a clearance experiment: the fluctuation is usually less than this. With a plasma inulin level of 15 mg % a 10 mg % departure from the blank would produce an error of one % in the inulin value determined.

A series of determinations on different solutions containing both glucose and fructose were run in the same heating batch with the corresponding separate glucose and fructose concentrations. The ratios of the observed additive optical densities to the calculated were 0.993, 0.993, 1.003, 1.007, 1.015, 0.994, 0.994, 0.985, 1.010, 1.006, 1.033, 1.006, 1.020 and 0.987.

Summary. A modification of Harrison's diphenylamine method for fructose or inulin determination is described, heating being carried out at 75°C for 60 minutes. With this procedure the ratio of fructose to glucose color production is 64, as compared with a ratio of 8 at 100°C for 30 minutes. Inulin hydrolysis is complete, the standard error of the method is less than 1 percent, the color is light stable and the low color production by glucose permits one to omit fermentation except in the presence of unusual glucose fluctuations.

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False Positive Trichina Precipitin Reactions in Neoplastic Disease. (17430)

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(Introduced by C. P. Rhoads)

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Because of high fever, palpebral edema, painful inflammation of feet and hands, and eosinophilia of 5% in a child with atypical lymphosarcoma, a trichina precipitin test was performed. The reaction was strongly positive in a dilution of 1:1280, the highest titre routinely tested. The clinical signs rapidly subsided during treatment with 4-aminopteroylaspartic acid, a trichina complement-fixation test was negative, and x-ray examination demonstrated lesions of bone of the "moth-eaten" type commonly seen in acute leukemia. Hence, although the precipitin test remained unchanged, there was no longer any clinical reason to consider a diagnosis of trichiniasis and it was felt that the trichina precipitin reaction was a false positive.

This occurrence of an apparently false positive trichina precipitin test in a patient with lymphosarcoma led to a study of sera from other patients with lymphosarcoma, Hodgkin's disease, leukemia, and other neoplastic diseases. Positive reactions were so frequently seen that it seemed desirable to report the phenomenon.

Method. Sera were obtained from hospitalized and clinic patients and personnel of Memorial Hospital. Three categories were studied: (1) those neoplastic diseases which involve principally the reticuloendothelial system (Hodgkin's disease, lymphosarcoma, the leukemias, and multiple myeloma), (2) widespread metastatic disease of other tissue, both carcinomas and sarcomas, (3) apparently healthy controls. Group 2 was included as controls who showed advanced and debilitating disease comparable to that seen in the first group.

Precipitin tests were performed by the standard technic of the Bureau of Laboratories of the New York City Department of Health. The antigen consisted of a saline extract of *Trichinella spiralis* larvae obtained from infected rat muscle by digestion with pepsin and hydrochloric acid. Undiluted serum was pipetted into small bore test tubes and overlaid with antigen in dilutions of 1:160, 1:320, 1:640, and 1:1280 on a basis of weight of dried larvae. A positive test was indicated by the formation, after two hours at room temperature, of an opaque ring. A

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TABLE I.

Results of 171 Trichina Precipitin Tests from 128 Persons With and Without Neoplastic Disease. Numerals indicate number of patients, not number of serum samples. Figures in parentheses indicate patient on whom skin tests were done (all negative), and those in brackets indicate patients on whom complement fixation tests were done (all negative).

Diagnosis	Total No. patients	Trichina precipitin titre					
		Neg.	160	320	640	1280	variable
Hodgkin's disease	13	1			4	8[1](1)	
Lymphosarcoma	14	5		2	2	4[2]	1
Acute leukemia	25	10			2	7(3)	6
Chronic leukemia	13	10		1	1	1	
Multiple myeloma	3	2			1		
Nieman-Pick's disease	1	1					
Osteogenic sarcoma	3				1(1)	1	1
Wilm's tumor	1				1		
Rhabdomyosarcoma	1	1					
Bronchogenic carcinoma	3				1	2	
Cancer of breast	8	4	2	1	1		
Cancer of prostate	5	3		2			
" " tongue	1	1					
" " uterus	2				1	1	
Normal healthy adults	26	26					
Normal healthy children	9	9					

titre of 320 is generally considered significant for diagnosis of trichiniasis.

Results. Tests have been done on 171 serum samples from 128 persons. Results are summarized in Table I.

All normal controls tested† (26 adults and 9 children) had negative reactions.

Of 13 patients with Hodgkin's disease, 12, in all stages of disease, had highly positive reactions. The negative reactor was a 10 year old boy; all others were adults. Of 14 patients with lymphosarcoma, 5 had negative reactions. These 5 were all adults in good condition. Seven (including 4 children) had positive reactions in a high titre and all of these patients had terminal and rapidly progressive disease. One case of lymphosarcoma in good condition and one in the terminal stage of the disease gave intermediate titres (320). Of 13 patients with chronic leukemia (7 myeloid, 5 lymphatic), only 3 had positive titres. Each of these was in the terminal phase of myeloid leukemia and showed a large percentage of blasts in marrow and peripheral blood. Results in 25 cases of acute leukemia were variable. Nine patients with acute leukemia had negative titres on all serum samples tested, 8 had consistently positive titres, and 8 had variable titres on serial specimens. Those who consistently had high titres all died without remission. Most patients who had hematologic remissions (on treatment with antagonists of pteroylglutamic acid) had either consistently negative titres (5 patients), or on serial tests reverted from positive titres to negative (3 patients).

No generalization can be made concerning patients with other types of neoplastic disease. Of the 3 patients with bronchogenic carcinoma and 3 with osteogenic sarcoma who were tested, all gave high positive titres. Thirteen patients were tested who had metastatic carcinoma of breast or of prostate. Only one of these had a high titre and 7 were negative. It is noteworthy (in view of the positive titres found in bronchogenic and osteogenic neoplasms) that most of the patients with these 2 diagnoses had metastases to bones or lungs or both. Other diagnoses are represented by too few cases to merit discussion.

Three sera showing highly positive precipitin titres (2 patients with lymphosarcoma and one with Hodgkin's disease) were tested by John Bozicevich of the National Institutes of Health for complement-fixing antibodies with trichina antigen. All 3 were negative. Skin tests were performed with trichina antigen

† Twelve of the adult control sera were obtained by Dr. Joseph J. Bunim of The New York University Medical School.

diluted 1:8000 on 5 patients having strongly positive precipitin reactions. All were negative (Table I).

Discussion. The frequency of false-positive reactions in the presented data naturally raises questions as to the significance of these results, and the cause and mechanism of the reaction.

Reliability of data. All tests were performed by one person (A.E.T.) and were done without any knowledge of the diagnosis. The reproducibility of results in serial specimens from many of the patients (chiefly those with Hodgkin's disease, lymphosarcoma, and leukemias) indicate that the data as presented are reliable. Thirty-six patients had at least duplicate tests and only 10 have showed variation of more than one dilution. Those who showed variation in titre also showed concurrent variations in the disease process.

Reliability of the method. In established trichiniasis the precipitin test shows a fairly high degree of reliability. In recent acute trichiniasis most workers have reported over 90% positive reactions (reviews of literature by Gould,[1] and by Shookhoff *et al.*[2]).

False positive reactions are known to occur. Gould[1] reports 51 patients in whom trichina could *not* be demonstrated at autopsy and in whom precipitin tests had been performed. Ten of these (19.8%) had a positive reaction at a dilution of 1:100. The diagnoses of these patients are not reported. Bachman *et al.*[3] studied 857 sera from an area where trichiniasis is not endemic and found 8.4% apparently-false positive tests in patients with a wide variety of non-neoplastic disease. Augustine and Theiler[4] in a similar study found 18 apparently false-positive reactions (12%) among 115 patients and felt that the false positives were related to medications (quinine, mercury, bismuth, and arsenic). There was no apparent relation to these same medications in Bachman's series. A single case of periarteritis nodosa reported by Reimann, Price, and Herbut[5] showed a false positive trichina precipitin test. Bassen, Thomson, and Silver[6] reported false positive precipitin tests in 5 cases of infectious mononucleosis.

Significance of present data. It is not probable that the reactions reported here indicate subclinical trichiniasis. No history suggestive of trichiniasis was elicited from any patient except the first patient tested. The available evidence indicates that the trichina precipitin test remains positive for only 2 to 3 years after infection, whereas skin reactions are more persistent.[1] In contrast to this, in the present study precipitin tests were positive, but skin tests and complement fixation tests were negative. Trichiniasis is rare in children,[1] while in the present study 14 of 21 children with leukemia or lymphosarcoma had high titres. Furthermore, if the present results were due to unrecognized trichiniasis an equal distribution of positive reactions would be expected in all diagnoses.

The major import, then, of the present study is that the trichina precipitin reaction is invalid as a test for trichiniasis in patients with certain neoplastic diseases, especially Hodgkin's disease, lymphosarcoma, and acute leukemia. The data also imply the possibility that this phenomenon might be utilized in prognosis, but the investigation has not yet proceeded far enough to permit valid discussion of such a possibility.

Indications at present suggest that the positive reactions are related in some way to the neoplastic process. There has been no correlation between positive precipitin reactions and fever or eosinophilia. The infrequency of positive reactions among patients with advanced carcinoma of the breast or prostate and the frequency of positive tests among

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3 Bachman, G. W., Rodriguez-Molina, R., and Oliver-González, J., *Am. J. Hygiene*, 1934, **20**, 415.

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6 Bassen, F. A., Thomson, A. E., and Silver, A., *J. Lab. and Clin. Med.*, 1949, **34**, 543.

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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