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Uranium and Plutonium in Hair as an Indicator of Body Burden in Mice of Different Age and Sex

K. W. Bentley, J. H. Wyatt, D. J. Wilson, and Rhoda J. Dixon

Australian Atomic Energy Commission, Lucas Heights Research Laboratories Private Mail Bag, Sutherland, NSW 2232, Australia

The comparatively recent development of analytical techniques of great power and sensitivity has permitted investigators to establish correlations for ingestion and elemental hair levels of several metals from differing environmental exposures (e.g. YURACHEK et al. 1969, EADS & LAMBDIN 1973). Ease of collection, storage and analysis of human hair, together with its potential as the "recording filament" (STRAIN & PORIES 1966) to reveal retrospective information about an individual and his exposure, has increased its popularity as a forensic biopsy and autopsy material. For some trace elements, levels in hair have been examined for possible applications in assessing nutritional status, medical diagnosis and the determination of both acute and chronic exposure to toxic elements. The entire topic of trace metals in human hair has been discussed in a recently published book (VALKOVIC 1978).

However, while some authors such as KLEVAY (1970a,b) and KELLO & KOSTIAL (1978) have found positive correlations between plasma and hair elemental concentrations for particular population groups, others (e.g. DEEMING & WEBER 1978) could find no correlation between plasma and hair levels, when they are related to diet, age and sex.

As part of a program to develop alternative bioassay techniques for potentially occupationally exposed uranium and plutonium workers (BENTLEY & WYATT 1980) hair is being examined as a potential practical biological dosimeter for these elements. For uranium, the results of toxicity (LD_{50}), organ deposition and metabolic animal studies (mainly conducted in the wartime Manhattan Project) are such that quantitative comparisons are not possible. In many reported results, no reference is made to diet, age, sex or strain of the animal used although the importance of these parameters for uranium had been documented in early work (e.g. JACKSON 1910, VERNE 1931). For intraperitoneally injected rats, an age-dependent increase in acute toxicity and sex differences (males more resistant) was noted. Using four mice strains TANNENBAUM (1951) noted that males were more resistant than females but did not find an age difference in this species.

Available human data for uranium and plutonium are at best fragmentary, being generally obtained from autopsy of occupationally exposed workers.

The present work examines, in a controlled animal study, the uptake of uranium-235 and plutonium-239 in mice of different age and sex.

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MATERIALS AND METHODS

Four experiments were performed: two using plutonium-239 and the remainder uranium-235, to study the retention of these isotopes in the whole body and hair in relation to age and sex. Each experiment was performed on six groups of male and six groups of female albino QS strain mice aged 3-18 weeks. The animals were cube fed ('Barastoc', Melbourne, Australia) with *ad lib* access to water.

The animals received a single intraperitoneal dose of either plutonium-239 nitrate or uranium-235 nitrate at amounts of 0.2 mg/kg and 1.0 mg/kg respectively. The injection solutions were prepared in acid and citrate-buffered to pH 4.2 immediately before use to minimize colloid formation. Uninjected animals from the 12 and 18 week groups were individually marked and jointly housed as controls for surface contamination. Because no uranium or plutonium was detected in the hair from uninjected controls, the hair of the experimental animals was not washed.

Seven days after radioisotope administration, the animals were sacrificed by ether narcosis and the whole body weight of each animal determined. The animals were skinned and the weight of skin with hair recorded for each one. Means and SEM for each group were derived from the sum of the weight of whole body and of the skin and hair from each individual group. The errors shown (Figures I-IV) are based on the assumption that the weight of the carcase is a constant proportion of the total body weight (PITTS & BULLARD 1968). The uranium (or plutonium) content of the hair (including skin) was measured directly by delayed neutron analysis as described elsewhere (AMIEL 1962).

The carcases were ashed in platinum dishes in a muffle furnace before their uranium or plutonium content was measured by delayed neutron analysis. The possible losses incurred in the muffle ashing procedure have been measured using control animals injected with uranium-235 immediately before sacrifice. For animals in the weight range used the recovery was 93 ± 4%.

RESULTS

Older mice retained a significantly lower percentage of plutonium and uranium (Figure I) in the whole body than weanlings. The residual whole body burdens for both plutonium and uranium can be expressed as linear functions having slopes of -0.22 ± 0.03% per day and -0.09 + 0.03% per day respectively, i.e. the ability to retain material in the whole animal is decreasing twice as fast for the plutonium-239 as for uranium-235. The percentage of plutonium retained in the hair increases with the age of the animal (0.013 ± 0.002% per day), although for uranium the observed values are similar for both young and adult mice, suggesting that the uptake is not age-dependent (0.0006 ± 0.001% per day).

The relative uptake of plutonium and uranium into the hair with respect to the whole body is shown in Figure III. For plutonium, there is a rapid increase with age (0.036 ± 0.001% per day), whereas

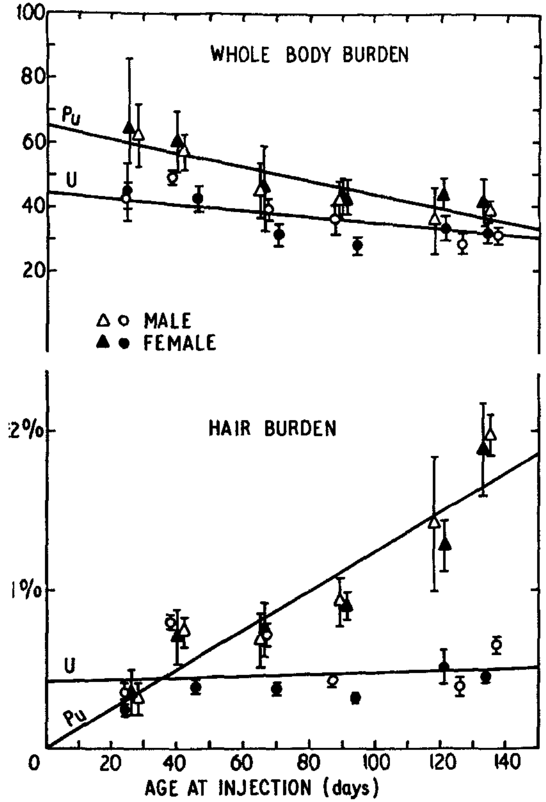

Figure I: Percentage retention of plutonium and uranium in whole body and hair in mice of different age and sex.

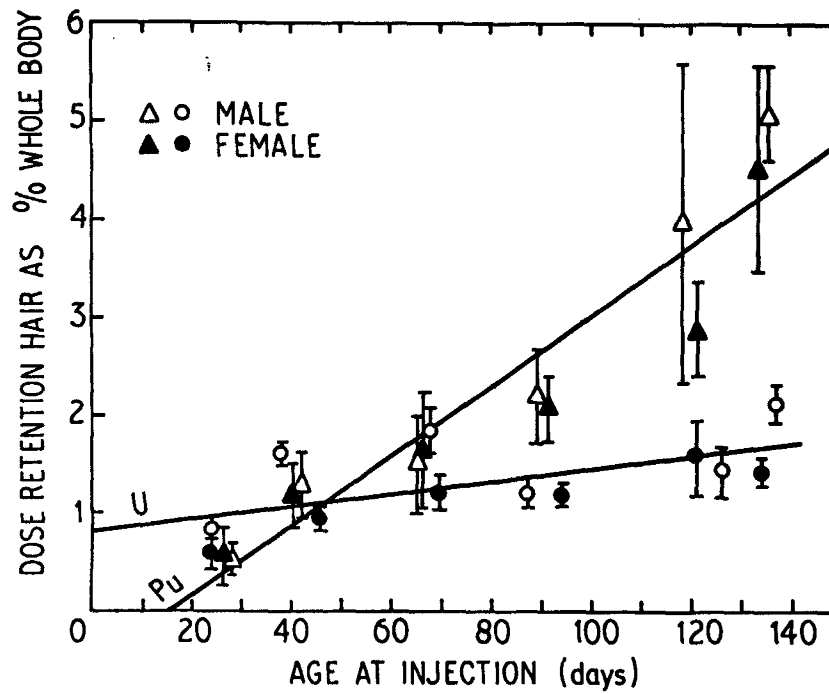

Figure II: Retention of plutonium and uranium in hair as a percentage of whole body burden.

for uranium the increase is slight (0.006 ± 0.003% per day).

Comparisons for specific burdens (i.e. residual dose/g fresh weight) (Figure III) show a marked increase with age for plutonium (0.0017 ± 0.0003% per day) but a decrease for uranium (-0.008 ± 0.0003% per day).

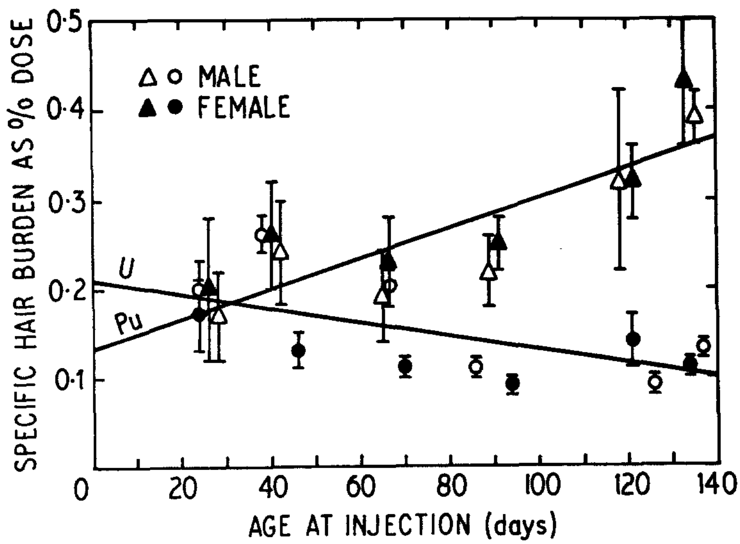

Figure III: Specific hair burden as a percentage of dose.

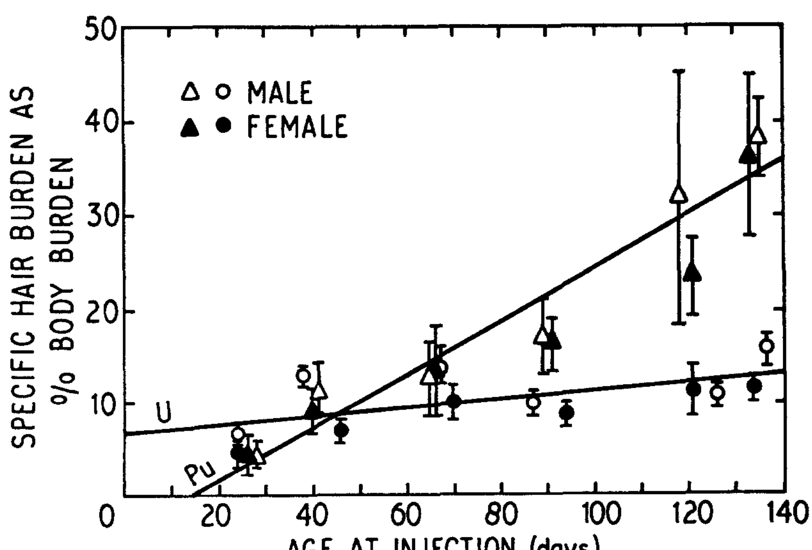

Figure IV: Specific hair burden as a percentage of body burden.

Finally, (Figure IV) a comparison of the specific burden of hair as a percentage of the specific whole body burden i.e.

$\frac{\text{Burden of hair/g of hair}}{\text{Burden of body/g of body}}$ shows increases with age for plutonium of $0.29 \pm 0.021\%$ per day. Uranium increases at about 20% the rate for plutonium ($0.047 \pm 0.02\%$ per day).

For both uranium and plutonium, sex does not appear to have any significant influence on the residual whole body or hair burdens when the results are expressed either as a percentage of the dose retained (Figures I, II) or as a percentage of the dose per gram of fresh tissue (Figures III, IV).

DISCUSSION

The evidence that age or sex influences metal metabolism in humans is still scarce, and that available is frequently contradictory. Data on concentration of heavy metals in hair in relation to age and sex are, therefore, of special importance.

Data obtained from short-term controlled animal studies are necessarily of limited value for interpreting results on hair concentrations in humans. However, it is generally not possible to undertake controlled human experiments using fissionable radionuclides. Such human evidence which exists has either been derived from environmental studies (e.g. following atmospheric nuclear testing), autopsy examination of tissues from occupationally exposed individuals who have had a number of involuntary, ill-defined exposures during incidents, or a very limited number of voluntary exposure experiments. In these experiments hair uptake, being a minor excretory pathway, was not reported separately. Some plutonium data obtained following exhumation of early volunteers are now available (TOOHEY et al. 1981).

In the present experiment we estimated uranium and plutonium not only in the hair but also in the skin in order to assess the quantity deposited in the hair follicles where endogenous metal deposition is expected to start (HOPPS 1977). Our results show that, contrary to earlier report (e.g. TANNENBAUM 1951, VOEGTLIN & HODGE 1953), for the mouse strain we examined (QS), sex does not have any effect, on either the total residual burden or the specific burden at any age from weaning to adult.

Discrepancies between the results of our present work and those of earlier uranium and plutonium experiments can be attributed primarily to the physicochemical state of the material injected. For both plutonium and uranium, the injection solution must be both freshly prepared and buffered to a pH which is as low as physiologically acceptable. Polymerisation in unbuffered or aged solutions results in tissue accumulations varying by up to $\times 10^3$ in liver (^{239}Pu) and $\times 10^2$ in kidney (^{235}U), the respective primary soft tissue target organs.

KELLO & KOSTIAL (1978) examined the influence of age on the uptake of cadmium and lead in rats and concluded that young animals retained significantly higher percentage burdens of both elements than adults. However, if their results are expressed as percentage dose retained in the whole body, then for lead there was no difference relative to age. Cadmium was considered age-dependent because of the higher accumulation in the hair of young animals. For uranium and plutonium, we also noted a higher percentage retention in the whole body of young animals, but for specific whole body burden there was a marked increase with age for plutonium and only a slight increase for uranium. The plutonium content in hair was age-dependent because of the higher selective accumulation of ^{239}Pu in the hair of older animals and, therefore, it was not a good indicator of the total body burden. There was a similar, if much less marked, increased accumulation in the hair of uranium-dosed animals with age.

Although our results cannot be directly applied to human experience they are a definite indication, particularly for plutonium-239, that age should be taken into consideration when using hair concentration as an indicator of body burden.

REFERENCES

AMIEL, S.: Anal. Chem. 34, 1683 (1962).

BENTLEY, K.W., AND J.H. WYATT: Environ. Res. 21, 407 (1980).

DEEMING, S.B., AND C.W. WEBER: Am. J. Clin. Nutr. 31, 1175 (1978).

EADS, E.A., AND C.E. LAMBDIN: Environ. Res. 6, 247 (1973).

HOPPS, H.C.: Sci. Total Environ. 7, 71 (1977).

JACKSON, D.E.: Amer. J. Physiol. 26, 381 (1910).

KELLO, D., AND K. KOSTIAL: Bull. Environ. Contam. Toxicol. 20, 618 (1978).

KLEVAY, L.M.: Am. J. Clin. Nutrit. 23, 284 (1970a).

KLEVAY, L.M.: Am. J. Clin. Nutrit. 23, 1194 (1970b).

PITTS, G.C., AND T.R. BULLARD: Body Composition in Animals and Man. Ed. J.T. Reid. Washington D.C.: Nat. Acad. Sci. 1968.

STRAIN, W.H., AND W.J. PORIES: Zink Metabolism. Ed. A.S. Prased. Illinois: Thomas Pub. 1966.

TANNENBAUM, A.: Toxicology of Uranium. New York: McGraw-Hill 1951.

TOOHEY, R.E., C.G. CACIC, R.D. OLDHAM AND R.P. LARSEN: Health Physics 40, 881 (1981).

VALKOVIC, V.: Trace Elements in Human Hair. New York: Garland STPM Press 1978.

VERNE, J.: Ann. Anat. Path et Anat. Normale Med. Chir. 8, 757 (1931).

VOEGTLIN, C., AND H.C. HODGE: Pharmacology and Toxicology of Uranium Compounds, Vol. IV. New York: McGraw-Hill 1953.

YURACHEK, J.P., G.G. CLEMENA AND W.W. HARRISON: Anal. Chem. 41, 1666 (1969).