gastrointestinal tract into the vascular system has been determined in man by adapting an integral equation approach for use with a digital computer. A single tracer dose of Ca^{47} and of Sr^{85} was given both by the oral and intravenous route in separate studies and serial samples of plasma were obtained for radioassay. The maximal rate of initial entry of Ca^{47} per 15-minute interval ranged from 2.2% to 3.8% of the dose and was reached within 1½ hours. This rate was sustained for about one hour and decreased thereafter with time. The rate of initial entry for Sr^{85} was less than that for Ca^{47}, not exceeding 1.5% of the dose in any 15-minute interval, but was relatively more sustained from the first to the fourth hour After the fourth hour, the rates of initial entry of Sr^{85} and Ca^{47} were almost proportional.

APPENDIX I

```
0   $IBFTC   FHGJ
1   Dimension B(30), F(30), G(30)
2   Read 100, (F(J), G(J), J = 1,30)
7   B(1) = 0.0
10  Print 120, B(1), F(1), G(1)
11  Do 80 J = 2,30
12  K = J - 1
13  S = 0.0
14  Do 70 L - 1,K
15  M = J + 1 - L
16  70 S = B(L) * F(M) + S
20  B(J) = (G(J)-S)/F(1)
21  80 Print 120, B(J), F(J), G(J)
23  100 Format (2F8.4)
24  120Format (1H, F8.4,3X,F8.4,2X,F8.4)
25  Stop
26  End
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Effect of X-irradiation on Host Resistance to the Dwarf Tapeworm.* (32448)

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It is known that the course of certain infectious processes is aggravated in animals following sublethal doses of ionizing radiation. To date most studies have been concerned with the role of bacteria. There is some information on host susceptibility to parasitic infections following radiation exposure, but there is no information on cestodes and interest has centered primarily on a single nematode, *Trichinella spiralis*(1).

Although man and rodents are susceptible to infection with the dwarf tapeworm, *Hymenolepis nana,* host resistance to egg infection is relatively pronounced in that only a small percentage of ova consumed develop into adult forms. Furthermore, acquired host resistance to reinfection is striking following

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the intake of tapeworm ova, but not following the intake of cysticercoids which permit autoinfection to take place(2). Immune globulins appear to be formed and later directed against both the tissue and lumen stages of this parasite(3,4). In contrast to the more pathogenic trichina worm, considered in other studies(1), this cestode does not cause the death of parasitized hosts. It is the purpose of this paper to report a marked decrease in the ability of the irradiated host to resist infection by *Hymenolepis nana*. Cellular and humoral defense mechanisms were disturbed in the irradiated host to the extent that significantly decreased host survival was observed in parasitized animals as compared to uninfected, irradiated mice.

Materials and methods. Infection. Swiss Webster ICR female mice, ranging in weight from 17 to 18 g, were employed as definitive hosts for the dwarf tapeworm, *Hymenolepis nana*. Infection was induced by ova which were recovered from gravid segments of worms lightly homogenized in normal saline (30 sec at 0°C). Approximately 10,000 eggs, as determined by hemacytometer counts, were administered into the stomach of control and experimental mice by means of a syringe with attached oral catheter. Mice were infected 24 hours after radiation exposure.

X-irradiation. Mice were placed in a circular, compartmented, plexiglass container on a revolving turntable and exposed to dose levels of 450 and 650 R of total body irradiation. An exposure dosage of 34 R per minute at a T-O distance of 94 cm was delivered by means of a General Electric Maximar unit operating at 250 KV and 15 ma with an inherent filtration equivalent to 4 mm of aluminum. A 0.25 mm copper filter was used as additional filtration.

Survival. The course of host resistance and survival was followed for a period of 21 days following radiation exposure. At this time surviving mice were sacrificed and serum samples were examined for the presence or absence of antibody. After autopsy, worm loads in terms of number and size were established. In a few instances surviving mice were observed for periods up to 63 days following x-irradiation. In one investigational series, streptomycin was employed to determine whether or not resistance of irradiated hosts to helminth infection might be enhanced by antibiotic treatment. The antibiotic (300 μg/g body weight) was administered daily by intraperitoneal injection to infected and control mice following radiation exposure until death or sacrifice 21 days later.

Antibody Assay Techniques. Whole worm homogenates were prepared in phosphate buffered saline (pH 7.2) and centrifuged at 110,000 *g* for 90 minutes in a preparative ultracentrifuge (Spinco Model L). That volume of supernatant material containing 1.5 mg of protein was utilized in the sensitization of tanned human formocells (Difco Laboratories) which were to be used in the indirect hemagglutination test of Boyden(5) as modified by Daniel *et al*(6). To determine newly formed antibody 2 uCi of C^{14} L-lysine (u.l. and specific activity = 0.658 mg/millicurie) were injected intraperioneally into each animal 10 hours before collection of serum samples. Control and experimental sera were absorbed with formocells sensitized with worm cell sap antigens (or bovine serum albumin as controls). Radioactive content of washed, lysed and dried cell samples was determined by means of a windowless gas flow proportional counter (Baird Atomic). Sample self-absorption was not a problem and corrections were made for background.

Cultures. Blood samples were taken aseptically by means of cardiac puncture from irradiated and irradiated, infected mice 9 to 10 days following radiation exposure. Heart infusion broth, eosin methylene blue and blood agar plates were each inoculated with 0.1 ml of a collected sample.

Statistical evaluations(7) of the data were carried out using the "t" Distribution and Chi Square analyses where appropriate.

Results and discussion. As shown in Table I, mice infected with *Hymenolepis nana,* following exposure to 450 R of whole body x-irradiation, have a significantly ($P<0.05$) lower percentage of survival than that observed for mice exposed to similar radiation dose but without subsequent tapeworm infection. Although infection with this cestode does not normally cause the death of mice,

TABLE I. Effect of X-irradiation on Host Resistance to the Dwarf Tape Worm, *Hymenolepis nana*, 3 Weeks Following Radiation Exposure and infection.

Treatment	Original No.	No. of survivors	% survival
Non-irradiated group			
Infected	24	24	100.0
Irradiated group			
450 R, uninfected	42	35	83.3
Infected	55	30	54.5
Uninfected + streptomycin	24	23	95.8
Infected + streptomycin	24	21	87.5
650 R, uninfected	33	8	24.2
Infected	36	7	19.4

results indicate that it is capable of decreasing host survival in irradiated hosts by more than 28%. This overall effect is similar to that reported by Stoner and Hale(8) where it was observed that the susceptibility of mice to infections with the nematode, *Trichinella spiralis*, is markedly increased following exposure of the host to ionizing radiation.

When radiation exposure was increased to 650 R, the differential level of survival between infected and uninfected mice was not as striking. Nevertheless, even in this case where survival was reduced from 83% (with 450 R) to about 25% (with 650 R), superimposition of the parasitic infection reduced the chances of host survival even further, namely to less than 20%.

Increased susceptibility to the tapeworm infection (Table II) was observed in mice that survived to autopsy (21 days after radiation exposure and/or 20 days after tapeworm infection in that the number of worms present in irradiated hosts (450 R) was significantly higher ($P<0.01$) than that found in non-irradiated mice. However, in the former case the individual worm size was observed to be consistently smaller. With rare exception (only one case noted) the worm load in mice observed 6 to 9 weeks after 450 R exposure does not suggest autoinfection. Rather, there appears to be a persistence of the initial infection but at a higher level (in terms of worm number) and for a longer period of time than observed in non-irradiated series composed of 14 mice, whereas no more than 1 or 2 worms were present per animal in a non-irradiated series of 12 mice. Incomplete suppression or partial recovery of the host's ability to form antibody against worm antigens was observed in mice 3 weeks after radiation exposure in that hemagglutination titers on pooled serum samples from irradiated mice were less than 1:12. Furthermore, the amount of radioactivity found in adsorbed C^{14} labeled anti-worm globulin was only 20 to 50% of that observed in non-irradiated, infected mice.

TABLE II. Effect of X-irradiation on Host Susceptibility to the Dwarf Tapeworm, *Hymenolepis nana*, as indicated by worm loads observed in 6 survivors 3 weeks after exposure (450 R) and 6 non-irradiated, infected survivors.

Worm load (No. of worms per animal)	
Non-irradiated Series	Irradiated Series
398	595
417	718
440	703
475	626
452	640
412	674

$t = 10.06$
$P <= 0.01$

Yarinsky(9) reported increased mortality of x-irradiated mice when infected with the trichina worm and postulated that worm migration through the tissues opened a path for bacterial invasion. Miller *et al*(10) reported a high incidence of bacteremia in mice following radiation exposures of 450 and 650 R. In the present study survival of irradiated animals that were uninfected was increased approximately 13% when given streptomycin (Table I). Streptomycin treatment of irradiated, infected animals resulted in a significant ($P<0.05$) increase in survival over irradiated, infected mice not receiving therapy. It should be noted that superimposition of the tapeworm infection on irradiated mice receiving streptomycin did not result in a significant difference in host survival, in contrast to observations noted for non-treated mice. Examination of blood cultures from 26 irradiated and 22 irradiated, infected mice, however, did not show any appreciable difference in the incidence of bacteremia 9 to 10 days post radiation exposure.

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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