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INTERSPECIES COMPARISON OF THE LUNG CLEARANCE OF INHALED MONODISPERSE COBALT OXIDE: TRANSLOCATION FROM THE LUNGS TO BLOOD

Kreyling W.G.[1], Bailey M.R.[2], André S.[3], Batchelor A.[4], Collier C.G.[2], Drosselmeyer E.[6], Ferron G.A.[1], Foster P.[7], Haider B.[1], Hodgson A.[2], Masse R.[3], Metivier H.[3], Morgan A.[5], Müller H-L.[6], Patrick G.[4], Pearman I.[7], Pickering S.[8], Ramsden D.[7], Stirling C.[4], and Talbot R.J.[5]

[1]Gesellschaft für Strahlen- und Umweltforschung, Neuherberg, FRG. [2]National Radiological Protection Board, Chilton, UK. [3]Commissariat á l'Energy Atomique, ISPN/SPE/STCE Bruyéres-le-Chatel, France. [4]Medical Research Council Radiobiology Unit, Chilton, UK. [5]Harwell Laboratory, Oxon, UK. [6]Kernforschungszentrum, IGT, Karlsruhe, FRG. [7]Atomic Energy Establishment Winfrith, Dorset, UK. [8]CEC European Institute for Transuranium Elements, Karlsruhe, FRG.

An interspecies comparison of the lung clearance of a well-defined moderately soluble material was conducted to aid in the development of models used to relate inhalation of toxic particles to organ doses and bioassay measurements. Lung retention and excretion of ^{57}Co were followed for 6 months after inhalation of monodisperse 0.8 µm and 1.7 µm geometric diameter Co_3O_4 particles by human volunteers, baboons, dogs, guinea pigs, rats (3 strains) and hamsters and of the 0.8 µm particles by mice. Supplementary experiments were conducted to determine ^{57}Co excretion patterns following injection of $Co(NO_3)_2$ into the blood and following ingestion of Co_3O_4 particles. From these measurements, lung clearance rates due to translocation of dissociated ^{57}Co to the blood, S(t), and due to particle transport to the GI tract, M(t), were calculated as fractions of the contemporary lung content.

As expected from previous studies on dogs and as predicted on the hypothesis of a particle surface area dependent dissolution process, the translocation rate of 0.8 µm particles was greater than for 1.7 µm particles in each species. However, the initial translocation rate S(t) varied from 0.4 (0.2) %/d of the contemporary lung burden in men and baboons to 1.6 (0.6) %/d in HMT rats for the 0.8 (1.7) µm particles, respectively. For 0.8 µm particles, S(t) was constant in men over 6 months. It was constant during the first 3 months then it slightly increased in baboons and decreased in F-344 rats thereafter. For mice, hamsters and guinea pigs S(t) increased throughout the entire time up to about 2 %/d, and peaked for dogs and HMT rats at about 2 %/d after 3 and 1 months, respectively. For 1.7 µm particles, S(t) remained constant for the first 6 months in most species or increased slightly in men and hamsters. Only for dogs it peaked at about 1.5 %/d after 4 months while it increased up to 1 %/d in guinea pigs and plateaued thereafter.

As a result of these changes in S(t), the highest value of S(t) for 0.8 µm particles at any time is a factor 4-7 higher than the lowest at the same time. However, while the lowest values are always in men and baboons, the highest are firstly found in HMT rats, then in dogs, and finally in guinea pigs. For 1.7 µm particles, the highest initial value (in HMT rats) is about 3 times the lowest (in baboons), but S(t) in dogs increases, and at its maximum value is about 10 times that in baboons.

For comparison, a model for translocation to blood was derived based on the specific surface area dependent dissolution of particles in accordance with Mercer's theory (1967) and assuming a fraction of the dissolved Co to be indefinitely retained in the lungs. Varying the latter between 1-10 % and varying the initial translocation rate within the experimentally determined range the model was remarkably well able to account for the different forms of S(t) observed.

The dependence of S(t) on time showed a variety of different forms, but all were reasonably consistent with a simple dissolution model. This study identified slight interspecies differences in the initial translocation rates and subsequent rate patterns of a moderately soluble material from lung to blood, indicating the uncertainty associated with extrapolating translocation rates from ex-perimental animals to man.