INTRODUCTION

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Pulmonary dosimetry models provide quantitative information on the locations and amounts of deposition of inhaled toxins, both gaseous and particulate. The specification of location may be quite broad, as in an entire region (head, tracheobronchial airways, or parenchyma), or very specific, for example within each of the many generations of the tracheobronchial tree. The uses for such information include proper selection of laboratory animal species in toxicologic studies, refined interpretation of laboratory animal toxicologic data, and prediction of potential sites of high local-injury from inhaled materials. Further, dosimetry models tend to identify the roles of relevant factors in potential lung injury. Such relevant factors may be physical-chemical (particle size, gas water solubility, etc.), physiologic (air flow patterns, mucus characteristics, etc.), or anatomical (airway dimensions, branch angles, etc.).

Predictive dosimetry models are of two major types, theoretical and empirical. In both types, the ultimate requirements for acceptability are the same; they must be realistic, must be validated, and must be of use in predicting what would occur in unexamined circumstances. Theoretical dosimetry models are constructs which usually begin with simplifications of the real world. Such simplifications occur in the selection of equations describing movement of gases and particles toward airway walls, use of manageable airflow descriptions, and incorporation of anatomical geometries that represent averages of actual lung morphology. Such models are later made more sophisticated by the incorporation of additional complexities.

Empirical modeling usually involves analysis of dosimetric data obtained in constructed hollow models, or less often in actual lungs, which have been exposed to airborne material under conditions simulating breathing. The analysis of such data permits development of mathematical relationships that describe the distribution of material deposited. Such relationships are then used to predict deposition patterns in unstudied circumstances. In addition to their value for predicting dose patterns, the equations that result from theoretical and empirical models can shed light on the mechanisms which control such dose patterns. Knowledge regarding mechanism is a fuel which fires scientific inquiry, stimulating the design of future studies.

Deposition studies using hollow airway models are used to study airflow patterns and deposition sites of airborne particles. Such model studies have led to recognition of secondary airflows within the bronchial tree, the function of the larynx in modifying airflow, and to a better understanding of the detailed deposition patterns for particles. Representative publications in this area include those by Schroter and Sudlow (1969), Olson et al. (1970), Martin and Jacobi (1972), Bell and Friedlander (1973), and Schlesinger et al. (1982).

Validation of any model, theoretical or empirical, is essential to its utility and acceptance by scientists. Validation is a relative term because no model provides an exact description of the great variety of structure and situations that occur in the real world. What is a sufficient validation for one purpose may be insufficient for another. Validation procedures are often more extensive for theoretical models than for empirical ones, and can include testing the predictions in simplified airway models, making airflow measurements in lung or lung-like structures, and performing morphometric measurements on airways. Validation must however eventually include comparison of predicted phenomena with those which occur in living subjects.

The papers presented in this part are examples of current research related to pulmonary dosimetry. The papers by Gehr (1984) and Leith (1984) do not present dosimetric models per se, but rather describe quantitative approaches for generating useful basic anatomical information and air flow information, respectively. In both papers, comparative mammalian biology is stressed. Such a comparative approach is an essential ingredient for the work of extrapolating data acquired in one species to another species.

Because this topic covers a great deal of ground, many similar modeling-oriented anatomical efforts are not included. Among them are the detailed quantitative measurements by Jay Schreider and Otto Raabe on the mammalian nasal cavity and on the respiratory acinus (Schreider and Raabe, 1981a, 1981b), and on mammalian tracheobronchial airways published by a variety of scientists (Horsfield et al., 1971, 1982; Phalen et al., 1978; Weibel, 1963; Yeh and Schum, 1979, 1980; Klimet et al., 1972). Several authors have also published information on comparative mammalian ventilation (Guyton, 1947; Crosfill and Widdicombe, 1961; Boyd and Mangos, 1981; Mauderly, 1974; and Likens and Mauderly, 1979).

The paper on pulmonary dosimetry models by Overton (1984) is representative of recent theoretical dosimetry modeling efforts for inhaled gases. Additional gas (or very fine particle) deposition models have been described by others (Morgan and Frank, 1977; Miller et al., 1978; Hofmann, 1982).

Particle deposition models are not covered, but because of their long history and usefulness they should not be overlooked. Among these models many are quite detailed in their dose pattern predictions (Findeisen, 1935; Landahl, 1950; Morrow et al., 1966; Mercer, 1975; Yeh and Schum, 1980). The foregoing references are merely a small portion of those available.

It is difficult if not impossible to predict the future of scientific research efforts as this future is influenced by the availability of scientific expertise, availability and targeting of research monies, and the ever-changing status of knowledge. Nevertheless, several potentially fruitful research problems are identified. Among them are the following:

1. Additional morphometric information (of the type used as input to theoretical models) is needed on the nasal, tracheobronchial, and parenchymal airways of various mammalian species.
2. The nature of growth of the airways (particularly the human) should be quantitatively defined.
3. Gas dosimetry models require additional validation and sophistication. (For examples, see nos. 4–9 below.)
4. Measurements of gas uptake in whole animals (human and non-human) should be performed and compared to theoretical predictions.
5. Hollow models should be used to study airflow and gas uptake phenomena.
6. Gas uptake models for the nose are in need of further development.
7. Models are needed for the dosimetry of mixtures of gases and particles.
8. The nature of airflow in small airways (terminal bronchioles, respiratory bronchioles, alveolar ducts, and alveolar sacs) must be better defined.
9. The characteristics of normal airway mucus (with respect to dissolution and reaction chemistry) require better definition.
10. Individual variations of dose within a species are important for future research.
11. The persistence of deposited material, gaseous and particulate, in the respiratory tract warrants further study.
12. Alterations in dose and dose patterns during exercise require additional attention.
13. Abnormal situations such as occur in various disease states should be modeled.
14. Doses to specific cell-types within the respiratory tract should be given more attention.
15. Differences between males and females with respect to dosimetry of inhaled materials are potentially important.

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