Acetylation of P-Aminobenzoic Acid in X-Irradiated Rats. (21142)

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That the inactivation of Coenzyme A (CoA) may be of importance in the development of cellular damage in animals exposed to ionizing radiation has been suggested by several authors(1-3). It has been shown that: a) the protective effect of cysteamine is enhanced by simultaneous administration of pantothenic acid prior to irradiation(1); b) CoA preparations are superior to cysteamine in the pre-irradiation treatment of mice(4); and c) CoA is highly sensitive to oxidation by X-radiation *in vitro*(5). In regard to the first of these, small numbers of animals were used, and the results are far from conclusive. Further, the demonstration by Pierpoint and Hughes(6) that cysteamine is not involved in the biosynthesis of CoA in bacteria, suggests that any beneficial effects of pantothenic acid in supplementary radiation prophylaxis may be attributable to some other effect. The increased protection observed in mice injected with CoA prior to irradiation may be a reflection of the pronounced pharmacologic effects of the impurities in the CoA preparations employed(4). Finally, it has been shown several times that high radiation sensitivity of a compound *in vitro* does not necessarily bespeak a high sensitivity in the intact animal.

We have studied the capacity of the irradiated rat to acetylate p-aminobenzoic acid (PABA) and sulfanilamide, and have concluded that irradiation does not interfere with this process.

Methods. Female Sprague-Dawley rats, weighing 160 to 200 g, were used in these experiments. Because of differences in rates of excretion of the free and acetylated drugs, the renal vessels and ureters were ligated prior to intravenous injection of 50 mg/kg PABA or sulfanilamide. Blood samples (0.2

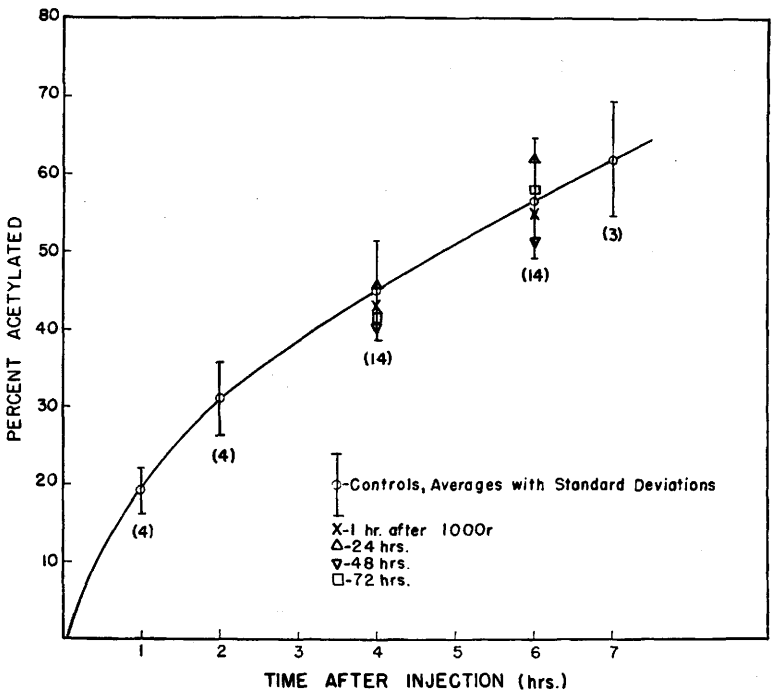

FIG. 1. Rate of acetylation of PABA in control and X-irradiated rats. Numbers of control rats indicated in parentheses.

ml) were taken at varying intervals after ligation and injection from irradiated and non-irradiated animals and were analyzed for free and total compound by the method of Bratton and Marshall(7).

Irradiated rats received 1000 r of X-irradiation at a rate of 225 r/min from a machine operated at 250 kv, 15 ma, 0.5 mm Cu and 3.0 mm bakelite filters, 27 cm distance. At 1, 24, 48, and 72 hours after exposure, groups of 4 rats were treated as above.

Results. Fig. 1 shows the percent acetylation of PABA at various times after injection. It is apparent that during the first 3 days after exposure the irradiated animals did not differ significantly from the controls in their ability to acetylate PABA, an indication that this particular reaction, requiring CoA, was not affected by irradiation. Similar results were obtained with sulfanilamide on a small number of animals.

Discussion. Acetylation of PABA and its analogues is considered to be a function of the liver, an organ generally believed to be radio-resistant. The fate of CoA in the sensitive hematopoietic tissues, the gonads, and the intestinal mucosa is not known; however, it appears that CoA, measured in terms of an *in vivo* function, is not indiscriminately destroyed. Van Heyningen *et al.*(8) have measured CoA levels in the lens after irradiation, and have found that the concentration decreased as opacities developed; however, the decrease is a delayed effect, and not an immediate action of X-radiation.

Summary. Rats exposed to 1000 r X-radiation retained their capacity to acetylate p-aminobenzoic acid and sulfanilamide for at least 3 days after exposure, an indication that Coenzyme A is not indiscriminately destroyed by whole-body irradiation.

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Intravenous Infectivity of Type 2 Poliomyelitis Virus in Mice.* (21143)

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After Armstrong(1) had demonstrated the susceptibility of mice to intracerebral infection with Type 2 poliomyelitis virus (Lansing strain), Casals, Olitzky and Anslow(2) were successful in adapting the MEF-1 strain of the same type intracerebrally in suckling mice. It was noted that the concentration of virus in the CNS increased with progressive serial passages in suckling mice. Similar observations have been reported by others(3,4) working with the MEF-1 strain of poliomyelitis virus in young hamsters as well as in young mice. Using the suckling mouse adapted line of the MEF-1 strain, Hammon, Cheever and Sather(5) have demonstrated the susceptibility of 4 to 15 days old mice to intraperitoneal infection. Similar results were observed by Moyer, Accorti, and Cox who inoculated their strain adapted to suckling hamsters intramuscularly or intraperitoneally into 21 to 28 day old mice(3). Though the precise portal of entry of poliomyelitis virus in

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