PNL-SA-17594
CONF-891290--2
CONF-900733--1

DEC 17 1990

PNL-SA--17594

DE91 005086

REVISION OF THE ICRP DOSIMETRIC MODEL FOR THE HUMAN RESPIRATORY TRACT

W. J. Bair

December 1990

Presented at the
21st Annual NIRS Symposium on Inhalation
of Airborne Particles & Induction Mechanisms
of Biological Effects
Japan
December 8-9, 1990

Work supported by
the U. S. Department of Energy
under Contract DE-AC06-76RLO 1830

Pacific Northwest Laboratory
Richland, Washington 99352

W.J. Bair
Life Sciences Center (K1-50)
Pacific Northwest Laboratory
Richland, Washington, USA

REVISION OF THE ICRP DOSIMETRIC MODEL FOR THE HUMAN RESPIRATORY TRACT

ABSTRACT

Although the dosimetric model of the respiratory tract used in ICRP Publication 30 had not been shown to be seriously deficient for the purpose of calculating Annual Limits on Intake (ALIs) for workers, the availability of new information led the ICRP in 1984 to create a special Task Group to review the dosimetric model of the respiratory tract and, if justified, propose revisions or a new model. The Task Group directed its efforts towards improving the model used in Publication 30 rather than developing a completely new model. The objective was a model that would 1) facilitate calculation of biologically meaningful doses; 2) be consistent with morphological, physiological, and radiobiological characteristics of the respiratory tract; 3) incorporate current knowledge; 4) meet all radiation protection needs; 5) be user friendly by not being unnecessarily sophisticated; 6) be adaptable to development of computer software for calculation of relevant radiation doses from knowledge of a few readily measured exposure parameters; 7) be equally useful for assessment purposes as for calculating ALIs; 8) be applicable to all members of the world population; and 9) consider the influence of smoking, air pollutants, and diseases of the inhalation, deposition, and clearance of radioactive particles from the respiratory tract. Rather than calculating an average dose to the total lungs, emphasis was given to calculating doses to tissues and cells of most concern, those that had shown evidence of susceptibility to radiation induced cancers either in humans or in experimental animals.

Since both the radiation dose and the cancer susceptibility of each region determine the overall risk to the respiratory tract of a given radionuclide intake, the model provides for calculation of a committed dose equivalent for each region, adjusted for the relative cancer sensitivity of that region, and for the summing of these to yield a committed dose equivalent for the entire respiratory tract.

PREPARED FOR THE U.S. DEPARTMENT OF ENERGY UNDER CONTRACT DE-AC06-76RLO 1830

INTRODUCTION

The ICRP is currently undertaking a number of efforts leading to a revision of its basic recommendations on radiation protection, as described in Publication 26. These efforts include reviews and reassessment of its system of dose limitation as well as the values of primary limits. ICRP Committee 2 is preparing for a possible revision of secondary limits, which could include the annual limits on intake (ALI). To support this work a task group on human respiratory dosimetric models was appointed.

The members of the ICRP task group on human respiratory tract models for radiological protection were selected to assure that the broad spectrum of biological, physiological, chemical, radiological, and health physics aspects of inhaled radioactive aerosols and gases could be competently addressed. The members of the multinational task group are: Frederick Cross, USA; Richard Cuddihy, USA; Peter Gehr, Switzerland; Anthony James, USA; John Johnson, USA; Roland Masse, France; Monique Roy, France; Willi Stohlhofen, West Germany; and William Bair, USA, chairman. In addition, numerous corresponding members were invited to provide technical assistance and to review drafts of the task group's report.

The task group was asked to review the current ICRP lung dosimetry model, advise on its inadequacies, develop a plan for needed revisions of the current model, and recommend to the ICRP a revised model.

Review of ICRP Lung Dosimetry Model

The current ICRP lung dosimetry model, used in Publication 30 (ICRP 1979) to calculate ALIs and derived air concentrations (DACs), was a slight modification of that published in 1966 by a special task group on lung dynamics of ICRP Committee 2, chaired by Dr. Paul Morrow (ICRP 1966). Major innovations were introduced by this task group, including a deposition model not only based on but using dust-sampling data. Deposition was described for three anatomical compartments, which both physiological and radiobiological implications. The model made possible consideration of both particle size of inspired aerosols and respiratory rate with respect to fraction deposited in each region: nasal, bronchial, and pulmonary.

A quantitative kinetic clearance model was introduced that accounted for material deposited in each of three regions. Perhaps of greatest impact was the classification of chemical compounds according to the estimates of their expected tendency to be retained in the respiratory tract. This is the D, W, and Y classification; D class for those compounds expected to be cleared from the respiratory tract with a half-time less than 1 day; W class for compounds with clearance half-time of a few days to months; and Y class for compounds that are expected to be retained with half-time of 6 months to years. This model also provided for the transfer of inhaled particles to the thoracic lymph nodes. The effort of the task group was a major scientific accomplishment. It used and expanded upon the total relevant technical data available and reflected the outstanding expertise and extraordinary insight of the members.

The deposition and retention models developed by the task group provided a sound scientific basis for ICRP Committee 2 to calculate radiation doses from

inhaled radionuclides leading to recommendations for ALIs and DACs that appeared in Publication 30. Task group models went further than Committee 2 was prepared to go in some areas, such as the transfer of radionuclides to thoracic lymph nodes (Committee 2 elected to combine the lymph nodes and lungs for Publication 30); but it failed to address others, such as deposition and clearance of particles from the nasal passages. However, the omissions were insignificant compared with the magnitude of the advances in knowledge about inhaled particles that were stimulated by the task group's report. After publication of the 1966 report, research on the deposition, retention, clearance, and translocation of inhaled aerosols intensified with studies on both humans and experimental animals. This new knowledge suggests a model can be constructed that more accurately describes inhalation of particles and gases by workers, but more importantly, it provides a basis for applying a lung model to all members of the world population.

Following a review of the current ICRP lung model, a plan was prepared for a revision. Principal inadequacies of the current model would be addressed, such as calculation of radiation doses to the nasal and oral passages; replacement of the D, W, and Y classification system for clearance of inhaled materials where adequate information is available; and calculation of doses for inhalation of gases. The revised model would use new knowledge of deposition and retention of very small particles (well below 0.1-μm diameter), regional deposition of inhaled particles, the distribution and absorption of inhaled gases, and clearance kinetics for numerous radioactive compounds determined in humans and experimental animals. Knowledge of the morphology and the physiology of the respiratory tract has increased, the relative regional sensitivities of the respiratory tract to cancer induction are better understood, and dosimetry modeling concepts and approaches have greatly expanded. The major developments in computer technology during the last few years have opened numerous possibilities for not only modeling the intake of radioactive materials but also utilizing the model for both projecting and assessing radiation doses. The task group determined that a new model should facilitate calculation of biologically meaningful doses; should be consistent with morphological, physiological, and radiobiological characteristics of the respiratory tract; should incorporate current knowledge; meet radiation-protection needs and be user-friendly (i.e., not too sophisticated); should be adaptable to development of computer software to allow calculation of relevant radiation doses from knowledge of a few readily measured exposure parameters; should be equally useful for assessment purposes as for calculating ALIs; should apply to all members of the world population; and should consider the influence of smoking, air pollutants, and disease.

A Revised Model

In developing a revised model the task group began with a number of assumptions. These are:

- The site of cancer induction is determined by both regional dose and regional sensitivity.
- Therefore, averaging the dose over the lungs is inappropriate because it does not reflect the variability in dose distribution or differences in regional sensitivity.

- A more appropriate approach is to calculate regional doses that relate to the relative cancer sensitivities.

- It was assumed that lung cancer risk factors apply to the total respiratory tract (risk factors are not specific to cancer site or cell type)

- That it is appropriate to weight regional doses by relative sensitivities to obtain a dose equivalent applicable to total respiratory tract.

The task group's approach was to converge separately developed morphological, radiobiological, physiological, deposition, clearance, dosimetric, and bioassay considerations into a comprehensive multiparameter dosimetric model for the complete respiratory tract. All will be addressed in considerable detail in the task group's report. An anatomical representation of the model is shown in Figure 1. It identifies the regional compartments that can be correlated with measurements of deposition, clearance, and retention of inhaled aerosols as well as with the occurrence of neoplastic diseases, the somatic effects of principal concern in radiation protection. These compartments are: the extrathoracic, ET, comprising the nose, mouth, pharynx, and larynx; the tracheobronchiolar region, TB, comprising the airway generations 0 through 15 (trachea through the terminal bronchioli) and the alveolar interstitial region, AI, comprising the airway generations 16 through 23 (respiratory bronchioli through alveolar sacs), plus the thoracic lymph nodes.

The proposed revised model addresses inspirability of aerosols and deposition in extrathoracic tissues, such as the nasal passages, pharynx, larynx, and vocal cords. Deposition in the TB region is assumed to include material rapidly cleared essentially by mechanical processes from airways generations 0 through 15, the bronchioli (Figure 1). Deposition in the AT region includes material slowly cleared from airway generations 16 through 23 by both mechanical and solubilization processes, as well as material infinitely retained, such as in lymphatic tissues. Calculations of the deposition of particles in these regions will be based on morphometric models and experimental data from human subjects inhaling test aerosols over a broad range of particle sizes.

In the proposed model, clearance of particles is competitive, occurring either by mechanical or absorption processes. It is also assumed to be nonlinear, with excretion a time-varying factor of the residual amount. Mechanical clearance rates will be obtained from studies with human subjects. For compounds for which reliable human data exist or for which data can be extrapolated from animal experiments, the model will use observed rates of absorption. For other compounds, default values will be used based on the current D, W, and Y classification system.

A proposed compartment model to represent mechanical clearance is given in Figure 2. This describes the behavior of a completely insoluble material. Absorption or translocation into blood acts on each compartment except the anterior nasal passages, represented by compartment ET_1, and it is assumed to occur at the same rate. Translocation to blood is essentially a two-stage process, Figure 3.

a. The dissociation of the particles into material which can be absorbed into the blood. For simplicity this will be termed dissolution.

b. The absorption into blood of material dissolved from particles, or if material deposited in a soluble form.

Mathematical models for calculating radiation doses to various tissues of the respiratory tract will be developed, incorporating expressions describing the deposition and retention of radionuclides. Rather than treat the lung and lymph nodes as a single organ and then calculating an average dose, the revised model will provide for calculating doses to radiation sensitive tissues in all anatomical regions identified in Figure 1.

The calculation of doses will follow the method of ICRP 30, in which the committed dose equivalent in a target tissue is determined by the energy absorbed per unit mass from the radiation emitted from a source organ. Compared with the current model, the proposed model is expected to simplify calculating respiratory tract doses from bioassay data. The task group expects computer software will facilitate, but not be necessary for, using the revised dosimetric model for the respiratory tract.

The tissues of the respiratory tract identified as among the most sensitive to radiation induction of cancer are:

- Keratinized epithelium of ET_1 (anterior nose)
- Stratified squamous epithelium of ET_2
- Ciliated epithelium of TB
- Alveolar-interstitium, AI
- Thoracic and extrathoracic lymph nodes, LN_{TH} and $LN4_{ET}$

Radiation doses to these tissues will be calculated. These regional doses will be weighted by the relative susceptibility to cancer induction and summed to obtain a single value of committed dose equivalent for the entire respiratory tract.

The approach used by the task group to derive estimates of the relative susceptibilities of the different tissues to radiation induced cancer was to assume that the entire respiratory tract is susceptible to radiation-induced cancer, but not all regions are equally susceptible. Since data are inadequate to provide risk estimates for each region or tissue, it was assumed that induction of cancer by radiation is proportional to spontaneous incidence in each region and that the relative distribution of spontaneous regional cancers in unexposed persons reflects relative sensitivities of the regions to radiation-induced cancer.

Reviewing data on cancers of the human respiratory tract, relative risks were assigned to each region and tissue as shown in Table 1.

Region	Relative Risk	Apportionment of Risk Coefficient
Extrathoracic		0.2
Nose & nasopharynx	0.03	
Mouth & oropharynx	0.12	
Larynx	0.05	
Tracheobronchiolar	0.64	0.64
Alveolar Interstitial	0.16	0.16

TABLE 1. Partition of Risk and the proposed appointment of the risk coefficient for radiation induced respiratory tract cancer among the most sensitive tissues

It is proposed then that the dose equivalent H_{50}, to the total respiratory tract would be calculated as follows:

$$H_{50} = H_{50,ET}R_{ET} + H_{50,TB}R_{TB} + H_{50,AI}R_{AI}$$

where R_{ET}, R_{TB}, and R_{AI} are factors from Table 1 for apportionment of risk among three regions of the respiratory tract.

COMMENT

Completion and publication of the task group report is expected to occur in 1991. The above description of the approach taken by the task group is not likely to change, but specific aspects of the model may change before publication.

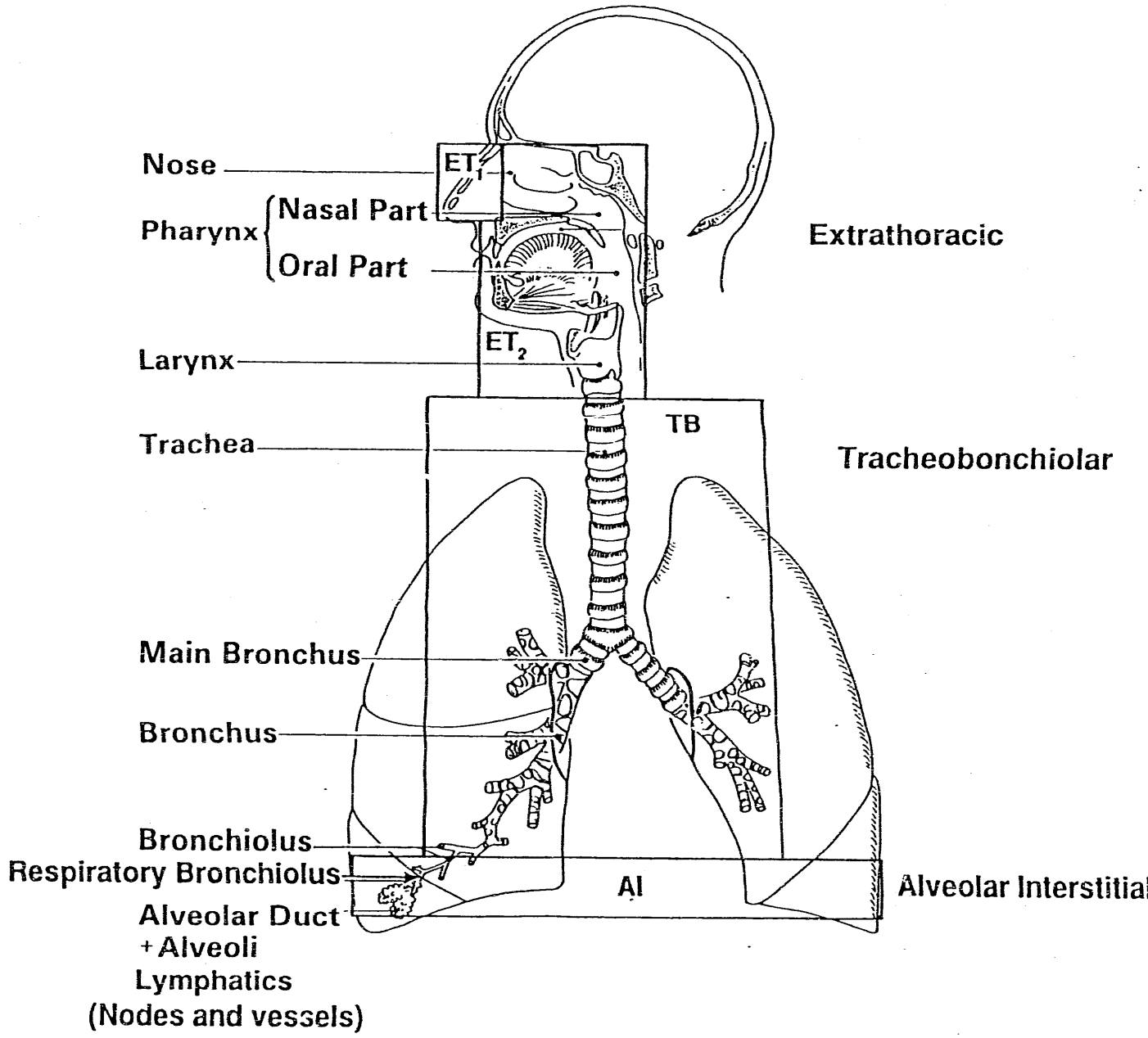

FIGURE 1. Morphometric Model - Respiratory Tract

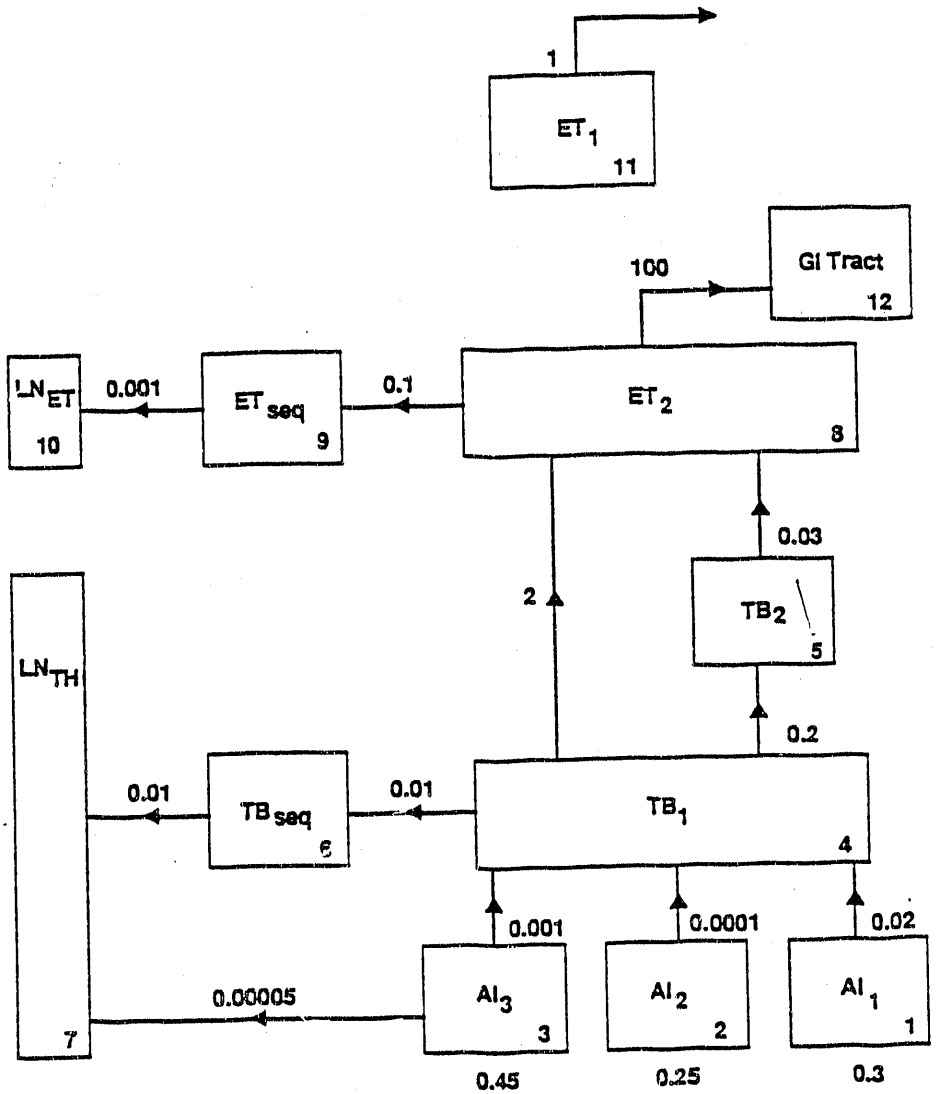

FIGURE 2. Compartment Model to Represent Time-Dependent Mechanical Transport From Each Region. Clearance rate constants shown are representative values in d^{-1}. Compartment numbers shown are to define clearance pathways, thus $m_{4,5}$ is the mechanical clearance rate from the TB_1 to TB_2 ($0.2\ d^{-1}$).

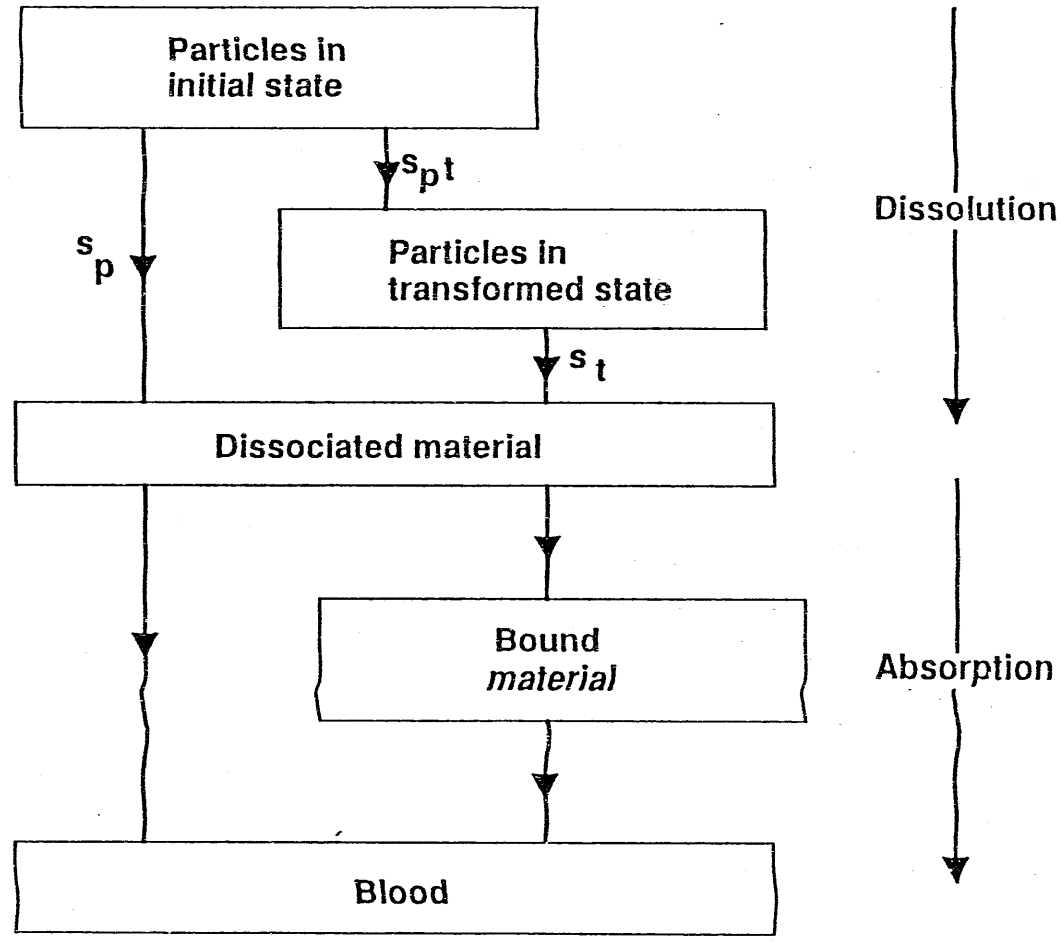

FIGURE 3. Clearance Model - Translocation to Blood

END

DATE FILMED

02/07/91