

d-enantiomorph. If the acetylation is preceded by the formation of the corresponding keto acid from both isomers, as Knoop's theory postulates, then the *d*-isomer is apparently less readily deaminized than the *l*-isomer. *d*-Benzylcysteine is undoubtedly directly acetylated, as is indicated by the excretion of *dl*-acetylbenzylcysteine in the urine. We are not excluding the possibility of racemization of *d*-benzylcysteine *in vivo*, neither do we imply that some oxidative deamination of either or both isomers of benzylcysteine does not occur *in vivo*.

The work is being continued and extended to benzylhomocysteine and phenylaminobutyric acid, particularly with reference to the possibility of racemization and preferential rate of acetylation of the optical isomers of these amino acid derivatives *in vivo* as contrasted with Knoop's acetylation theory.

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Some Effects of Experimental Trichinosis in the Dog.*

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In view of the fact that encysted trichina larvae become calcified in the muscles of the host, it appeared desirable to determine the changes which occur in the blood picture of dogs suffering from experimental trichinosis. The present report presents the results of cytological studies in which concurrent determinations were made on the level of blood calcium, hemoglobin and inorganic phosphate at periodic intervals before and during the period of infection.

Methods and Technic. The 13 mature mongrel dogs, used in these experiments, were kept under observation for several weeks to determine whether or not they were suffering from any disorder. Each was treated with arecoline hydrobromide (Parke, Davis) to insure freedom of the gastro-intestinal tract of parasites. The dogs were kept in separate cages in a room in which the temperature fluctuated very little. Purina dog biscuit was supplied *ad libitum*.

* The authors wish to acknowledge the assistance of John E. Krettek with the blood counts.

TABLE I.
Blood Picture in Trichina-infected Dogs.

Sex and Number	Wt in kg	Control period in days	Control period			Experimental period			
			R.B.C. in millions per mm ³	Hematocrit	Grams % Hemoglobin	Organisms fed (in thousands)	R.B.C. in millions per mm ³	Hematocrit	Grams % Hemoglobin
M3	6.81	13	5.80-7.25	44-49	14.9-16.9	90	5.30-6.70	40-44	12.4-16.7
M2	11.81	20	6.90-7.25	46-48	14.7-17.7	160	6.45-7.00	44-48	15.3-18.1
M1	15.90	20	6.85-7.45	47-48	14.2-18.0	220	5.85-7.00	42-56	13.9-16.4
M4	8.63	13	6.50-8.90	55-66	16.3-19.4	292	5.48-7.56	44-55	13.5-16.7
M9	7.50	13	6.20-6.50	41-42	11.4-12.6	300	5.33-6.74	42-45	12.6-13.4
F5	7.27	8	6.00-7.10	44-49	15.0-15.2	400	5.07-6.12	39-46	9.5-12.6
M7	7.27	22	5.07-5.44	41-47	10.5-11.8	480	4.19-5.22	32-42	10.4-12.6

TABLE II.
Leucocyte Variations in Trichina-infected Dogs.

Sex and Number	Control period		Experimental period				After recovery*	
	W.B.C. in thousands	Eosinophils %	Days after infection	W.B.C. in thousands	Eosinophils %	W.B.C. in thousands	W.B.C. in thousands	Eosinophils %
M3	10.1-18.0	1-3	11-17	16.7-11.5	14-11	12.7	12.7	2
M2	14.0-15.0	0-5	10-23	14.7-14.5	21-10	15.2	15.2	7
M1	15.2-16.0	0-3	10-14	20.3-18.1	11-17	14.6	14.6	2
M4	9.3-15.0	2-10	6-22	12.0-13.0	21-24	10.9	10.9	9
M9	12.4-17.6	2-4	15-30	20.0-17.0	18-8	14.8	14.8	14
F5	9.5-12.5	4-6	10-17	19.2-10.8	38-15	15.0	15.0	3
M7	11.1-12.8	0-8	14-22	10.6-14.2	25-8	10.1	10.1	5
M10	14.1-17.3	2-7	12-26	14.9-13.0	19-8	12.3	12.3	7
M12	11.7-16.0	0-3	12-18	12.2-15.3	22-4	12.9	12.9	4
F13	15.5-18.8	0-2	12-20	16.0-14.0	16-6	13.2	13.2	4

* After 30 days.

Blood was drawn from the jugular vein using 30 mg of potassium oxalate as an anticoagulant for each 5 cc sample. Samples were taken in the forenoon on animals which were fasted 16 hours.

Total counts were made with a bright-line Neubauer hemacytometer. Blood smears were made on a coverslip and stained with Wright's stain. Two hundred to 400 cells were tabulated, alternately, in the differential counts. Hematocrit determinations were made with a Wintrobe tube using 1.1 as the shrinkage correction factor.

Serum calcium was determined by the Clark-Collip¹ modification of the Tisdall method. Hemoglobin and inorganic phosphate were determined according to the method of Van Slyke² and Kuttner-Lichtenstein³ respectively. All analyses were made in duplicate.

The dogs were infected by feeding them 90 to 480 thousand trichina larvae contained in fresh rabbit muscle. Three of them were discarded during the period of infection due to poor physical condition. All animals were shown to be infected at autopsy.

Results. The normal blood picture of each dog was followed for a period of 13 to 22 days since it appeared desirable that emphasis should be placed upon changes observed rather than on absolute values. Table I shows the results of determinations conducted on these animals for a period of 60 days. Normal erythrocyte values and differential counts fall within the range of normal values.^{4, 5, 6}

TABLE III.
Blood Picture in Trichina-infected Dogs.

Sex and Number	Control period			Experimental period		
	Serum Calcium in mg per 100 cc	Eosinophils, %	Inorganic phosphate, mg%	Serum calcium, mg%	Eosinophils, %	Inorganic phosphate, mg%
M3	11.06-12.68	1-3	5.58-5.88	14.50-10.40	14-11	4.01-7.20
M2	10.50-11.85	0-5	4.40-5.30	12.50- 9.60	21-10	4.06-7.30
M1	9.50-11.60	0-3	4.50-6.00	13.00-10.60	11-7	3.69-5.20
M4	10.60-13.20	2-10	3.90-4.80	16.50-11.00	21-24	3.30-3.80
M9	10.30-10.90	2-4	5.75-5.88	18.70-12.00	18-8	5.30-7.40
F5	12.30-13.80	4-5	4.85-7.20	12.60-10.50	38-15	4.40-6.98
M7	11.06-11.88	0-8	4.58-5.13	16.13-11.10	25-8	4.04-5.65
M10	9.81-11.17	2-7		9.76-10.52	19-8	
M12	10.44-10.96	0-3		11.28-10.83	22-4	
F13	10.60-11.14	0-2		10.49-10.36	16-6	

¹ Clark, E. P., and Collip, J. B., *J. Biol. Chem.*, 1925, **68**, 461.

² Hawk and Bergeim, *Practical Physiological Chemistry*, 11 Ed., 533.

³ Kuttner, T., and Lichtenstein, L., *J. Biol. Chem.*, 1930, **86**, 671.

⁴ Scarborough, R. A., *Yale J. Biol. and Med.*, 1930, **3**, 359.

⁵ Wintrobe, M. M., Shumaker, H. B., and Schmidt, W. J., *Am. J. Physiol.*, 1936, **114**, 502.

⁶ Morris, M. L., Stelton, N. J., Allison, J. B., and Green, D. F., *J. Lab. and Clin. Med.*, 1940, **25**, 353.

White blood counts were slightly higher (Table II) than those found by Morris, *et al.*⁶ The variations observed in serum calcium ranged from 9.8 to 13.8 mg %, average 11.3. Inorganic phosphate ranged from 3.9 to 6 mg % with an average of 4.87.

During the period of infection the cell volume, total erythrocyte count and hemoglobin remained essentially unaltered (Table I). The white cell counts, both total and differential, showed striking variations from the normal in all animals. The leucocyte count (Table II) showed an increase in those animals having the most severe infection. Even those dogs receiving 13 to 14 thousand trichina larvae per kilogram body weight showed marked changes. The most marked variation in the blood picture was in the differential count. There was a gradual increase in the eosinophiles (Column 6, Table II) which reached a maximum (11 to 38%) 10 to 15 days after infection. No significant changes were observed in other leucocytes which is in contrast with the findings of Beahm and Downs⁷ in the albino rat.

Significant increases in the serum calcium level (Table III) were

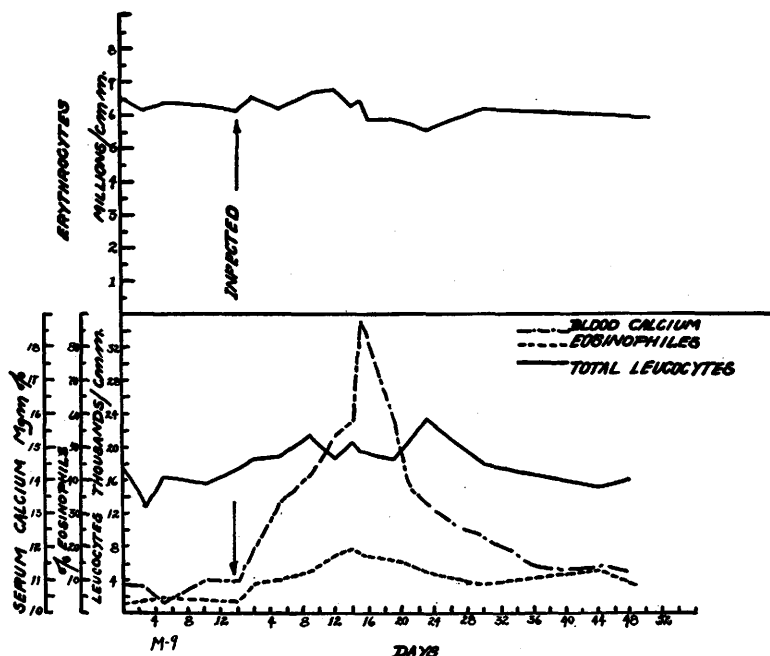


FIG. 1.

Graph showing comparison of results from control and experimental period of trichina-infected dog M9.

⁷ Beahm, E. H., and Downs, C. M., *J. Parasitol.*, 1939, 25, 405.

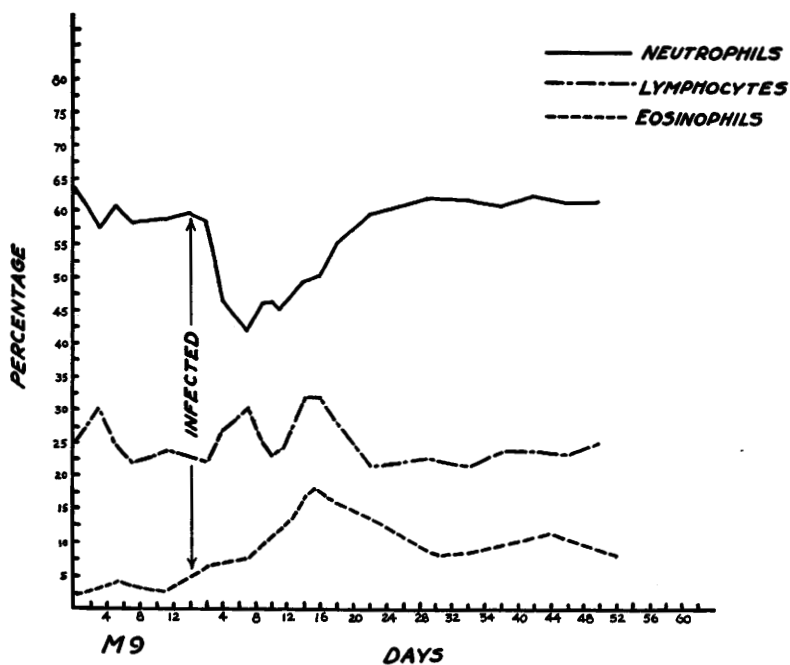


FIG. 2.
Differential count of trichina-infected dog M9.

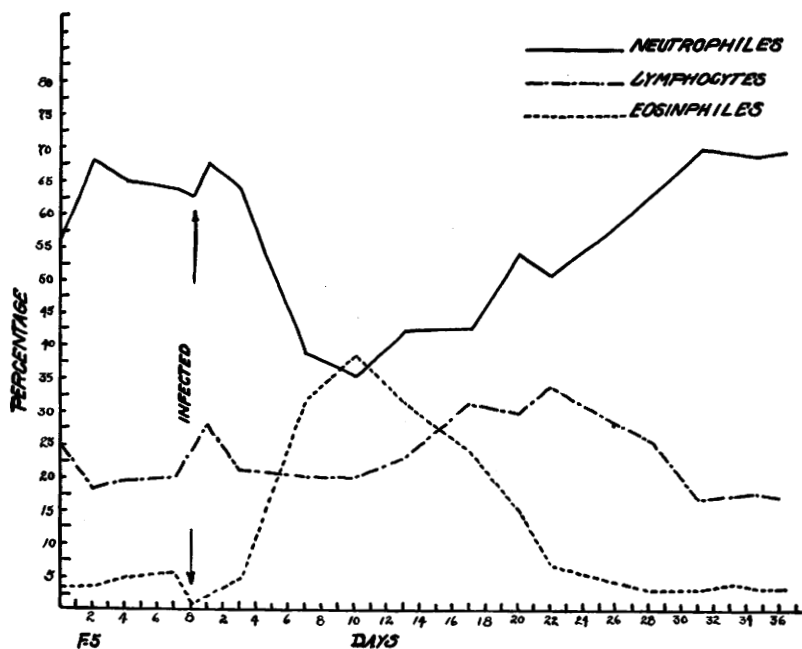


FIG. 3.
Differential counts. Graph showing comparative data obtained during control and experimental period on dog F5.

observed in only 4 dogs suffering from severe trichinosis. These animals (M12, M4, M9, M7) that received 32, 33, 40 and 66 thousand trichina larvae per kilogram of body weight exhibited increases in serum calcium, eosinophiles and total leucocytes. At the same time a moderate decrease was exhibited in the level of inorganic phosphate. Figs. 1 and 2 depict these changes as observed in M9. In contrast with these findings, M10, F13, and F5 had marked eosinophilia but no rise in calcium was observed although they received 34, 40, and 55 thousand larvae per kilogram of body weight. Fig. 3 graphically represents findings observed in F5 which are typical of these animals.

Summary. No significant changes in cell volume, total erythrocyte count and hemoglobin values were observed in trichina-infected dogs. All animals exhibited increases in eosinophiles which reached a maximum 10 to 15 days after infection. Significant increases in serum calcium, which reached a maximum (16-18 mg %) 11 to 18 days after infection, were observed in only 4 dogs. It would appear that hypercalcemia can only be elicited by a massive infection, whereas an eosinophilia will always result from ingestion of fewer organisms.

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Absorption of Drugs Through the Bone Marrow.

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For years the writer has been studying the penetration of drugs into the body through unusual channels and has published papers on their absorption through the bladder, urethra, ureters, vagina, eyes, ears, nose, pharynx, esophagus and pathological versus normal skin and mucous membranes.^{1, 2} Having observed that drugs penetrate the tooth pulp and canaliculae,³ the author determined to investigate what drugs and poisons in general can be absorbed through bone marrow and how rapidly. Such a research was deemed especially desirable because of the recent work of Morrison and Samwick⁴

¹ Macht, D. I., *J. A. M. A.*, 1938, **110**, 409.

² Macht, D. I., *Arch. internat. de Pharmacodyn. et de Therap.*, 1938, **58**, 221.

³ Macht, D. I., *J. Pharmacol. and Exp. Therap.*, 1923, **22**, 123.

⁴ Morrison, M., and Samwick, A. A., *J. A. M. A.*, 1940, **115**, 1708.