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RADIOBIOLOGICAL ASPECTS OF HIGH ALTITUDE FLIGHT: RELATIVE BIOLO--ETC(U)
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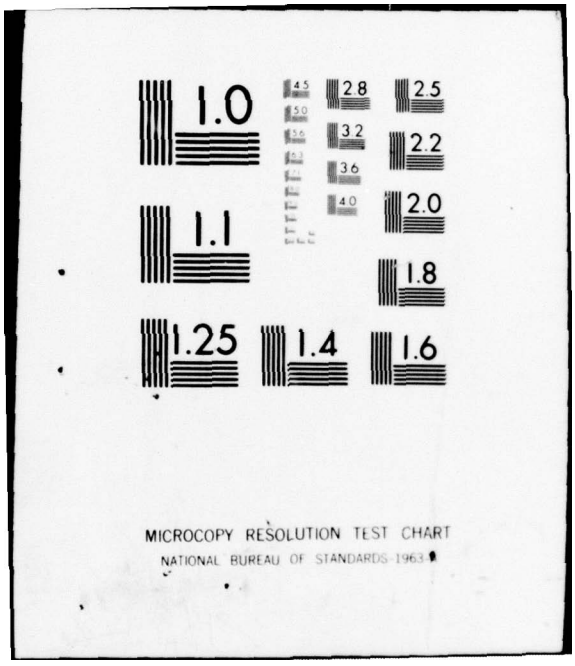
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16. Abstract

We investigated the relative biological effectiveness (RBE) of fast neutrons compared with X-rays in impeding development of immunity to an infective agent, the intestinal cestode Hymenolepis nana. Mice were irradiated with neutrons or X-rays and 2 days later given an immunizing dose of H. nana eggs. After another 2 days, the mice received a challenge dose of the eggs. Challenge egg doses were also given to sham-irradiated unimmunized and immunized controls. All mice were killed 90 to 92 hours after challenge, and the H. nana larvae (cysticercoids) that developed in the intestinal tissue were counted. An increased cysticercoid count in the irradiated mice, as compared with the count in unirradiated immunized controls, reflects suppression of immune capacity by the radiation. The results indicate a neutron RBE of 4 at 50 and 101 rad.

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RADIOBIOLOGICAL ASPECTS OF HIGH ALTITUDE FLIGHT: RELATIVE BIOLOGICAL EFFECTIVENESS OF FAST NEUTRONS IN SUPPRESSING IMMUNE CAPACITY TO AN INFECTIVE AGENT

I. Introduction.

Neutrons, produced by interaction of primary galactic and solar cosmic radiation particles with the earth's atmosphere, are a major component of the radiation environment at flight altitudes. Estimating the potential of neutrons for producing changes in biological indicator systems is germane to establishing risk estimates for humans.

There is extensive literature on effects of X-rays on immune mechanisms; however, relatively little attention has been given to immune changes caused by neutrons or other high-LET radiation. Gottlieb and Gengozian (1972 a,b; see also Gengozian, Carlson, and Gottlieb, 1968) compared fast neutrons with X-rays in suppressing the primary hemagglutinin response to sheep erythrocytes in mice. They found that suppression of immunity was dose-rate dependent with X-rays and independent of dose rate with neutrons. When X-rays at a high dose rate were the reference radiation, the relative biological effectiveness (RBE) of the neutrons was 3.4 at 66 rad (neutrons) with an in vitro culture system and 2.1 at 252 rad with intact animals.

We report here the RBE of fast neutrons in impeding development of immunity to an infective agent, the intestinal cestode Hymenolepis nana. In its direct life cycle in the mouse, from egg to egg-producing tapeworm, H. nana goes through a larval (cysticercoid) stage in the villi of the upper small intestine. Mice immunized to H. nana by infection with the eggs resist a subsequent challenge infection, as indicated by a reduced cysticercoid count.

II. Methods.

Nine-week-old male mice (C3H/Anf Cum ♀ X C57Bl/Cum ♂, Cumberland View Farms, Clinton, TN) were irradiated with neutrons or X-rays and 2 days later they were given an immunizing dose of approximately 5,000 H. nana eggs. After another 2 days the mice received a challenge of approximately 50,000 eggs. Two types of unirradiated control groups were used: unirradiated-unimmunized control mice that were sham irradiated and challenged 4 days later--these animals did not receive an immunizing egg dose--and unirradiated-immunized controls that were sham irradiated and given both the immunizing egg dose and the challenge dose. All animals were killed 90 to 92 hours after challenge, and cysticercoids were counted. We decided on a challenge of 50,000 eggs on the basis of a preliminary investigation with X-rays which indicated that a challenge of this size partially overwhelmed acquired immunity and thereby reduced the amount of radiation necessary to show a detectable effect (increased cysticercoid count) on

immune capacity. In the preliminary study essentially the same protocol described above was used except that challenges of 5,000 and 25,000 eggs were also tested.

The source of neutrons was the Health Physics Research Reactor at the Oak Ridge National Laboratory. The dose rate of neutrons was 2 rad/min and the average neutron energy was 1.2 MeV. The X-rays were generated by a General Electric Maxitron 300 operating at 300 kVp and 20 mA. The half-value layer of the X-rays was 1.2 to 1.4 mm Cu and the dose rate was 67 rad/min. Nylon tubes were used to restrain the mice during both kinds of irradiation. For other details of the irradiation procedures see Friedberg et al. (1973).

The doses of eggs were prepared as described previously (Friedberg et al., 1970) and administered by esophageal tube. The method of Heyneman and Sindell (1959) was used to prepare the small intestine for counting cysticercoids. Counts were made at a magnification of 20-40X by use of a dissecting microscope.

III. Results and Conclusions.

An increased cysticercoid count in the irradiated mice, as compared with the count in unirradiated immunized controls, reflects suppression of immune capacity by the radiation.

From results in Table 1 we estimated by linear interpolation between the X-ray doses that 393 rad of X-rays would be equivalent to 101 rad of neutrons with respect to median cysticercoid count. The neutron RBE for suppression of immune capacity is therefore 3.9. A similar treatment of the data in Table 2 indicates that 50 rad of neutrons would be equivalent to 200 rad of X-rays giving a neutron RBE of 4.0. These results are in reasonably good agreement with the neutron RBE of 3.4 at 66 rad reported by Gottlieb and Gengozian (1972 b) although different immunologic endpoints were measured. The neutron RBE of 4 determined in these experiments is a minimum estimate of the expected RBE value for neutrons at the low doses of cosmic radiation to which air travelers are exposed.

Table 1. Radiation Effects on Immune Capacity: 101 rad of Neutrons Compared with 300 and 400 rad of X-rays.*

Unirradiated (controls)		Irradiated before immunizing egg dose		
		Neutrons	X-rays	
Unimmunized	Immunized	101 rad	300 rad	400 rad
317	0	41	0	185
360	0	71	16	262
363	0	90	84	335
416	0	194	103	341
472	0	221	107	385
548*	2*	370*	118*	390*
569	10	421	199	444
812	16	438	215	478
912	63	444	225	569
931	79	540	273	618
963	233	561	281	659

*Immunization: 5.2×10^3 *H. nana* eggs.
Challenge: 47.0×10^3 eggs. Each table entry is the number of cysticercoids that developed in a single mouse after the challenge egg dose. Median values are indicated by asterisks (*).

Table 2. Radiation Effects on Immune Capacity: 45 and 60 rad of Neutrons Compared with 200 rad of X-rays.*

Unirradiated (controls)		Irradiated before immunizing egg dose		
		Neutrons		X-rays
Unimmunized	Immunized	45 rad	60 rad	200 rad
336	0	0	2	0
404	0	0	16	0
430	0	0	18	2
445	0	0	22	12
486	1	1	30	23
525*	1*	1*	72*	24*
537	8	2	97	27
569	20	5	136	39
682	44	7	171	51
684	56	10	220	133
812	378	229	363	284

*Immunization: 4.9×10^3 *H. nana* eggs.
Challenge: 50.0×10^3 eggs. Each table entry is the number of cysticercoids that developed in a single mouse after the challenge egg dose. Median values are indicated by asterisks (*).

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