A MODEL FOR THE AGE-DEPENDENT SKELETAL RETENTION OF PLUTONIUM*

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INTRODUCTION

The metabolic model for plutonium given in Publication 30 of the ICRP[1] assumes that 90% of Pu reaching blood is divided equally between the skeleton and liver, with the remainder going to other tissues and early excreta. Plutonium deposited in the skeleton is assumed to be apportioned uniformly on cortical and trabecular surfaces, where it is retained with a biological half-time of 100 years. For the liver, a biological half-time of 40 years is assigned.

This model was designed principally for use in estimating long-term dose commitments and was not intended to be an accurate mathematical description of the actual metabolic and physiologic processes involved in the retention and translocation of Pu in the body, even for an average adult. In this paper we describe a model intended to more accurately depict these processes, and we examine the implications of our model concerning the dose as a function of age to radiosensitive tissues of the skeleton. To describe the model concisely it is convenient to view the body as subdivided into the liver, the skeletal compartments shown in Fig. 1, and all remaining tissue.

UPTAKE AND TRANSLOCATION OF PU BY THE SKELETON

Experimental data for beagles together with limited human autopsy data indicate that the fraction of circulating Pu depositing in the skeleton decreases from about 0.7 in newborns to about 0.5 in adults.[2-6] Plutonium is deposited initially on bone surfaces (pathways K and L in Fig. 1), with higher deposition being at sites with red marrow and lower deposition at sites with yellow marrow.[7] In the adult, nearly all of the red marrow is in trabecular bone,[8] and deposition on trabecular bone appears to be greater than on cortical bone. In children, some or all of the marrow in cortical bone is active,[8] and a fairly uniform distribution on cortical and trabecular bones is expected. Thus it is assumed that Pu is divided evenly between cortical and trabecular surfaces in children; in adults, 60% of the initial deposit in the skeleton is assumed to be on trabecular surfaces and 40% on cortical surfaces (cf. Ref. 5).

Bone surfaces labeled with Pu may remain unchanged, or they may be buried by formation of new bone (pathways A and C) or resorbed by osteoclasts (pathways B and D).[9] The rate of removal from surfaces by burial or resorption depends on the age of the individual and on the bone surface type (trabecular or cortical).[9] To a large extent, bone addition and resorption occur on opposite sides of a bone or bone trabecula, so that the bone may be pictured as continually drifting in a given direction.[10] Bone drift apparently occurs at all ages but may not be the predominant type of bone remodeling in mature bone. Rather, resorption and addition may often occur at the same location in mature bone; first an area of bone is excavated by osteoclasts, and then the same area is refilled with osteoid, which is later mineralized.[11] It is assumed that all bone remodeling in nonadults involves bone drift, and the removal rate of Pu from bone surfaces is estimated as the sum of the resorption rate and the formation rate (since these processes are assumed not to overlap). For the adult, an intermediate scenario involving both types of bone remodeling is assumed; the burial rate in bone is assumed to be one-half the formation rate, and the removal rate from surfaces is estimated as

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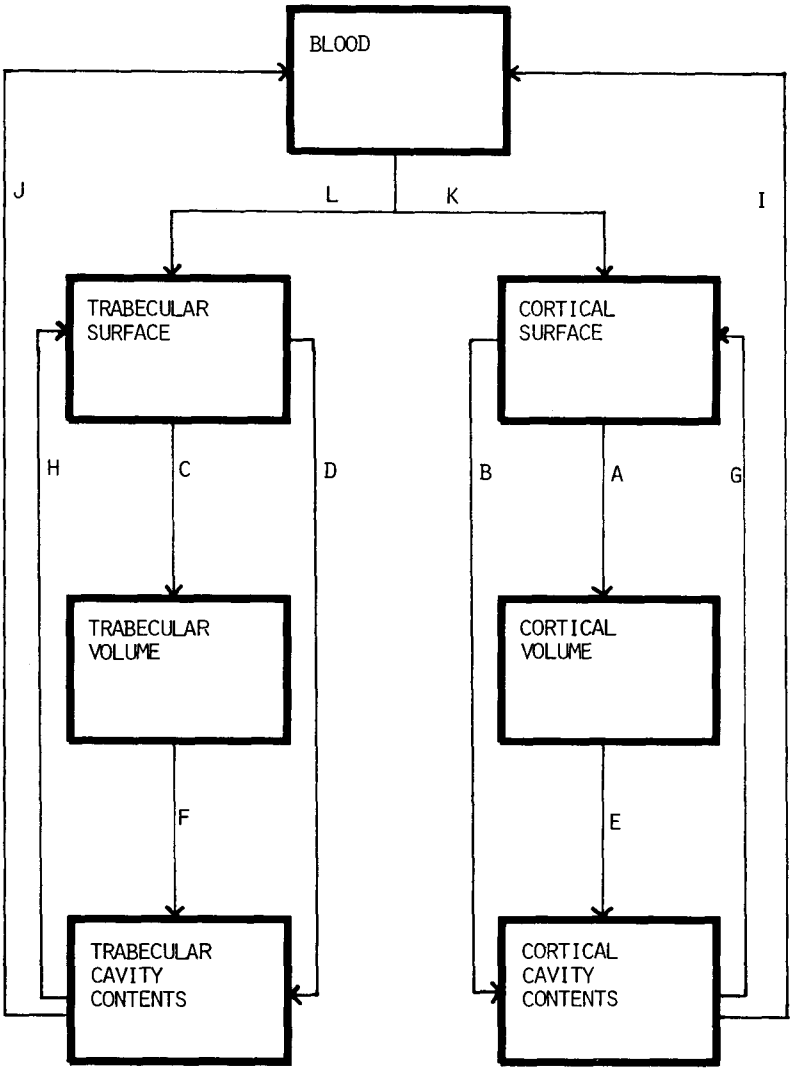

Fig. 1. Compartments and pathways in the model of the skeleton.

the resorption rate plus one-half the formation rate. The age-dependent formation rate is estimated for cortical bone from tetracycline data and for trabecular bone from strontium removal rates from vertebrae.[11-13] Resorption and formation rates are assumed to be equal; this may result in an overestimate of the half-time of Pu on bone surfaces in children.

Plutonium resorbed by osteoclasts may be released and concentrated by macrophages in bone cavities, particularly in marrow.[9] The length of time that Pu remains in these macrophages is not known. Experiments with beagles suggest that several half-times have elapsed after two years.[9] For the present calculations we have arbitrarily assumed a half-time of 0.25 years.

Pu buried in bone volume may eventually become distributed in volume as the bone section is remodeled.[9] If the resorption rate for trabecular bone is k per year, then buried Pu may begin to be resorbed about 1/k years or more after exposure, depending on the fraction of remodeling attributable to bone drift. Here account must be taken of the fact that k varies with age. Because of the slow turnover time for cortical bone at most ages, much of the Pu buried in cortical bone of adolescents and adults may never be recycled.

Experimental data suggest that both local (pathways G and H) and systemic (pathways I and J) redeposition onto bone surfaces occur, although we suspect that systemic redeposition may predominate in the highly vascularized bone of children. For lack of information, we have attempted to minimize errors in the present calculations by assuming that all Pu released from marrow is channeled through blood.

PU IN NON-SKELETAL TISSUES AND EXCRETA

Experimental data indicate that the fraction of Pu depositing in liver increases with age, from about 0.1 in very young animals to about 0.3 in adults.[3-4,6] It is known from animal studies[14-16] that Pu may leave the liver both in blood and in bile, that soluble Pu is taken up by hepatocytes but is later transferred to reticuloendothelial (RE) cells, and that Pu may reside for years in the RE system. It is also suggested by autopsies of persons occupationally exposed that Pu may reside for many years in the human liver. No differences with age in removal of Pu from liver are discernable from animal studies or from autopsy data for non-occupationally exposed humans. Our model assumes that, at all ages, about 4% of Pu going to liver is removed in feces with a relatively short half-time (a few days) and the remainder is removed to blood with a half-time of 10 years. These values were chosen because they lead to reasonable agreement with human data.

The biological half-time of Pu in soft tissues other than liver appears to be on the order of a few hundred days.[6] In this model we have assumed a half-time of 500 days; estimated doses to sensitive skeletal tissues are fairly insensitive to this value within reasonable limits of the half-time.

Plutonium released to blood may be excreted or may be recycled to the skeleton, liver, and remaining tissue. The effective half-time of Pu in blood is about one day, although an accurate description of retention in blood over a few weeks or months requires several exponential terms.[6] The amount excreted per day at equilibrium is estimated as 8.4% of the integrated activity in blood, on the basis of data for humans. Plutonium reaching blood after release from skeleton, liver, or remaining tissue is assumed to be redeposited or excreted in the same percentages as the original deposition in blood. Processes of retention and translocation outside the skeleton and liver are assumed to be independent of age.

IMPLICATIONS FOR SKELETAL DOSIMETRY

Integrated doses over 50 years were calculated for various age groups, assuming that one unit of activity of Pu-239 was injected into the bloodstream. It is estimated using this model that about three-fourths of the alpha energy released in the skeleton over a period of 50 years is deposited in non-sensitive tissues, for all ages at injection. Moreover, for an adult, the ICRP model leads to an estimated dose commitment to active marrow that is about 2 times higher than that

estimated using the present model. According to our model, there is little age dependence in 50-year dose commitments to sensitive skeletal tissues, mainly because of the large amount of recycling that occurs over 50 years among the skeleton, liver, and other tissues. This example refers only to an initial unit injection and does not consider the potentially large difference with age in the amount of Pu-239 that may reach the bloodstream in a more typical exposure situation, particularly through the ingestion pathway.

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