subject rose to 29 seconds several hours after a transfusion of 500 ml of normal whole blood. Two days later the serum prothrombin time had returned to 19 seconds. The serum prothrombin time of chronically ill hospitalized subjects averaged about 10 seconds higher than the young healthy control group. The significance of relatively high serum prothrombin time values found in some chronic disease states has not yet been determined.

Discussion. The 3 phases of serum prothrombin activity described in this report are suggestive of the presence of a substance which develops as clotting progresses, and interferes with prothrombin activity of serum if separated with the serum. This substance is apparently removed by the clot if the serum is not separated from the clot. Thus, during the first phase, only a small amount is formed and promptly neutralized. During the second phase some of the active substance is separated with the serum, and may destroy some of the protein moieties which contribute to prothrombin activity. If the serum remains with the clot, however, (third phase), all of this substance may be removed by the clot. This sequence is consistent with the concept that the substance is thrombin, since early in coagulation, thrombin is present only in traces (phase 1). Later it develops in appreciable amounts which may be separated with the serum (phase 2). This thrombin in serum, free from its normal adsorbents (fibrinogen, fibrin, and platelets), may exert a binding or proteolytic effect on other serum proteins, and may destroy some component of the prothrombin complex. However, if the serum is permitted to remain in contact with the clot (phase 3), the thrombin is adsorbed by the clot, leaving the residual prothrombin unaltered in the serum. This concept removes the necessity for postulating a new inhibitor substance to explain the observed facts. It is consistent with the data reported by others (3). Thus phase 1 represents only the initiation of prothrombin consumption; phase 2 represents a labile period of free thrombin activity; phase 3 represents a relatively stable period of residual prothrombin, reflecting the prothrombin consuming capacity of the blood.

The data demonstrate that prothrombin consumption can be estimated adequately by determining serum prothrombin time after one hour of clot incubation with the aid of a single, relatively stable, dry reagent preparation. The normal serum prothrombin time obtained with the preparation is about 40 seconds, as compared with about 25 seconds by the Quick technic. This difference is probably due to the difference in thromboplastin preparation plus the fact that only fibrinogen, free from extrinsic accessory clotting factors, is added. Much of the clinical significance of altered prothrombin consumption remains to be determined.

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Received January 14, 1952. P.S.E.B.M., 1952, v80.

Comparison of Parenteral and Oral Protein Feeding on Radiation Susceptibility in Protein-Depleted Rat. (19503)

F. LAMONT JENNINGS.* (Introduced by Paul R. Cannon.)

From the Department of Pathology, University of Chicago.

The damage that is apparent histologically in the intestinal epithelium following radiation has stimulated several investigations of intestinal absorption following radiation. Meed, Decker, and Bennett found no marked impairment of fat absorption from the intestine due

* Atomic Energy Commission Postdoctoral Research Fellow in Medical Sciences, National Research Council.

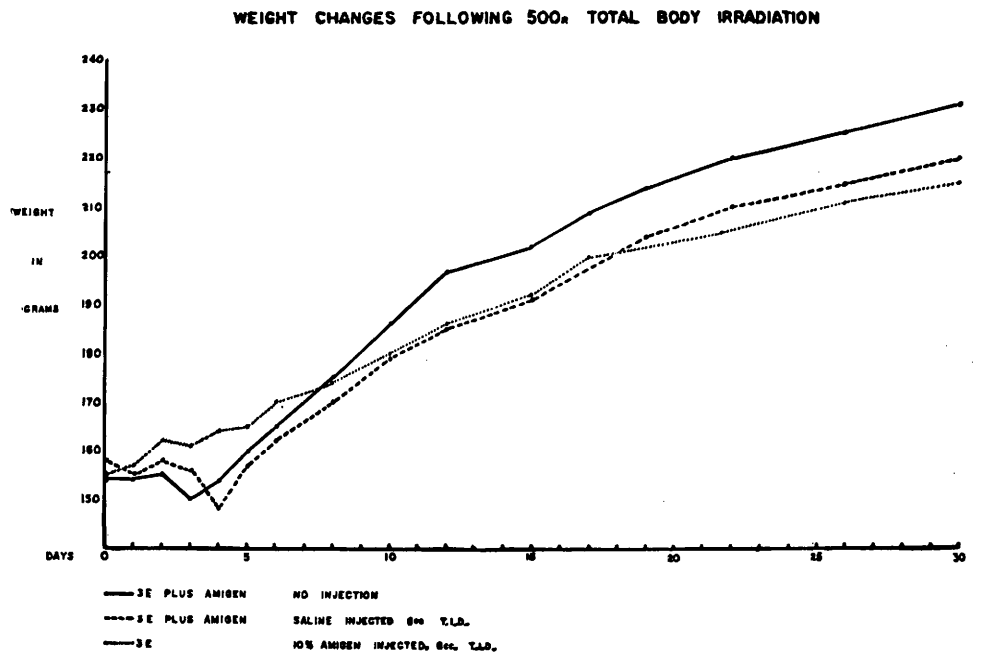

FIG. 1.

to radiation(1) though earlier investigators reported decreased fat absorption in dogs following radiation(2). Buchwald reported that the rates of absorption of glucose, fructose, and mannose were markedly diminished in rats 20 and 40 hours after sublethal radiation (3). These observations were recently confirmed by Barron(4). Since this present experiment has been completed Bennett and his group have reported that they found no change in the absorption rate of radioiodinated human serum from the intestinal tract of mice following sublethal radiation(5). In view of previous studies showing that the state of protein nutrition of an animal has considerable effect on the radiosensitivity of that animal(6), it seemed advisable to determine if parenteral administration of protein hydrolysate could produce more effective protein utilization than oral feeding following total body x-ray. For this reason the following experiment was undertaken in which groups of irradiated rats were given equal quantities of a protein hydrolysate (Amigen) orally and parenterally.

Procedure. Protein-depleted rats were used in this study since they are more sensitive to radiation than animals that have adequate protein reserves(6) and they have been shown to be a good test animal for assaying protein utilization(7,8). Ninety Sprague-Dawley male rats with an initial weight of 200 g were depleted of their protein reserves according to the procedure developed by Cannon and his group(9,10). When the animals had lost about 25% of their body weight after being maintained on the low protein diet for 10 weeks, they were random distributed into 3 series of animals of 30 rats each. Each series was then divided into 5 groups of 6 rats each and subjected to total body irradiation with the dosage ranging from 450 to 650 r. Following radiation all animals were housed in individual cages. All of the animals were weighed at 2-day intervals through the 30-day observation period. The enzymatic hydrolysate of casein, Amigen, was used in this study since the preparation was available both in powdered form for oral feeding and in 10% solution for parenteral administration. Previous studies have shown that Amigen promotes weight recovery in the protein-depleted rat comparable to that produced by the feeding of high quality protein(11). All of the animals in all groups received approximately

TABLE I. 6 Rats in Each Series. Diet: 3E + Amigen.

	Dose	Deaths
No inj.	450 r	0
	500	1
	550	3
	600	5
	650	6
Saline inj. 6 cc t.i.d.	450	0
	500	1
	550	3
	600	5
	650	5
Diet: 3E, 10% Amigen inj. 6 cc t.i.d.	450	2
	500	1
	550	3
	600	5
	650	6

1.8 g daily which is equivalent to 1.35 g of protein per day (NX 6.25). In all animals a basal low protein diet (3E) was fed to supply the caloric and vitamin requirements(9) and this diet was supplemented by the Amigen. The first series of rats received the basal ration (3E), to which 128 g of powdered Amigen had been added per kg, at the rate of 15 g per rat per day. No injections were given in these animals. The second series of animals was also fed 15 g per rat per day of the basal diet to which powdered Amigen had been added at the rate of 128 g per kg. All of the animals in the second series were injected with 6 cc of saline subcutaneously 3 times a day to serve as controls for the fluid intake of the third series. The third series was fed the low protein diet at the rate of 15 g per rat per day. These animals were given 6 cc of 10% Amigen subcutaneously 3 times a day.

Results. The weight changes for all the animals given 500 r of radiation are shown in Fig. 1. It is noted that the animals given Amigen subcutaneously did not undergo the weight loss during the first 3 or 4 days shown by the 2 groups fed orally. Weight loss during early radiation recovery is the usual finding. There was a somewhat greater rate of weight gain between the 3rd and 12th days in those animals not subjected to the trauma of injection.

The mortality results in this experiment are summarized in Table I. Mortalities were almost identical in all 3 series with the exception of 2 deaths at 450 r in the series given Amigen subcutaneously. Calculation of mortality regression lines, according to the method reported by Bliss(12), showed very little difference in the LD50/30 for the animals in the 3 series. The LD50/30 for the animals given Amigen subcutaneously was about 544 r, for the animals given saline subcutaneously about 554 r, and for those given no injections about 547 r.

Discussion. The weight curves show that there is no essential difference in weight recovery in the protein-depleted rat whether that animal is given protein hydrolysate orally or parenterally. The fact that the weight curve for those animals given Amigen subcutaneously rises almost steadily from the start of the administration of Amigen suggests that possibly intestinal absorption was impaired for the first 3 or 4 days in the other groups. It is doubted that this early weight increase is due to water retention for a similar rise is not seen in the series injected with saline. The weight recovery curves suggest that protein utilization is similar in the protein-depleted irradiated rat whether the hydrolysate is given orally or parenterally.

There is a slight divergence of the weight curves between the 6th and 12th days for the animals given no injection and those injected with saline. No reason can be offered for this divergence but it is noted that the curves are parallel for the last half of the experiment. For this reason it is felt that the trauma of multiple injections and the forcing of large volumes of subcutaneous fluid into the animal had very little, if any, deleterious effect on the animal. Autopsy of the injected rats at the conclusion of the experiment showed no edema, fibrosis, or infection in the subcutaneous area of the back despite the fact that the animals had been subjected to 90 subcutaneous injections and 540 cc of fluid.

The mortality regression lines indicate that there is no difference between feeding a protein hydrolysate orally or parenterally following radiation in the protein-depleted animal. The lines also indicate that multiple injections under sterile conditions do not have an adverse effect on survival in the radiated rat.

While this experiment shows that parenteral feeding of protein hydrolysate during radia-

tion recovery offers no advantage over oral feeding as measured by long-term weight gain or mortality, it does suggest that parenteral feeding may be advantageous during the first few post-irradiation days. For this reason further work with parenteral hydrolysate administration during the early post-irradiation period is indicated. In view of the earlier work of Buchwald reporting impaired intestinal glucose absorption in the immediate post-irradiation period(3), the effect of complete parenteral feeding in the early period following radiation should be studied.

Conclusions. 1. Parenteral feeding of protein hydrolysate following radiation offers no advantage over oral feeding in the protein-depleted rat as measured by radiation susceptibility. 2. Parenteral hydrolysate administration may be advantageous in preventing early post-irradiation weight loss.

The animals were irradiated through the kind cooperation of the Biology Division, Argonne National Laboratory, Chicago, Ill.

The author wishes to express his appreciation for the aid and assistance of the following: Paul R. Cannon, Robert W. Wissler, and Randolph H. Hughes, Department of Pathology, University of Chicago and Austin M. Brues, Biology Division, Argonne National Laboratory, Chicago, Ill.

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Received January 31, 1952. P.S.E.B.M., 1952, v80.

Inhibition of Growth of a Green Flagellate by the Antihistamine, β-dimethylaminoethyl (Benadryl).* (19504)

THEODORE L. JAHN AND WILLIAM DANFORTH.

From the Department of Zoology, University of California, Los Angeles.

The antihistamines and related drugs have been shown to have a variety of effects upon living systems, including growth inhibition of micro-organisms(1-5), inhibition of glutamate oxidation by rat brain tissue(6), and production of conduction block and depolarization of frog nerve(7). Of these effects, only one case of bacteriostatic activity(4) and one case of fungistatic activity(3) were reversible by histamine. Experiments in this laboratory have shown that β-dimethylaminoethyl benzhydryl ether (Benadryl hydrochloride, Parke, Davis Company) is a potent inhibitor of the growth of the green flagellate, *Chlorogonium tetragamum.*

Experiments were carried out in a modification of the medium of Hutner *et al.*(8) for fresh-water chlamydomonads, produced by reducing the concentrations of trace metals and chelating agent to one-fifth those described for the original medium. Dilution of this medium by one-sixth its volume, changes in initial pH from 5.5 to 8.0, and the addition of the metabolites and biological

* Aided by a grant from the California Cancer Institute.