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THE COMPARATIVE METABOLISM OF INTRAVENOUSLY
INJECTED PROMETHIUM IN SWINE AND HUMANS (a)

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THE COMPARATIVE METABOLISM OF INTRAVENOUSLY
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Promethium-147 is a major constituent of long-lived fission product wastes and is currently available in megacurie amounts for a variety of industrial, space, military and medical applications. In general, these applications involve the use of ^{147}Pm as beta sources in instruments and batteries and, more importantly, as fuel for isotopic heat sources. As promethium technology expands and more uses and applications are developed, the likelihood of accidental intake and deposition by workers involved in promethium production and handling may be increased.

Since ^{147}Pm decays primarily by beta emission to the ground state of ^{147}Sm , assessment of the extent of internal deposition by conventional whole body counting techniques is precluded. The extent of internal depositions must, therefore, be assessed by analysis of excreta samples and the use of appropriate excretion models based on the results of animal or human metabolism studies.

An experimental program has been in progress for some time at Battelle-Northwest to develop such excretion models for ^{147}Pm using volunteer human test subjects and various experimental animals. Promethium chloride injection studies with both humans and swine have been completed and the results reported. Further experiments are planned to investigate the fate of inhaled Pm_2O_3 in humans, the mode of exposure and chemical form of promethium most likely to be experienced in accident situations.

Using available animal and human experimental data, the present study was undertaken to develop, with the aid of an analog computer, a kinetic model of the metabolism of PmCl_3 in humans. The model was constructed from the results of swine experiments for tissue distribution at sacrifice, urinary and fecal excretion, whole blood activity measurements and whole body counting data. The final model was then adjusted for human application using available experimental data.

The first slide (Slide 1) presents promethium injection information for both the human and the swine experiments. The conditions of both experiments were quite similar except that in the human studies, the injected activity and resulting mass of promethium were substantially less than in the swine studies in order to control the dose to the human volunteer test subjects within acceptably low levels. In the human studies, ^{143}Pm , containing a small amount of ^{144}Pm , was substituted for ^{147}Pm , again in order to limit the dose to the test subjects. Promethium-143 decays by electron capture to stable ^{143}Nd with the emission of a 740-keV gamma ray which was used for whole body counting measurements. In the swine experiments, the $^{148\text{m}}\text{Pm}$ was used for the whole body counting measurements.

The next slide (Slide 2) shows a block diagram of the kinetic model for promethium chloride injection based on the results of the swine experiments. The times indicated in each compartment are turnover times and the fractions from the blood to the body compartments and back again to the blood are indicated on the connecting arrows. The turnover times listed for the intestinal compartments are those recommended by the ICRP. Six body compartments plus intestinal compartments were found to be sufficient for a model which fit the existing data. Various combinations of turnover times and fractional removals were tried until the numbers seen here were arrived at, which best described the experimental data.

The next series of slides presents computer derived predictions of the activity in each of the model compartments with experimental data points shown for comparison. Slide 3 shows the blood compartment, indicating the rapid translocation of PmCl_3 from the blood that has been observed. After the first day post-injection, promethium activity in the blood of the pigs was barely above detectable levels. Urine and fecal excretion levels are shown in the next slide (Slide 4). The blood data points shown in the previous slide and the urine and fecal data points shown here are based on mathematical expressions derived to describe the experimental

data. This was done to provide smooth line data points which could be more easily used by the computer and provide a better visual comparison with the kinetic model predictions. In the next slide, (Slide 5), showing the whole body counting results, actual data points from the experiment are shown. The swine experiment was terminated at 104 days post injection with sacrifice of the animals. About 75% of the injected PmCl_3 was found in the skeleton and liver of the animals at sacrifice which explains why we used these two tissues for our kinetic model and grouped all other tissues in a body pool compartment. The next slide (Slide 6) shows the model predictions of activity in the bone and liver along with corresponding data points. Unfortunately, data points are available from this experiment at only 104 days post injection. However, similar data has been observed at shorter times after injection in other experiments with different chemical forms of promethium.

Using as a basis the model developed from the swine experimental data, another kinetic model to describe the human data was developed. A block diagram of this model is shown in the next slide (Slide 7). Parameters of the swine model, where different from those of the human model, are shown in parentheses. These changes were found to be necessary in order that the human model might better describe the human urinary and fecal excretion rates which were slightly different than those observed in the swine experiment although the total excretion rate was the same in both experiments. The excretion rates predicted by the model for humans is shown in the next slide (Slide 8). The method of arriving at the data points was the same as previously indicated for the swine experiment. Human fecal sampling was terminated 22 days after exposure. The next slide (Slide 9) shows actual whole body counting data points for humans versus the promethium activity remaining up to 105 days post injection as predicted by the kinetic model. Based on the good correlation observed here between the model prediction and the data points, we were encouraged that the model, as shown, adequately described the translocation

and elimination of PmCl_3 in humans following intravenous injection.

Using the human kinetic model, estimates were made of the biological half life of promethium in the total body, bone and liver of humans. Estimates were also made of the fraction in the organ of reference to that in the total body and the fraction translocated from the blood to the organ of reference. These estimates are shown in the last slide (Slide 10) along with the corresponding values recommended by the ICRP which are shown in parentheses. Our results would indicate that the biological half life of promethium in the bone is much longer than the value recommended by the ICRP (35 yrs. vs. 4.1 yrs.) and that the fraction of promethium translocated from the blood to liver and retained in the liver is significantly higher than the ICRP values. All other values from this study agree fairly well with the ICRP values. ✓

In conclusion, the results of this brief study have indicated that (1) metabolic data in swine is quite similar to that found in humans, (2) the ICRP value for the biological half life of promethium in bone may be low by as much as a factor of 8, and (3) liver deposition of promethium following intravenous injection of PmCl_3 may be higher than the ICRP recommended value by a factor of 5.

FIGURE 1

PROMETHIUM INJECTION INFORMATION

	<u>HUMAN</u>	<u>SWINE</u>
NO. OF SUBJECTS	6	11
RADIONUCLIDE	^{143}Pm (^{144}Pm)	^{147}Pm ($^{148\text{m}}\text{Pm}$)
CHEMICAL FORM	PmCl_3	PmCl_3
pH	3.0	3.5
INJECTANT VOLUME (cc)	1	5
ACTIVITY INJECTED (μCi)	0.1	517 (1240)
MASS Pm INJECTED (μg)	$\sim 3 \times 10^{-5}$	~ 0.6

FIGURE 7

BLOCK DIAGRAM OF THE PROMETHIUM
INJECTION MODEL BASED ON HUMAN DATA

FIGURE 10

BIOLOGICAL CONSTANTS PREDICTED
BY PROMETHIUM MODEL

	BIOLOGICAL HALF LIFE T_b (DAYS)	FRACTION IN ORGAN OF REFERENCE TO THAT IN TOTAL BODY - f_2	FRACTION FROM BLOOD TO ORGAN OF REFERENCE f'_2
TOTAL BODY	2100 (656)	1.0 (1.0)	1.0 (1.0)
BONE	12800 (1500)	0.6 (0.8)	0.4 (0.35)
LIVER	500 (656)	0.3 (0.06)	0.5 (0.06)

ICRP Values in parentheses