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MEETING REPORT

Respiratory Tract Morphology: Summary of a Conference

The role of the mammalian respiratory system, as both a portal of entry for toxic agents and as a target site for various disease processes, was considered at the 1973 Respiratory Tract Morphology Conference. The relatively informal meeting, held 7 and 8 May 1973, at the Lovelace Foundation's Inhalation Toxicology Research Institute in Albuquerque, New Mexico, afforded the opportunity for communication among anatomists, physiologists, pathologists, medical practitioners, physicists, and engineers, all working in the respiratory field. The meeting was cosponsored by three organizations; the National Institute of Environmental Health Sciences, the U. S. Atomic Energy Commission, and the Lovelace Foundation for Medical Education and Research, each having strong interests in inhalation toxicology.

Needs for New Information

The desirability of a multidisciplinary approach to the problem of environmental inhalation diseases, utilizing the strengths of both physical and biomedical scientists, was emphasized by the lead speaker, Roger O. McClellan (Lovelace Foundation, Albuquerque). McClellan pointed out that although man, dog, and rat exhibit many similarities in terms of the deposition of inhaled materials there are important differences between these species in their clearance patterns and in the development of pathophysiological responses.

Phillip Walsh (National Institute of Environmental Health Sciences, Re-

search Triangle Park, North Carolina) described the importance of evaluating the health effects of long-term, low-level exposures to biological, chemical, and physical agents in the environment. Of central concern is the assessment of hazards when several airborne agents are acting together. Improved respiratory-tract deposition models for inhaled particles and gases are needed to help relate exposure parameters to health impact.

A clinician's view, particularly that of the chest physician, was presented by David R. Sanderson (Mayo Clinic, Rochester, Minnesota). An improved terminology and understanding of the bronchial tree would improve the communication between the endoscopist, the pathologist, and the chest surgeon in the pinpointing of lesions.

Descriptive Models of the Airways

Mathematical models of the bronchial tree, in the form of sets or tables of numbers, were discussed by Keith Horsfield (Midhurst Medical Research Institute, Sussex, England). Horsfield described branching system models as either "symmetrical," i.e., having the same number of branches to each termination along all paths, or as "asymmetrical." A "continuous" model is one which can be used to uniquely reconstruct the branching system from the data of the model, maintaining the proper connections of one branch to another. In "discontinuous" models, a single set of data can be used to construct various branching systems. By defining an average asymmetry (of di-

ameters) at each bronchial junction, Horsfield has developed a model that is both asymmetrical and continuous. He also stressed that the often-heard term "generation" is not generally useful in describing the mammalian bronchial tree. For example, a tenth generation bronchus in man can be as large as several millimeters in diameter or as small as 0.5 mm and respiratory in character.

Replica Casts of the Respiratory Tract

Replica casts of the respiratory tract are becoming increasingly popular in scientific studies as improved materials and methods become available. Discussion of the problems associated with preparing casts brought out several points. It is important that mucous membranes not be allowed to dry, and thereby shrink, before a casting is made. When casts are used in particle deposition studies the presence of nasal hairs and the airway surface character are of importance and should not be overlooked.

Comparative Morphology

Subgross comparative lung anatomy in mammals was discussed by Richard McLaughlin, Jr. (Burlingame Medical Group, Burlingame, California). An outgrowth from the study of thousands of sections from latex-injected lungs was the classification of several mammals into three basic subgross lung types. Lung Type I, which includes the cow, sheep, and pig, has a thick pleura, well developed secondary lobulation, and marked interlobular septa. The dog, cat, and rhesus monkey, examples of Type II, have very thin pleura, absent secondary lobulation, and ill-defined interlobular septa. Type III, which includes the horse and man, is an intermediate type having thick pleura, incompletely developed lobules, and haphazard interlobular septa. With respect to the anatomy of the distal airways, McLaughlin observed that the cow, rat, and guinea pig have very little alveolarization of airways proximal to the alveolar duct. At the other extreme are the dog, cat, and rhesus monkey with heavily alveolarized respiratory bronchioles. Man, horse, and rabbit appear to fall between the extremes, showing an intermediate degree of alveolarization of the distal airways.

Walter Tyler (University of California, Davis) further discussed the distal airways in various mammals. Using the

scanning electron microscope one can see scattered alveoli, opening into the lumens of partially ciliated distal airways, in rats and hamsters. In contrast, the ciliated airways of the horse did not have alveoli opening into them. The rhesus monkey had alveoli opening into bronchioles lined with cuboidal epithelium, but no alveoli were seen opening into ciliated airways. Mammalian alveoli were always observed as having polyhedral shapes with flat interior wall surfaces.

The distal airway, a critical site of both experimental and spontaneous disease of the mammalian lung, shows tremendous interspecies variability. Additional information is clearly needed to describe this important anatomical region within the mammalian respiratory tract.

Growth and Pathology

Differences in the lungs of humans of different body size were described by William Thurlbeck (Midhurst Medical Research Institute, Midhurst, Sussex, England). Postmortem morphometric studies were organized around three anatomical compartments; the large airways, the small airways (bronchioles), and the alveoli. The same number of large and of small airways were found in all adult lungs, but the bigger lungs had larger airways. Both the number and size of alveoli were larger in the bigger lungs. Thurlbeck hypothesized that the full number of air-conducting airways is present at birth and does not vary with body size; but, that the final number and size of alveoli are influenced by individual growth patterns.

Edwin Boatman (University of Washington, Seattle, Washington) discussed his observations of the ultrastructure of mammalian lungs after exposure to ozone. Observations after brief (≈ 4 hours) exposures of cats and rabbits to low concentrations (< 1 ppm) of ozone indicated focal lesions in large airways (3 mm or more in diameter), occurrence of mitochondria with thickened and disoriented cristae, and denudation of alveolar epithelium. It appeared that the smaller airways of the acinus were more susceptible to damage from ozone than the larger ones.

Charles Plopper (Fitzsimmons Army Medical Center, Denver, Colorado) reported on ultrastructural studies of the acinus of the rat lung after exposure to 3 ppm of ozone for 4 hours. He observed damage to capillaries and that

the number of Type I alveolar cells was decreased. Damage was concentrated in, though not limited to, the central portions of the acinus. Both the degree and location of damage seen in such studies depend upon many factors, including the exposure and sacrifice times and whether or not the exposure bypassed or included the nasopharyngeal region.

Particle Deposition and Airflow Patterns

The complex problem of calculating where particles of a given size, density, and composition will deposit in the respiratory tract was addressed by Herbert Landahl (University of California Medical Center, San Francisco, California). Major physical mechanisms contributing to the deposition of inhaled particles are inertial impaction at bends or bifurcations in airways, sedimentation under the influence of gravity, and Brownian diffusion of particles within the respiratory tract. The glottis, which has an opening of variable size, can cause increased impactional particle deposition in the trachea by increasing the airflow velocity.

Air flows in the airways were discussed by respiratory physiologist Robert Schroter (Imperial College, London, England). Schroter described helical and retrograde secondary flow patterns that result from the interaction of moving air with the flow divider portion of a bifurcation. These secondary flows, seen in models of bifurcations, can have velocities as high as 25% of the axial flow velocity at physiologically realistic flow rates.

Hsu-Chi Yeh (Lovelace Foundation, Albuquerque, New Mexico) described attempts to improve the traditional particle deposition calculations in the lung by the use of an improved anatomical model. The anatomical model, based on hand measured morphometry data from lung cast replicas, contains the asymmetric aspects of branching found in mammalian lungs and expresses the anatomic differences between various lobes.

A series of particle deposition studies in hollow bronchial tree casts was described by Morton Lippman (New York University, New York). After the addition of a larynx cast, he found increased deposition of particles in the trachea and in the subsegmental bronchi. Monodisperse particles with aerodynamic diameters above 1 micron were used in the studies.

Nonuniformities in the particle deposition pattern in idealized models of airway bifurcations were reported by Carl Bell (California Institute of Technology, Pasadena, California). The greatest deposition occurred at the leading edge of the flow divider with deposition generally decreasing downstream and radially away from the apex of the bifurcation. Deposition maxima were seen downstream and sometimes on the walls opposite to the apex of the bifurcation. The locations of these deposition maxima appeared to be consistent with the helical secondary flow patterns described by Robert Schroter earlier in the meeting.

An isolated perfused lung system developed by Elias Tombropoulos and John Hadley was described by Bruce Stuart (Battelle Pacific Northwest Laboratories, Richland, Washington). This preparation, used to keep an isolated hamster lung in reasonably good condition for about 90 minutes, may prove useful in studying particle deposition and early solubilization within the lung.

Differences in aerosol deposition and clearance between normal people and people with disease of the small airways were described by Michael Newhouse (St. Joseph's Hospital, Hamilton, Ontario). Normals exhibited an initial aerosol deposition pattern that appeared uniform throughout the lung field, very little deposition in the trachea or hilar region, and very little clearance of the particles from the lung during the first 24 hours. People with airways obstruction showed only spotty deposition in the peripheral lung fields, marked deposition in the trachea and hilar region, and nearly complete clearance of the particles by 24 hours.

The basic problem of accounting for all of the aerosol in an animal inhalation study was discussed by Douglas Craig (Battelle Pacific Northwest Laboratories, Richland, Washington). In Craig's dog exposure apparatus, inspired and expired air were separated, breathing monitored with a venutri flow meter, and cascade impactors used for obtaining aerodynamic samples from both inhaled and exhaled volumes.

Progress in generating labeled, spherical monodisperse aerosols with a spiral centrifuge for use in inhalation studies was described by George Newton (Lovelace Foundation, Albuquerque, New Mexico).

Comments

A subject discussed informally at the meeting was the difficulty of obtaining

fresh human lungs for study. The scientific need for all types of human tissue is great and procedures should be devised whereby proper access can be quickly obtained.

A major outgrowth of this meeting was an emergent interest in the small airways of the lung. These airways, lying between the ciliated surfaces of the airway and the fully alveolarized parenchyma, have been recently regarded as important sites for pathophysiological processes, the nature and severity of which are strongly dependent on the species involved. The relationships between the structure of small airways and their susceptibility to disease emerge as a research area with considerable immediate promise.

A more complete summary and set of selected references prepared by the author and his associates for conference attendees are available upon request.

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