, 272.

[2] Snell, E. E., and Shive, W., *J. Biol. Chem.*, 1945, **158**, 551.

[3] Pfalz, H., *Z. f. Vitaminforsch.*, 1943, **13**, 236.

[4] Burlet, E., *Z. f. Vitaminforsch.*, 1944, **14**, 318.

[5] Rubin, S. H., Cooperman, J. M., Moore, M. E., and Scheiner, J., *J. Nutrition*, 1948, **35**, 499.

[6] Hegsted, D. M., and Lipmann, F., *J. Biol. Chem.*, 1948, **174**, 89.