patients in good condition with Hodgkin's disease, make it unlikely that the positive reactions reflect merely debilitation. There have been no changes in titres in serial specimens which would suggest that the presence in the serum of folic acid, folic antagonists, or nitrogen mustards cause the positive reactions. Many highly positive reactions were observed in sera obtained before any treatment had been given. The addition of folic acid (pteroylglutamic acid) or 4-amino-pteroylglutamic acid (10 γ/cc) to serum having a negative precipitin reaction did not change the reaction.

Mechanism of the reaction. The cause of these false positive trichina precipitin reactions is not known.

Summary. Patients with certain neoplastic diseases involving the reticuloendothelial system (Hodgkin's disease, lymphosarcoma and acute leukemia) exhibited a high percentage of false positive trichina precipitin reactions. Such reactions were much less frequently encountered in sera from patients with metastatic carcinomas and no positive reactions were observed in the normal controls. The false-positive reaction does not appear to be related to medication.

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Tissue Distribution and Elimination of DDD and DDT Following Oral Administration to Dogs and Rats.* (17431)

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Although the tissue distribution of ingested DDT (2,2-bis-(p-chlorophenyl)-1,1,l-trichloroethane) has been reported by several workers,[1-7] in most cases with particular reference to its storage in fat, similar data concerning its analog, DDD (2,2-bis-(p-chlorophenyl)-1, 1-dichloroethane), is limited.[5]

The increasing agricultural use of DDD (Rhothane) against insect pests infesting fruit and vegetable crops makes desirable further knowledge concerning its tissue distribution following ingestion. Although it has been demonstrated that DDD is less toxic on both an acute[8,12] and chronic[5,11,12] basis than is DDT, it has not as yet been made clear whether this difference is attributable to DDD being inherently a less toxic molecule, or whether it is due to differences in absorption, storage or excretion.

In an attempt to clarify this question of absorption, storage and excretion of DDD, the following experiments were done:

Experimental. Dogs. Ten female dogs were used, 5 receiving DDD and 5 DDT in a dose of 25 mg per kg daily except Sunday, for a maximum period of 4 weeks. The insecticides were administered orally once daily in the form of a 10% solution in corn oil in gelatin capsules at the time of the daily feeding.

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TABLE I.
DDD and DDT Content of Tissues of Dogs to Which the Insecticides Had Been Administered Orally Daily for Periods of 2 and 4 Weeks.

Insecticide	Insecticide content, mg per kg of tissue									
	DDD					DDT				
Duration	2 wks		4 wks			2 wks		4 wks		
Dog No.	D-4	D-5	D-1	D-2	D-3	T-4	T-5	T-1	T-2	T-3
Liver	0	0	1.6	0	24	0	0	0	0	0
Kidney	15	4.3	13	14	15	4.9	0	14	7.2	9.6
Heart	3.8	0	11	12	13	0	3.4	4.9	8.1	3.4
Brain	0	0	3.5	4.1	5.2	1.3	0	2.5	3.9	1.2
Lung	0	0	1.9	3.9	lost	0	0	0	0	0.8
Pancreas	0	0	8.9	29	12	0	3.4	14	9.4	8.8
Spleen	0	1.7	0	12	4.7	0	0	2.2	3.6	0
Adrenal	0	0	150	0	210	0	0	83	63	62
Fat	76	270	880	360	300	29	100	910	400	200
Muscle (gastroc.)	7.6	5.2	lost	20	28	8.4	5.5	12	14	18
Skin	90	7.2	28	128	18	82	73	0	6.4	3.3
Mammary gland	—	—	—	—	—	—	—	2.2	—	21
Fecal excretion mg/kg body wt, 48 hr	0.9	4.2	3.9	2.2	3.9	lost	0.03	0.01	0.5	0.8

Twenty-four hour urine samples were taken at the end of the first, second, and fourth weeks for subsequent analysis for DDD, DDT, or their acid end-product, DDA (2,2-bis-(p-chlorophenyl) acetic acid). The total feces of each dog was collected over the 48 hour period just prior to the time of sacrifice for similar chemical analysis.

At the end of 2 weeks, 2 of the dogs in each insecticide group were sacrificed, the remaining dogs being sacrificed at the end of 4 weeks. Samples of the tissues listed in Table I were removed, frozen quickly in a dry-ice-alcohol mixture and preserved in the frozen state for subsequent analysis for DDD and DDT. In the case of 2 dogs receiving DDT that were lactating at the end of the experiment a sample of mammary gland tissue was similarly prepared. Because the presence of blood in the tissue sample appears to interfere with the analytical procedure used, as much as possible was removed (ca. 90% as determined by hematocrit) from the circulation by saline perfusion before death.

During the course of the experiment, 3 of the dogs bore litters. One of the 4-week DDD dogs (D-1) bore 5 premature stillborn pups 13 days after beginning of the experiment. All of these were frozen whole for subsequent chemical analysis. On the same day, one of the 4-week DDT animals (T-1) bore 5 pups, 2 of which were sacrificed as soon after birth as they were discovered and frozen whole. The other 3 were sacrificed at the end of the experiment and the organs listed in Table II removed, pooled as to organ and frozen. Another 4-week DDT dog (T-3) bore 6 pups 2 days before the termination of the experiment. Two were killed and frozen whole before having an opportunity to nurse; the other 4 were killed at the end of the experiment and the same organs removed, pooled and frozen. Because of their small size, no

TABLE II.
DDT Content of Pooled Organs from Pups Nursing from Mothers Receiving Daily Doses of DDT Orally.

Tissue	DDT, mg per kg organ weight	
	4 pups from T-3 (2 days old)	3 pups from T-1 (2 wks old)
Liver	220	0.51
Kidney	6.3	8.3
Heart	0	10
Lung	3.5	1.3
Brain	0	0
Skin	26	12
Fat	205	0
Pancreas	149	46
Spleen	9.8	0
Muscle	8.4	5.8

attempt was made to perfuse out the blood of the pups.

Rats. The rats used in this experiment were survivors from a series of animals that had been subjected to a 2-year feeding program comparing the chronic toxicity of DDD with that of DDT. Finely ground Purina Dog Chow served as the basic diet, and into this was incorporated predetermined amounts of 5 or 10% DDD or DDT in Pyrax† to achieve the dietary concentrations listed in Table III. Only analyses of the fat were done on these animals.

All DDD, DDT and DDA determinations were done according to the Schechter-Haller method.[9,10]

Results and Discussion. Dogs. Table I shows the amounts of DDD and DDT in mg per kg of organ weight found in the tissues of the treated animals.

It will be noted that in the animals sacrificed at the end of 2 weeks the fat and the skin were the main sites of storage of both DDD and DDT. Muscle and kidney showed a measurable level of both insecticides, however, the other tissues that were studied showed either none or very small amounts.

In those animals sacrificed at the end of 4 weeks the fat, again, showed the highest content of both DDD and DDT, whereas, the skin content, which was relatively high for both insecticides at the end of 2 weeks, was found to be low in the case of the DDT animals. This lower skin content of DDT may be related to the body weight loss and resultant probable decrease in cutaneous fat content incurred by this group.

It seems that, in general DDD and DDT were deposited in fat to a similar degree. This is in agreement with the thesis of von Oettingen and Sharpless[8] that since the 2 compounds have similar solubilities in olive oil they would probably be stored to about the same degree in fat.

The other tissues in which little or no insecticide was found at the end of the 2 week period contained definite quantities of DDD or DDT at the end of 4 weeks. This is particularly noticeable in the case of the adrenal gland and is most apparent here in those animals which received DDD. This latter observation is of interest in relation to the adrenal cortical atrophy that has been described in dogs receiving DDD orally[5,13] and which has also been noted in this laboratory (unpublished).

Analysis of the pooled carcasses of the 5 stillborn pups from one of the 4-week DDD dogs (D-1) showed a content of 3.7 mg per kg DDD. Similar analyses of individual carcasses of the 2 newborn pups from dog T-1 and the 2 newborn pups from dog T-3 (both 4-week DDT dogs) gave average values of 1.3 mg per kg for the first pair and 0.04 mg per kg for the second. It was thought that the latter result was low owing to possible loss of part of the sample. These results demonstrate transfer of both DDD and DDT across the placenta.

Table II shows the amounts of DDT stored in the pooled organs of pups that were born to 2 of the dogs (T-1 and T-3) during the feeding period and nursed for the remainder of the time until the end of the experiment. It will be noted that the pups from dog T-3, which were 2 days old at the time of sacrifice, showed high levels of DDT in the liver, skin, fat and pancreas, whereas, those that had nursed for a period of 2 weeks (pups from dog T-1) showed much lower levels in these tissues, and, with the exception of heart tissue and perhaps kidney, showed lower levels in all other organs examined. This again seems indicative of a high degree of placental transfer of DDT and further suggests that the fetus is more liable to the accumulation of DDT than is the suckling offspring, despite the fact that DDT has been shown to be secreted in the milk.[3,4]

Included in Table I are data showing the amounts of the insecticides excreted in the feces in the 48 hour period just prior to sacrifice. Fecal excretion, in all cases, represented but a small proportion of the amount of the

† A pyrophylite diluent.

[9] Ofner, R. R., and Calvery, H. O., *J. Pharm. Exp. Therap.*, 1945, **85**, 363.

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TABLE III.
Averages of Fat Analyses for DDD and DDT in Rats at the End of Two Year Feeding.

Insecticide	Dietary concentration parts per million	No. of rats	Content of DDD or DDT in body fat, mg/kg (Avg and range)
DDD	150	3	220 (180-250)
	300	7	270 (140-830)
	600	4	480 (110-950)
	900	4	350 (280-500)
	1,200	10	420 (60-790)
	1,800	5	310 (210-430)
	2,500	5	680 (320-940)
	3,750	1	1,290
DDT	150	3	2,070 (400-5,400)
	300	5	470 (240-690)
	600	1	340

insecticide administered during that period. It is apparent that DDD is uniformly excreted to a greater degree in the feces than is DDT.

In contrast to the findings of Smith *et al.*[6,12] that orally administered DDT is excreted in the urine of rabbits, it does not appear to be excreted in the urine of dogs. Neither does the dog appear to excrete DDD by the way of the kidney. However, DDA appears to be a urinary end-product common to both insecticides in dogs. Thus the average 24 hour excretion of DDD as DDA was 0.63 mg per kg body weight at the end of the first week of administration, 0.50 mg at the end of the second week, and 1.25 mg at the end of the fourth week. In the case of DDT, the DDA excretion figures were 0.13 mg, 0.12 mg, and 0.17 mg per kg body weight at the end of the same intervals. These figures also indicate that the rate of DDD excretion in the form of DDA is greater than in the case of DDT.

Rats. It is apparent from Table III that both DDD and DDT are stored in considerable amount in the fatty tissues of the rat. Among the DDD-treated animals there appears to be a tendency for deposition of DDD to increase with its increasing dietary content, although this is not entirely consistent. The number of animals and dietary levels studied using DDT was too limited to permit similar comparisons.

Conclusions. 1. DDD and DDT when administered orally are stored in the tissues of the dog, the greatest storage appearing in the fat.

2. Similarly DDD and DDT are both stored in the fat of the rat.

3. Both DDD and DDT are transported across the placental barrier in the dog.

4. In the dog, a small proportion of orally administered DDD or DDT is excreted in the feces. Of the 2, DDD appears in greater amount.

5. When administered orally to the dog, neither DDD nor DDT are excreted as such in the urine. DDA is a urinary end-product common to both DDD and DDT, appearing in greater amount following DDD administration.

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