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RADON DECAY PRODUCTS: DMPA DECREASES TISSUE POLONIUM-210

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Studies designed to seek decorporating agents for polonium-210 have been limited in number since the initial work of Hursh in 1952 who showed the effectiveness of British Anti-Lewisite (BAL) for this purpose (2,3). Since BAL has many disadvantages as a drug, water soluble chemical analogs of it have been developed (1). The analogs of greatest interest are N-(2,3-Dimercaptopropyl)phthalamidic acid (DMPA), the Na salt of 2,3-dimercapto-1-propanesulfonic acid (DMPS) and meso-dimercaptosuccinic acid (DMSA). Of these, DMPS has been extensively studied as an antidote for polonium by other investigators (4,5) and found to have a major disadvantage. Until the experiments presented in this paper, neither DMPA nor DMSA had been evaluated as a decorporating agent for polonium-210, an alpha emitter with a physical half-life of 138 days and a biological half-life of 50 days. The purpose of the present investigation has been to find more effective decorporating agents that might be promising as eventual treatments for acute accidental exposure to this and other polonium isotopes. Only DMPA was found to be consistently effective as a decorporating agent.

When the dimercaptans were given at the dose of 0.20 mmol/kg, using the dosing schedule described (Fig.1), DMPA consistently and significantly lowered the ^{210}Po content of the tissues studied. DMPA decreased the ^{210}Po content of the kidney to a value 28% of that of the saline control group. DMSA treatment, however, as compared to the controls, increased the kidney content of ^{210}Po. Except for the kidneys of DMPS- or DMSA- treated animals, dimercapto treatment consistently and significantly decreased the tissue levels of polonium (Fig.1).

A time study of ^{210}Po levels in the kidney of animals treated with DMPA (Fig. 2A) indicated that after one day of treatment, the kidney content of Po increased about five fold as compared to the kidneys of the saline-treated control animals, but by seven days

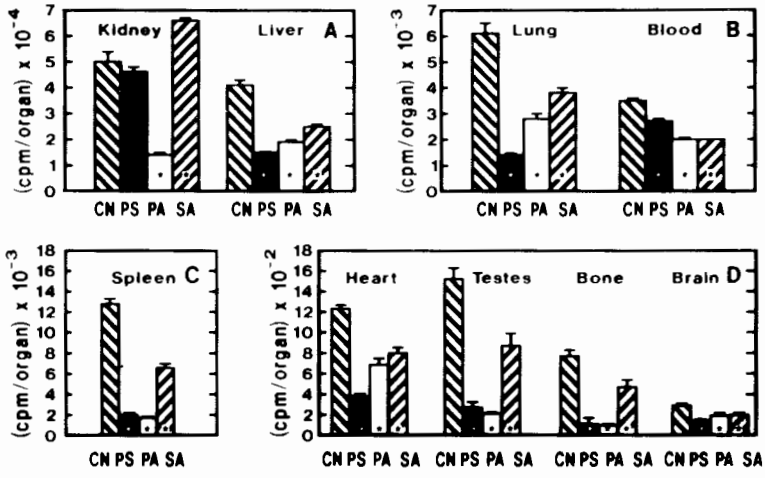

Fig.1. Polonium-210 content of tissues after dimercaptan treatment. Sprague-Dawley rats (n = 4), avg. wt = 233g, were given 0.4 μCi of ^{210}Po, sc in the right hind leg, followed by 0.20 mmol dimercaptan/kg at + 1 hr, 2.5 hr, 7 hr and at 8AM and 5PM on the second to the 20th day. Dimercaptan was injected sc in the anterior region of the back. Tissues were removed on day 21 and analyzed for ^{210}Po. Only the left kidney and left testis were removed, analyzed and the results recorded. indicates a significant difference between that group and the control at the 0.05 level. Standard error of the mean is indicated by the vertical line at the top of each bar graph. For blood the cpm are for 1.0 ml. Abbrev. - CN=control; PS=DMPS; PA=DMPA; SA=DMSA.

the kidney content had decreased but was still two fold greater than that of the controls. After 21 days of DMPA treatment, the Po content decreased to less than that of the kidneys of the control animals (Fig.2A). After 21 days of treatment, the radioactivity of the spleens of DMPA-treated animals was about one quarter that of the saline control animals and one-third that of the DMSA animals (Fig.2B). The Po content of the spleen of control animals increased with time while that of animals treated with DMPA decreased, clearly indicating a decorporation of ^{210}Po in the spleen by DMPA. A logical interpretation of these experimental observations is that the DMPA is mobilizing the Po from the injection site, as well as from other tissues, especially the spleen, and transporting it to the kidneys for excretion. With DMSA treatment, however, on the 21st day the Po content of the kidneys was twice as great as that of the control

and more than three times that of the DMPA-treated animals. It appears that the kidney is not excreting the DMSA-Po complex as rapidly as the DMPA-Po complex.

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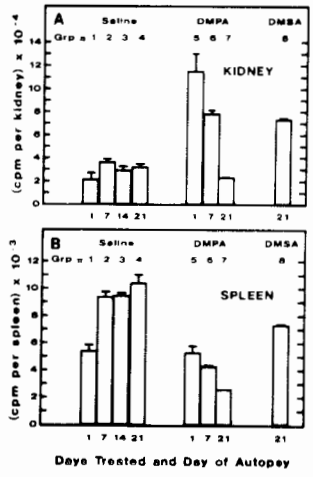

Fig.2. Changes in polonium-210 content of kidney and spleen with time after treatment with DMPA. Experimental methods including dose amounts and schedules were identical to those in the legend of Fig.1, except for additional times at which tissues were harvested. The number below each bar graph designates the days of treatment and autopsy. The following pairs of groups were significantly different at the 0.05 level: for the kidney 1vs5, 2vs6, 5vs6, 6vs7, 4vs8, 7vs8; for the spleen 1vs2, 1vs3, 1vs4, 2vs6, 4vs7, 7vs8 and 4vs8.

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