of these determinations it is conceivable that this approach might be used in devising an assay method for adrenocorticotropin.

Summary. The effect within 2 hours of adrenocorticotropin and adrenal hormone administration on the free amino acid content of rat tissues was determined. Liver and kidney showed a significant increase following administration of either hormone preparation and the adrenals showed an increase following adrenocorticotropin administration.

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Genetic Modification of Response to Spleen Shielding in Irradiated Mice.* (19481)

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Jacobson and his coworkers(1,2) have demonstrated that shielding of the exteriorized spleen will protect CF-1 mice against lethal doses of whole body x-radiation. Hematopoietic activity in the shielded spleen is greatly stimulated within the first 24 hours after irradiation and recovery of hematopoietic elements in the bone marrow occurs sooner than in sham-shielded irradiated controls. However, spleen shielding has reportedly been only partially protective in other species. Evidence is presented herein of a significant difference in response of two different inbred strains of mice, associated with apparent differences in histologic appearance of the shielded spleens after irradiation.

Procedures. Mice of strains A (Strong) and C57 black, of both sexes, were divided equally with respect to age (range 32-69 days) among 3 groups. One was kept intact and received a single whole-body dose of 550 r. Physical factors were 120 Kvp, 9 ma, 0.25 mm Cu + 1.0 mm Al added filter, 30 cm mouse-target distance, 32 r/min. The spleens of the other two groups were exteriorized under nembutal anesthesia and placed respectively in lead or paraffin shields during irradiation to the same dose, as described by Jacobson *et al.*(1). Some animals in these groups died during operation. Animals were maintained under identical laboratory conditions and had free access to Purina Laboratory Chow and water. One animal of each strain was sacrificed in each group at 3, 5, 7, 9, and 11 days after irradiation; complete autopsies were performed and the thymus, spleen, superficial lymph nodes, and liver were fixed in Bouin's fluid for histologic examination. In addition, sternal bone marrow smears were made and stained with Wright's and Giemsa's stains. The remaining animals were observed daily for deaths during the first 30 days after irradiation.

Results are summarized in Table I and Fig. 1. The earliest deaths among sham-shielded A mice occurred on the 4th day, whereas deaths among the intact irradiated controls were not observed until the 12th day. From this point on, however, cumulative curves of these 2 groups were parallel and final mortality was almost identical. A similar premature onset of death, without a greater final incidence, occurred in sham-shielded C57 black mice. Death started significantly earlier among all groups of this strain than among strain A animals. The 2 strains also differed in the greater effect of

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TABLE I. Effect of Spleen-Shielding on Radiation Mortality in Two Strains of Mice.

	Strain A						Strain C57 Black				
Treatment group	32-41* days	42-51	52-61	62-71	Total	%	32-41 days	42-61	62-71	Total	%
Spleen shielded	0/7†	0/21	0/10	0/4	0/42	0	4/7	2/11	2/17	8/35	23
Sham "	6/7	18/22	5/10	3/4	32/43	74	6/6	11/16	5/18	22/41	54
Intact	6/8	15/19	7/11	3/7	34/45	76	8/8	14/19	3/16	26/44	59

* Age at time of exposure to single dose of 550 r.
† Expressed as: No. dying/No. irradiated.

age upon susceptibility among C57 blacks (3); mortality decreased only moderately with age among the albino mice.

Spleen shielding protected strain A mice completely against mortality after 550 r. In contrast, mortality in spleen-shielded C57 blacks attained 23%, despite the lower final death rate in controls of this strain.

Histologic examination revealed essentially the same degree of initial damage in the thymus glands, lymph nodes, and bone marrows in all groups of each strain. The shielded spleens of both strains showed distinct enlargement and increased cellularity within 3 days. Those of strain A seemed enlarged primarily by the proliferation of hematopoietic elements in the red pulp, with rather small Malpighian corpuscles, whereas the shielded spleens of the serially sacrificed C57 blacks showed approximately the same areas of enlarged white pulp and red pulp in cross-sections. The numbers of animals are too small, however, to convey more than a suggestive difference. Recovery of the lymph nodes and thymus glands was not apparently influenced by spleen-shielding under these conditions. Bone marrow preparations were not technically satisfactory for quantitative comparison of the 2 strains.

Summary. It appears that the protective effect of spleen-shielding in irradiated mice may be genetically conditioned, and related

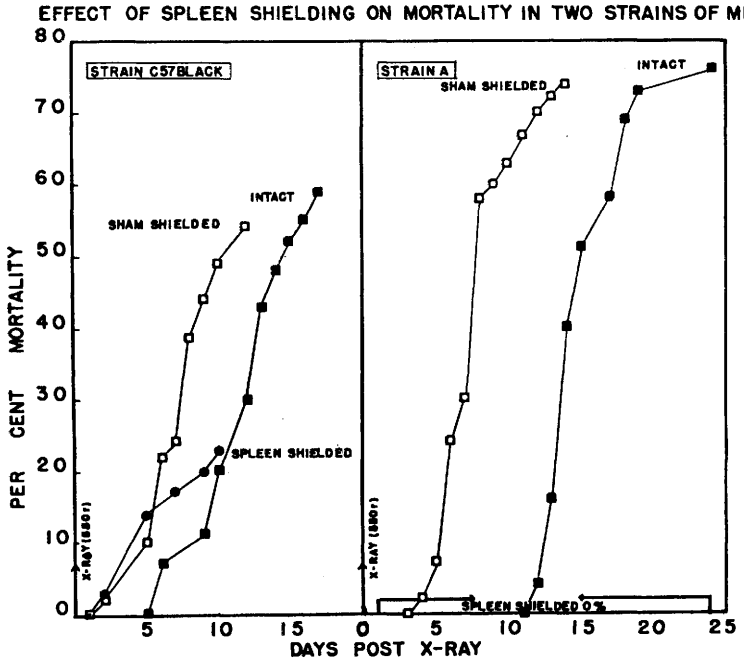

FIG. 1.

to the importance of the spleen in the hematopoietic system of each strain.

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Salicylates and Experimental Beryllium Poisoning. (19482)

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Acute beryllium poisoning in mice, readily produced by the intravenous injection of soluble beryllium salts, usually terminates fatally in 3 days(1,2). Death results from acute liver failure following hepatic focal and mid-zonal necrosis(1,3). Additional pathological changes in the kidney and spleen have also been described. Recently, aurintricarboxylic acid, a substance of relatively low toxicity, was found to be an effective antidote when it was administered to mice up to 8 hours after they had received LD_{95} amounts of $BeSO_4$ intravenously(2). This protection was attributed to its chelating and lake-forming properties. The present study was undertaken to ascertain if the salicylic acid portion of the aurintricarboxylic acid molecule would be as effective in reversing experimental beryllium intoxication.

Experimental. $BeSO_4$ was injected intravenously into young adult female CF#1 mice in an aqueous solution containing 0.07 mg Be per ml at a pH of 3.6-3.7. The animals were injected with 0.7 mg Be per kg, an amount which kills approximately 95% of the mice within 2 weeks. Compounds tested for antidotal properties were administered intravenously one hour later, except as otherwise noted. Control animals given only beryllium showed a 2.2% survival after 14 days with a 50% mortality time of 2.4 days.

Sodium salicylate was studied at various dose levels and the results, summarized in Table I, show this compound to be effective as an antidote when given in adequate doses either intravenously or intraperitoneally. Of the sodium salts of various analogues of salicylic acid tried, those without the ortho-hydroxy, carboxylic acid structure were uniformly ineffective. However, not all compounds with this grouping showed protective properties. Sodium *p*-aminosalicylate gave only equivocal results. Sodium gentisate, a product of salicylate metabolism(4), and its analogue, sodium 2,4-dihydroxybenzoate, were ineffective.

Disodium catechol disulfonate, which has been found to be effective in the treatment of experimental uranium poisoning(6), was partially successful.

Sodium salicylate afforded protection when treatment with 400 mg per kg was delayed 8 hours but not when treatment was postponed 24 hours. Pretreatment 8 hours before the beryllium was administered was ineffective, probably because of metabolism and excretion of salicylate during this period.

Discussion. The toxicity of beryllium to tissues has been ascribed by several investigators to its soluble, ionized form(1,5). Among the factors believed to be involved in effective antidotal action against beryllium ions is the chelating action of the ortho-hydroxy, carboxylic acid structure, which reduces the availability of the toxic ionized beryllium(7). Such chelation is presumed to occur with salicylate as well as with aurintricarboxylic acid, which in addition forms a stable lake. Undoubtedly, factors other than chelation are involved in successful protection against acute experimental beryllium poisoning. For example, on a molar basis about 35