Although it is clearly impossible to be certain as to what factors lead to increased small intestinal serotonin concentration in rats fed a diet which is deficient in both tryptophan and niacin, it is felt that this finding may explain the diarrhea that is observed in pellagrous patients. Furthermore, it may be that the elevated levels of serotonin encountered in patients with sprue may be a reflection of niacin-tryptophan deficiency.

Summary. Groups of rats were fed tryptophan-deficient diets and niacin-tryptophan deficient pellagragenic diets. The former group showed significantly decreased concentrations of serotonin in the small intestine, brain, and colon, while pellagrous rats showed a significant increase in the small intestinal serotonin levels and no decrease in the brain or colonic concentration was observed. The elevated small intestinal concentration of serotonin in the N-T deficient rat is considered to be compatible with a diarrhea based on increased intestinal motility.

1. Krehl, W. A., Teply, L. J., Sarma, P. S., Elvehjem, C. A., Science, 1945, v101, 489.
2. Brodie, B. B., Pletscher, A., Shore, P. A., Science, 1955, v122, 968.
3. Sjoerdsma, A., New Eng. J. Med., 1959, v261, 181.
4. Denton, J., Am. J. Trop. Med., 1925, v5, 173.
5. Feldberg, W., Toh, C. C., J. Physiol., 1953, v119, 352.
6. Udenfriend, S., Fluorescence Assay in Biology and Medicine, New York: Academic Press, 1962, p170-176.
7. Boullin, D. J., Brit. J. Pharmacol., 1964, v23, 14.
8. Eber, O., Lembeck, F., Pflügers Arc. Ges. Physiol., 1958, v265, 563.
9. Paasonen, M. K., Kärki, N. T., Brit. J. Pharmacol., 1959, v14, 164.
10. Wood, M. M., Brit. J. Tuberculosis, 1955, v49, 20.

Received March 14, 1967. P.S.E.B.M., 1967, v126.

Serum Zinc Levels Following Exposure to Ionizing Radiation.* (32450)

M. A. QUAIFE AND R. E. OGBORN (Introduced by H. P. Jacobi)
Special Laboratory of Nuclear Medicine and Biology, Veterans Administration Hospital, Omaha, Nebraska

An investigation of the trace element zinc in serum as an indicator of exposure to ionizing radiation was predicated upon the role of certain trace elements in important biochemical processes in the living organism. Specifically zinc has been identified in several enzyme systems, *i.e.,* dehydrogenases and pancreatic carboxypeptidase(1,2), and alcohol dehydrogenase and glutamic dehydrogenase (3) in mammalian liver with evidence that zinc is the active enzymatic site and its presence is indispensable to their activity (4,5).

Alteration of enzyme levels in the serum of various mammalian species including man have been reported following exposure to significant amounts of ionizing radiation. In certain of these reports the enzymes were of the zinc containing metalloenzyme groups (6-8). By an investigation of the common denominator of these systems, *i.e.,* zinc, following the radiation insult, it was postulated that a useful pattern of response might evolve allowing application of this parameter as a biologic indicator of exposure to ionizing radiation. Additional support to this concept was given by Wolff(9) who noted increased serum zinc levels in patients undergoing radiation therapy.

Materials and methods. Pure bred Beagle dogs (equal numbers of male and female) in experimental groups of 30 each were utilized. The experimental subjects were individually irradiated using a Cobalt 60 teletherapy unit containing 989 curies of activity while the control group received sham irradiation. The clinical status of the experimental subjects was monitored throughout the post-exposure period. Radiation was delivered at 5.0 R/min,

* Supported in part by U. S. Air Force Contract AF29-601-62-5217.

Entrance Air Dose. The target skin distance was 162.5 cm. One half the total dose was delivered to each side of the animal. Constant geometry was maintained by a restraining box constructed of one half inch thickness of lucite (24″ × 12″ × 20″). A Siemens-Reinigewerke R-meter was used to calibrate the irradiation unit and to monitor each exposure.

After establishing baseline zinc levels by sampling from the external jugular vein using 20 gauge needles and antiseptic precaution, the subjects' zinc levels were determined at 6, 12, 18, 24 and 108 hours post exposure. The zinc level was determined on non-hemolyzed plasma samples by spectrophotometric analysis after diphenythrocarbozene complexing of the element. Percent recovery by this method was 100.3% ± 2.1%.

The data from this study were subjected to a mean percent of pre-exposure level transformation in order to allow for the individual biochemical variation in the experimental subjects' basal state.

Results and discussion. The zinc level following exposure is depicted in Fig. 1. The group response of the plasma zinc level in the dog following irradiation was that of elevation above the control group. This pattern was noted in all dosage groups except the

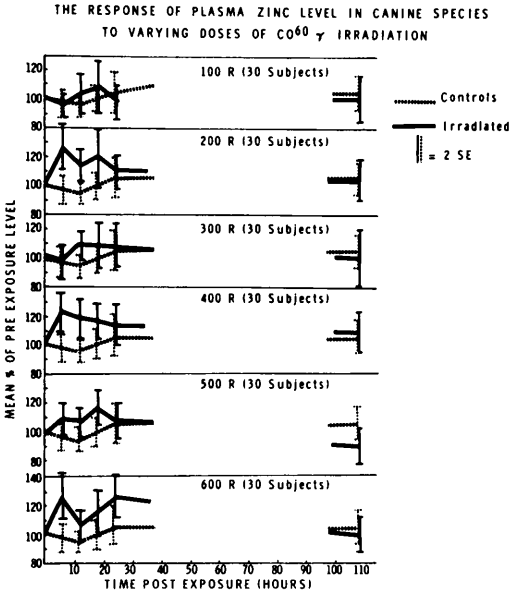

FIG. 1.

100 R group. In this group there is a suggestion of a similar response occurring at 12 and 18 hours post exposure. The remainder of the dose groups exhibit an elevation during the day of exposure and all have returned to control levels by 108 hours post exposure. In the case of the 500 R group the group mean was below that of the control group at 108 hours.

Observation of the physiological state of the experimental subjects did not reveal evidence of gastrointestinal disturbance during the time period of sampling. Alteration of blood volume does not appear to be a factor in the elevation of the serum zinc level. This fact is supported by evidence in irradiated beagles indicating a minimal alteration in plasma volume in the immediate post-exposure period(10).

The role of trace metal in metabolic processes is suggested as a useful area of exploration in discerning the biochemical alterations following exposure to ionizing radiation. This suggestion is based upon the fact that trace metals are in many instances the cofactors upon which enzyme activity is dependent. Alterations of plasma copper and magnesium have been reported(11) as well as serum manganese(12). Zinc as a cofactor in a number of metalloenzymes has been studied for its response in extracellular fluid, as reflected in the plasma level, to the effects of ionizing radiation. In the species studied the pattern of response was that of an increase over the pre-exposure level as well as that of the control group. The statistical variation within groups yielded varying degrees of overlapping.

As a mirror of the biochemical lesion of ionizing radiation, this parameter must be related to effects in the total organism. The more common endpoint utilized in radiation effects is that of lethality. Table I depicts the mortality in the experimental groups.

The dose mortality relationship suggests that the dose rate of 5.0 R/min influenced this study. The median lethal dose for this species is approximately 300 R for acute effects. The flattening of the dose mortality curve in this investigation with a median lethal dose between 500 R and 600 R introduces the dose rate factor as a possible ex-

TABLE I. 30-Day Mortality Following Exposure to Varying Doses of Gamma Radiation.

Dose (R)	No. of deaths/group	% Lethality
600	17/25*	68
500	7/25	28
400	6/25	23
300	1/25	4
200	0/25	0
100	0/25	0

* 5 animals chosen at random from each group were sacrificed on day 5 for histopathologic studies.

planation of the minimal elevation of serum zinc at lower total doses of radiation. Although no linear dose response relationship was found between groups in this study, the highest dose elicited the maximal elevation of serum zinc level, which was sustained for a longer period of time.

The technical assistance of Mr. T. J. Johnson, Mrs. Sheryl Swanberg, Mrs. Mary Haven and Mr. Henry Hahn is gratefully acknowledged.

1. Vallee, B. L., Hock, F. L., Proc. Nat. Acad. Sci., 1955, v41, 327.
2. Vallee, B. L., Neurath, H., J. Biol. Chem., 1955, v217, 253.
3. Vallee, B. L., Hock, F. L., ibid., 1957, v225, 185.
4. Vallee, B. L., Adelstein, S. J., Olson, J. A., J. Am. Chem. Soc., 1955, v77, 5196.
5. Vallee, B. L., Coombs, T. L., Williams, R. J. P., Fed. Proc., 1957, v16, 264.
6. Peterson, D. F., J. Occ. Med., 1961, v3, 155.
7. Peterson, D. F., Hughes, L. B., Rad. Res., 1958, v9, 166.
8. Brent, R. L., McLaughlin, M. M., Stabile, J. N., ibid., 1958, v9, 24.
9. Wolff, H., Deut. Arch. Klin. Med., 1950, v197, 263.
10. Odland, L. T., Ph. D. Thesis, Univ. of Rochester School of Med. & Dent., Rochester, N. Y., 1962.
11. Haley, T. J., Flesher, A. M., Komesu, N., Rad. Res., 1958, v8, 535.
12. Smith, H., Bates, T. H., Proc. Series, IAEA, 1965, March.

Received March 26, 1967. P.S.E.B.M., 1967, v126.

Rates of $C^{14}O_2$ Production from Labeled Ethanol, Acetate and Glucose in Alcohol Drinking and Non-Drinking Rats.* (32451)

JAMES L. MEEK, EDWARD MAJCHROWICZ AND MORRIS A. LIPTON†
Departments of Psychiatry and Biochemistry, University of North Carolina School of Medicine, Chapel Hill

Several investigations support a possible association between the acquisition of behavioral tolerance and an adaptive increase in alcohol dehydrogenase activity in animals subjected to chronic alcohol consumption. Some of these studies, as reviewed by Hawkins *et al*(1) employed too few animals, others too low a dosage level, and others too toxic a method of administration. In this paper we describe the rates of $C^{14}O_2$ formation after injection of ethanol-1-C^{14}, acetate-1-C^{14} and glucose-U-C^{14} into rats which had consumed dilute ethanol for up to 11 months.

Methods and materials. Male Wistar rats weighing 100 g were caged in pairs, and were allowed to eat a diet of Purina chows *ad libitum*. The control group consisted of 18 rats which were given tap water to drink. Three experimental groups of one dozen rats each were allowed only 5%, 10% or 20% solutions of ethanol in tap water for up to 11 months.

$C^{14}O_2$ monitoring system. A Nuclear-Chicago Dynacon (which consisted of an ionization chamber with a high precision DC voltmeter, a recorder, and an integrator) was used to measure rates of metabolism of labeled substrates by determining the appearance of $C^{14}O_2$ in expired air. For measurement of the current produced by the ionization chamber we used a method known either as the high resistance leak or as the equilibrium voltage method(2).

Rate of elimination of ethanol. Rats which had been drinking ethanol from 6½ to 11 months were injected intraperitoneally with

* This investigation was supported by USPHS grant AM-08329.
† Recipient of USPHS Career Development award AM-05062-05.