Absorption after a 6 hour test is increased from the 2nd to 6th days in irradiated animals. After a 10 hour test there was little difference between irradiated and control animals. Liver content of vitamin A is decreased in irradiated animals, and there is an increase in carcass vitamin A. Adrenal vitamin A is less in irradiated than control rats at 6 hours and is increased above control rats at 10 hours.

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Presence of Desoxyribonuclease Activity in Human Serum.* (17933)

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Greenstein and Jenrette(1) studied the depolymerization of thymonucleic acid by extracts from various tissues and body fluids. The enzyme responsible for this depolymerization was found to be present in the serum of the guinea pig, mouse, rabbit and dog, but not in that of man. McCarty(2) isolated the enzyme from beef pancreas, termed it "desoxyribonuclease", showed that it was activated by magnesium, and found that the optimal concentration for such activation was 0.003 M. In view of McCarty's findings, it was of interest to determine whether the addition of magnesium ion to human serum would reveal any desoxyribonuclease activity and, if so, to study this activity in normal individuals and in patients with cancer and noncancerous disease.

Desoxyribonucleic acid was prepared from calf thymus, essentially in accordance with Hammarsten's method(3), and dried in vacuum to constant weight. Analyses gave a value of 8.11% for the phosphorus content. The desoxyribonucleic acid was dissolved in 0.028 M veronal buffer of pH 7.5 so as to yield a concentration of 0.8 mg desoxyribonucleic acid per cc. Batches of this solution were filtered just before each series of determinations. McCarty's method for determination of the desoxyribonuclease activity was employed. A volume of 4.0 cc of the 0.08% solution of desoxyribonucleic acid was placed in an Ostwald viscosimeter immersed in a water bath at $37.0 \pm 0.1°$. The relative viscosity, η, of this solution was usually between 2.80 and 3.00. When this solution had attained the temperature of the bath, any substance such as Mg^{++} ion, the effect of which was being investigated, was added. The contents were mixed thoroughly by raising and lowering the solution several times, and several viscosity determinations were made in order to obtain an initial value. At a stated time, 1 cc of serum, brought to 37.0°, was added; the contents were mixed again and the change of viscosity with time was determined. In accordance with McCarty's procedure, the slope of the straight line portion of this curve was taken as the reaction velocity. In this paper, the velocity is expressed as the change in the relative viscosity, η, per 10^3 seconds.

Effect of Mg^{++} concentration. One-tenth cc of distilled water, or of various concentrations of Mg^{++}, was added to 4.0 cc of the desoxyribonucleic acid solution, and 1.0 cc of a pooled specimen of serum was then added. Table I shows that in agreement with the observations of Greenstein and Jenrette, only very slight activity was demonstrable in human serum in the absence of added magnesium over a period of several hours. If the reaction was allowed to proceed overnight (20 hours) measurable activity was manifest. The addi-

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1. Greenstein, J., and Jenrette, W. V., *J. Nat. Cancer Inst.*, 1941, v1, 845.

2. McCarty, M., *J. Gen. Physiol.*, 1946, v29, 123.

3. Hammarsten, E., *Biochem. Z.*, 1924, v144, 383.

TABLE I.
Effect of Mg^{++} Ion on Desoxyribonuclease Activity of Human and Animal Sera.

Final concentration of added Mg, M	Velocity			
	Human	Guinea pig*	Rabbit	Dog
.000	.023	.033	.305	.210
.0002	.059	.193	.370	.255
.003	.150	.345	.800	.301
.010	.098	.315	.790	.238
.020	.066	.280	.520	.190

* Undiluted guinea pig serum, even without the addition of Mg^{++}, gave such high activity that it could not be precisely measured. Consequently, 1 cc of a 1:5 dilution was used in these experiments.

TABLE II.
Thermolability of Human Serum Desoxyribonuclease Activity.
Serum heated for 20 min. at 55° to 60°. Final concentration of Mg^{++} was 0.003 M. Other conditions as described in text.

	Activity of unheated enzyme	Activity of heated enzyme	Decrease in activity, %
Serum 1	.180	.006	96
" 2	.150	.015	90

tion of magnesium chloride caused an activation of the desoxyribonuclease, sufficiently marked so that considerable changes in viscosity were obtained within one to 2 hours. The magnesium ion concentration necessary for optimal activation of human serum was found to be 0.003 M. Depolymerization of thymonucleic acid by the enzymic activity of the serum of the guinea pig, the rabbit, and the dog has been previously demonstrated(1). However, as shown in Table I, the addition of magnesium ion caused an increase in the desoxyribonuclease activity of all three sera. The concentration of magnesium ion necessary for optimal activity of guinea pig, rabbit, and dog sera was similarly found to be 0.003 M.

Thermolability of human serum desoxyribonuclease. In order to confirm the enzymic nature of the action, human serum was divided into 2 portions, one of which was kept at room temperature while the other was heated in a water bath at 55° to 60° for 20 minutes prior to determination of its activity. Table II shows that 90 to 95% of the enzymic activity was lost as a result of heating the human serum under the conditions described. This finding is in essential agreement with that of McCarty's observations on beef pancreas desoxyribonuclease.

Effect of pH. McCarty observed that the optimum pH for the action of beef pancreas desoxyribonuclease covered a broad range from 6.8 to 8.2. By using, as McCarty had done, a solution of desoxyribonucleic acid in veronal buffer of pH 7.5, we obtained, after the addition of human serum and at the end of the determination, pH values which, in practically all instances, lay between 7.50 and 7.80. Several series of determinations in quintuplicate showed that, within experimental error, there was no effect of pH upon activity within this pH range.

Desoxyribonuclease activity of serum in normal individuals, in patients with noncancerous disease, and in patients with cancer. In order to facilitate comparison, the desoxyribonuclease activity of the serum may be expressed in terms of units, where 1 unit is defined as a change of 1.0 in the relative viscosity produced in 10^3 seconds at 37° by adding 1 cc of serum to 4 cc of a 0.08% solution desoxyribonucleic acid in 0.028 M veronal buffer of pH 7.5. The control group consisted of sixteen apparently healthy individuals who ranged in age from about 21 to 65 years, and averaged 30 years. They showed serum desoxyribonuclease activities ranging from 0.14 to 0.54 unit and averaging 0.30 unit (Table III). The activities were not related to sex. The sera of 34 patients not having cancerous disease were tested for desoxyribonuclease activity.† This group ranged in age from 14 to 86 years and

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TABLE III.
Mean Value and Distribution of Serum Desoxyribonuclease Activity in Normal Individuals, Patients with Noncancerous Disease, and Patients with Cancer.

Group	No. of cases	Avg value in units	% of cases having activities, in units, of .00-.100	.101-.200	.201-.300	>.300
Normal individuals	16	.30	0	25	31	46
Noncancerous patients	34	.21	6	35	50	9
Patients with cancer	50	.15	31	52	10	6

The t value for the difference between the normal individuals and noncancerous patients was 3.2; for that between the normal individuals and cancerous patients, 5.7; and for that between the noncancerous and cancerous, 3.3.

averaged 50 years, and included a wide variety of noncancerous disease such as rheumatic fever, arthritis, cirrhosis, heart disease, benign tumors, diabetes, tuberculosis and diseases of the urogenital tract. The desoxyribonuclease activities ranged from 0.03 to 0.49 unit and averaged 0.21 unit. This average value was significantly lower than that for the group of normal individuals ($t = 3.2$; $P = <0.01$).

The group of 50 cancerous patients included cancers of the gastrointestinal tract, breast, genitourinary tract, Hodgkin's disease, melanoma, and liposarcoma. The ages in this group ranged from 24 to 75 years and averaged 52 years. The serum desoxyribonuclease activities ranged from 0.02 to 0.38 unit and averaged 0.15 unit. This average value was significantly lower than that for the group of normal individuals ($t = 5.7$; $P = <0.01$), and also than that for the group of patients with noncancerous disease ($t = 3.3$; $P = <0.01$).

The distribution of the desoxyribonuclease activities in the three groups is of interest (Table III). Thus, the incidence of activities less than 0.10 unit in the normal, noncancerous, and cancerous groups were 0, 6, and 31%, respectively, of the individuals in each group. 83% of the patients with cancer had activities less than 0.20 unit whereas only 41% of the patients with noncancerous disease and 25% of the normal individuals had activities below this level.

Discussion. The desoxyribonuclease activity of the serum has hitherto received scant attention. Because the activating effect of magnesium ion on this serum enzyme has not been recognized, it has been held that this enzyme is not present in human serum. The present work shows that the average serum desoxyribonuclease activity in the group of patients with cancer was significantly lower than the average in the normal group or in the group with noncancerous disease. The incidence of decreased serum desoxyribonuclease activities in the group of cancer patients does not appear to be sufficiently high to be of diagnostic value. No explanation for the occurrence of decreased serum desoxyribonuclease activity in disease can be offered at present. In general, such a decreased activity may reflect diminished output of the enzyme from one or more tissues of the body or the increased production of an inhibitor. Further study of the factors controlling the desoxyribonuclease activity of human serum is necessary before these possibilities can be evaluated.

Summary. The addition of Mg^{++} in a final, optimal, concentration of 0.003 M to human serum leads to distinct and readily measurable desoxyribonuclease activity. The average value of this activity in a group of fifty patients with cancer was significantly lower than the average value in a group of 34 patients, of comparable age, with noncancerous disease. Both average values were less than that of a normal group.

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