Damage to the intestional mucosa after exposure to moderate doses of irradiation (11, 12, and 13) coupled with damage resulting from the invasion of the villus by the tapeworm hexacanth embryo is of interest in terms of host and intestinal flora relationships. Since this tapeworm infection brought about a significant decrease in the survival of irradiated animals in the absence but not in the presence of streptomycin, a synergistic relationship is suggested. Although not precluded the parasite does not appear to enhance the invasion of bacteria since the incidence of bacteremia was not appreciably different in irradiated mice whether infected or uninfected. A possibility exists that the tissue phase of the cestode infection permits the passage of toxic microbial products from the gut. Some of the immunogens elaborated by this tapeworm during infection are esterases(14), and preliminary studies are being undertaken to investigate the role of active immunization (anti-enxyme-permeability factor) on survival of the irradiated host.

Summary. The superimposition of infection by the dwarf tapeworm, *Hymenolepis nana*, on mice exposed to either 450 or 650 R of whole body x-irradiation considerably lowered host survival. Larger worm loads were observed in mice surviving radiation exposure and infection. Infections persisted for longer periods of time and at higher levels (in terms of worm number) in irradiated hosts as compared to those not irradiated. However, increased susceptibility and lowered immunity, as exhibited by irradiated (450 R) hosts, did not appear to permit autoinfection to take place. Streptomycin therapy produced a striking increase in the survival of irradiated, infected mice.

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Alteration of Serotonin Metabolism in Rats Deficient in Niacin And Tryptophan.* (32449)

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The mechanisms responsible for the dermatitis, dementia, and diarrhea of pellagra remain obscure. Niacin deficiency alone will not result in pellagra. Tryptophan which can be converted by the body to niacin must also be deficient(1). One physiologically important product of tryptophan metabolism, serotonin (5-hydroxytryptamine), has a well recognized role in both gastrointestinal motility and cerebral function(2,3). The fact that serotonin is produced and stored chiefly by the enterochromaffin cells of the intestinal

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glands of Lieberkühn and that these glands undergo cystic and atrophic degeneration in pellagra(4), suggests that a disturbance of serotonin metabolism may exist in pellagra. This study was undertaken to ascertain if an alteration of serotonin concentration does occur in the gastrointestinal tracts and brains of niacin-tryptophan deficient (N-T deficient) rats.

Methods. Twenty-four-day-old, weanling male Sprague-Dawley rats were selected at random and placed on one of the following diets prepared by the Nutritional Biochemicals Corporation: 1) Tryptophan-poor, niacin-deficient (20 rats); 2) Tryptophan-poor (10 rats); 3) Normal diet for pair feeding the N-T deficient group (10 rats). A fourth group of 10 rats was fed Purina Laboratory Chow *ad libitum* to exclude anything intrinsic in the normal diet that might influence normal serotonin levels. Diet 1 contained the following nutrients: casein 80 g, casein hydrolysate 120 g, alphacel 20 g, sucrose 700 g, cottonseed oil 50 g, and salt mixture USP XIV 30 g totaling 1 kilogram. The following were added to the kilogram: codliver oil 10 g, thiamine hydrochloride 5 mg, riboflavin 5 mg, calcium pantothenate 10 mg, pyridoxin hydrochloride 10 mg, choline 1400 mg, inositol 250 mg, biotin 0.2 mg, pteroylglutamic acid 0.2 mg, para-aminobenzoic acid 50 mg. Diet 2 was the same as diet 1 except that 50 mg of niacin were added to the total. Diet 3 was the same as diet 1 except that it contained casein 200 g and no casein hydrolysate and also contained 50 mg of niacin.

Analyses of diets 1, 2, and 3 by the Wisconsin Alumni Research Foundation yielded the following results: Diet 1, niacin 2.64 μg/g and tryptophan 0.56 mg/g; Diet 2, niacin 60.9 μg/g and tryptophan 0.56 mg/g; Diet 3, niacin 94.8 μg/g and tryptophan 2.03 mg/g.

Fig. 1 shows the average weight gain of each of the dietary groups over a 15-day period. The deficient rats and control animals had comparable rates of weight gain while the *ad libitum* laboratory chow fed group showed a normal rate of weight gain.

In 3 to 4 weeks when symptoms of N-T deficiency were manifest in the rats by reddish pigmentation of the paws, snout, and ears,

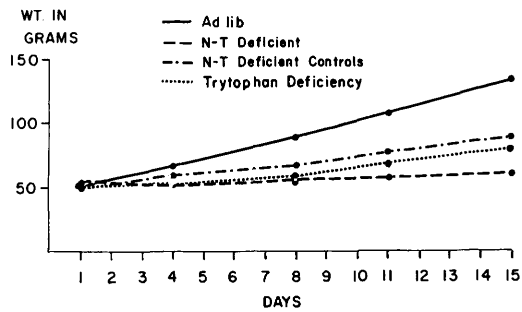

FIG. 1. The average weight gain of the various dietary groups over a 15-day period.

loss of hair, and diarrhea, 10 of the N-T deficient rats and their pair-fed controls were killed by guillotine. The small intestine of the N-T deficient and control rats from pylorus to cecum was stripped of mesentary, opened longitudinally, and washed in running tap water(5). The intestine was then cut in approximately 2 cm lengths with 3-4 mm at each cut being reserved for the determination of fat-free, dry solids (FFDS) which were used to calculate serotonin concentrations for the small intestine and colon so as to eliminate any variation due to the state of hydration of the animals and consequent water content of the tissues. The 2 cm segments were blotted dry, weighed, and homogenized in 0.1 N HCL. The homogenates were centrifuged and an aliquot of the supernate was used for determination of serotonin by the method of Udenfriend(6). Determinations were performed with a Turner fluorometer using a Baird Atomic A-11 filter and a 2mm Pyrex glass filter for the exciting wave length of 295 μm and a Corning 540 μm filter for the emission wave length. Standards of serotonin were prepared in 0.1 N HCL from serotonin creatinine sulfate (Nutritional Biochemicals Corp.) and were carried through the extraction procedure. The preparation of the colon included the cecum. The entire brain with the exception of the olfactory lobes was homogenized and extracted in butanol without centrifugation. Duplicate determinations for serotonin on standards and small intestine varied by less than 5%. Colon and brain levels were measured in single determinations because of limited quantities of materials. Following depolarization of the butanol with heptane, 2 ml of the final 0.1 N HCl solution were placed in 1 ml of 3 N HCL in a quartz cuvette and the fluorescent activity determined.

The remaining 10 N-T deficient rats were placed on a normal Purina laboratory chow diet with a multivitamin supplement, Berroca-C (Roche Laboratories) and 1 cc containing 40 mg of niacin was added to each 100 cc of their drinking water. Even so, 3 rats in this latter group died. The surviving 7 rats were killed after 4 weeks of the chow diet. The tryptophan-deficient and laboratory chow *ad libitum* dietary groups of rats were killed at 5 and 6 weeks respectively and their tissues studied in the same manner as described above.

Results. Table I shows the mean levels of

MEAN VALUES OF SEROTONIN CONCENTRATION OF THE SMALL INTESTINE, COLON, AND BRAIN

		AD LIB	CONTROL	TRYTOPHAN DEFICIENT	N-T DEFICIENT	N-T DEFICIENT	
SMALL INTESTINE							
	MEAN	20.9 (10)	22.9 (10)	13.6* (10)	42.5* (10)	25.8 (7)	μg/g FFDS
COLON							
	MEAN	41.3 (10)	38.6 (8)	27.3** (10)	40.6 (9)	46.0 (7)	μg/g FFDS
BRAIN							
	MEAN	0.39 (9)	0.40 (10)	0.24* (10)	0.36 (9)		μg/g wet wt.

* $P < .005$ (t test) compared to controls
** $P < .01$ (t test) compared to controls
( ) = Number of rats studied

TABLE I.

serotonin found in the small intestines, colons, and brains of the 4 dietary groups and in the 7 surviving treated N-T deficient rats. The laboratory chow *ad libitum* fed rats, the control fed rats, and the treated N-T deficient rats had similar mean concentrations of serotonin ranging from 20.9 μg/g of FFDS to 25.8 μg/g of FFDS. The tryptophan-deficient rats had significantly lower concentrations of serotonin in the intestines, colons, and brains than the control animals. The N-T deficient rats, on the other hand, showed a significant increase in the small intestinal serotonin concentrations being approximately twice the level of the controls. The brain and colonic concentrations remained unchanged from those of the control rats despite the deficiency of tryptophan in the diet. It is not clear as to why the colonic levels of serotonin failed to rise as they did in the small intestines of the N-T deficient rats, but it is possible that the local production of niacin by colonic bacteria may have prevented the striking elevation that was noted in the small intestine of these rats. Small intestinal serotonin concentrations in the N-T deficient rats subsequently fed a normal laboratory chow diet approximated those of the control and laboratory chow *ad libitum* fed groups. This points to the reversibility of the observed increase in small intestinal serotonin concentrations produced by niacin-tryptophan deficiency.

Discussion. It is apparent from these observations that a tryptophan-poor diet results in a reduction of serotonin concentration in the rat intestine, colon, and brain, in accordance with the findings of others(7,8). The further deletion of niacin from the tryptophan-deficient diet led to a significant increase in the concentration of this bioamine in the rat small intestine, an effect which was apparently reversed by normal diet and vitamin supplement. The 4-fold increase in the intestinal serotonin concentrations of the N-T deficient rats compared with tryptophan-deficient rats could be due to an increased production or a decreased destruction of serotonin. Increased production in the face of a diminished intake of the precursor seems unlikely. Since monoamine oxidase constitutes a major pathway in the catabolism of serotonin, it may be that niacin-deficiency leads to a decrease in activity of this enzyme in a manner similar to the monoamine oxidase inhibitor, iproniazid, which also results in elevation of tissue serotonin in the rat(9). The similarity of the chemical structure of iproniazid to niacin suggests that it could be a metabolic analog. This is further supported by the report that a similar drug, isoniazide, produced a marked delay in the healing of pellagra occurring in tuberculous patients, and in 3 patients who developed psychosis niacin therapy resulted in improvement(10). Since iproniazid raises serotonin levels in the otherwise normal rat, it seems unlikely that other catabolic pathways are adequate to maintain normal levels when monoamine oxidase activity is reduced.

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.

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

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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,

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