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REVIEW OF BIOENGINEERING CONFERENCE ON GAS FLOW AND PARTICLE TRANSPORT IN THE LUNG (JANUARY 22-23, 1968).

Birney R. Fish

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REVIEW
OF
BIOENGINEERING CONFERENCE ON GAS FLOW AND PARTICLE TRANSPORT IN THE LUNG

Birney R. Fish*
Health Physics Division
Oak Ridge National Laboratory**

February 21, 1968

*Work supported by Smoking and Health Lung Model Study for Division of Environmental Health Sciences, National Institutes of Health, U. S. Department of Health, Education and Welfare.

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Review of Bioengineering Conference on Gas Flow and Particle Transport in the Lung

Birney R. Fish*
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This conference was co-sponsored by the California Institute of Technology and the Air Pollution Study Section, National Center for Air Pollution Control, Public Health Service. It was held on the Cal Tech campus, January 22 and 23, 1968 and was attended by a mixed group of more than 130 engineering scientists and pulmonary physiologists. The aims of the conference are embodied in the following which served as a preamble to the program outline:

> "Engineering scientists have developed experimental and theoretical methods for studying fluid motion near surfaces and for determining rates of particle transfer from moving gases to surfaces. The purpose of this conference is to bring together engineering specialists in these fields with pulmonary physiologists concerned with transport in the lung.
>
> "From this meeting it is anticipated that the engineers will become aware of certain problems in their fields of specialization faced by the pulmonary physiologists. At the same time, the physiologists will familiarize themselves with the types of problems which can be solved by modern engineering methods. One result, it is hoped, will be improved methods for predicting rates of exchange of particles and gases with the surface of the lung."

The first session, Structure and Aerodynamics, was chaired by Doctor P. T. Macklem, Director, Respiratory Division, The Royal Victoria Hospital, Montreal, Canada. W. A. Briscoe, Columbia University, presented a paper on Pulmonary Architecture in which he gave a rather thorough review of the dichotomatous model of the lung described by Weibel [E.R. Weibel, Morphometry of Human Lung, Springer-Verlag, 1963] and referred to a table, which was handed out, listing the assumed dimensions of the various branches of the airways and the exchange regions of the lungs (see Appendix A). Professor Briscoe pointed out the distinction between the terms bronchus (cartilage in wall) and bronchiole (muscle in wall) and cautioned that at least one author of a published paper had erroneously left out one level of alveolar duct when referring to the

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Weibel model. He mentioned the curious observation of Dunhill that at birth a child has about 24 million alveoli, whereas by adulthood the lungs are found to contain about 300 million. His table included a calculation of pressure drop based on the assumption of laminar flow. The calculated value of ΔP from the mouth to the alveoli for a flow rate of 1000 cm^3/sec was 0.17 cm H_2O, in contrast with the observations of P. T. Macklem, et al., that $\Delta P = 0.3$ cm H_2O at a flow rate of 500 cm^3/sec. Thus, the assumption of fully developed laminar flow throughout the pulmonary airways is clearly not justified. Further review of the table and the indicated cumulative volume to the various levels of branching indicate that the anatomical dead space (volume of the transitory airways) is 215 cm^3 including the mouth through the terminal bronchioles. This is considerably in excess of 130 cm^3 which is usually taken to be the size of the anatomical dead space. The disparity may be due in part to a general expansion of the airways during the process of forming the cast of the air passages; further, it may well be that the single human lung used by Weibel to obtain his measurements, in fact, had a larger than average anatomical dead space.

Professor Y. C. Fung, University of California at San Diego, discussed Stress-Strain-History Relationship of Soft Tissue. This was one of the highlights of the meeting. Professor Fung, a most interesting speaker, gave an introduction to the experimental and theoretical treatment of the mechanics of mesentery tissue (in the absence of data on lung tissue). Various factors such as hysteresis, stress relaxation, fatigue and rupture are observed. He pointed out the distinction between the Lagrangian stress (force divided by the original area) and the Eulerian stress (force divided by the deformed area) and indicated his use of the Lagrangian stress in the theoretical treatment. In order to incorporate a dependence on prior history, Professor Fung assumes the Boltzman integral equation in time and was able to show rather good curve fits to stress-strain data. He pointed out the considerable difficulties to be faced in extrapolating the present work in 1-dimension to the 3-dimensional case of lung tissue in situ.

Doctor J. Mead, Harvard University, gave a paper on Pressure-Flow Characteristics of the Lung (External Measurement). In relation to the 1-dimensional case discussed by Professor Fung, Doctor Mead pointed out that respiratory physiologists refer to volume as the 1-dimensional unit = V (liters). The first ($\dot{V}$) and second derivatives ($\ddot{V}$) of the volume with respect to time also are measured parameters. The pressure drop P (inches H_2O) is assumed to be a function of V, $\dot{V}$, $\ddot{V}$; thus,

$$P = f_1 (V) + f_2 (\dot{V}) + f_3 (\ddot{V}).$$

In this $f_1 (V)$ is assumed to be related to lung tissue elasticity, $f_2 (\dot{V})$ is taken to be dependent on gas and tissue fluid flow resistance, and $f_3 (\ddot{V})$ is related to the mass of gas and tissue that is set into motion. The speaker described two means of measuring alveolar pressure: The gas compression technique, in which the subject is placed in a closed box; and the pleural pressure technique in which an esophageal balloon is used to obtain a measure of alveolar pressure. Both techniques are indirect, but it was pointed out that alveolar pressures obtained by the two methods are substantially in agreement. Using available data, Doctor Mead has obtained an expression for alveolar pressure (inches H_2O) during the inspiration cycle as follows:

$$P = 1.5\,\dot{V} + 0.3\,\dot{V}^2 + 0.01\,\ddot{V}.$$

At and below a volume flow rate of one liter per second, the first term dominates. For higher rates of flow, the second term dominates the equation. The pressure drop during the expiratory phase is approximately the same or, perhaps, 10% higher than that during inspiration. He suggested that the Weibel model probably represents the situation of the lungs inflated to about 80% of their maximum size.

The last speaker of the Monday morning session was Doctor D. L. Fry, National Heart Institute, Bethesda, whose subject was A Model of Pulmonary Pressure-Flow Relationships. Doctor Fry has developed an elaborate but potentially a powerful model which is intended to yield estimates of the shear stress on the walls of the pulmonary airways as a function of the flow parameters and of the location along the air pathway. In this model the total length of the air pathway is assumed to be directly

proportional to the cube root of the total volume of the lung. By means of a phenomenological argument, Doctor Fry arrived at an expression from which the wall shear stress may be estimated. The result includes a sizable number (14) of adjustable parameters; however, the speaker expressed confidence that many of these will be clarified as more intensive study of the lung produces additional data. [There is a definite need for such a model which may be able to produce estimates of the shear stress on the ciliated lining of the airways. This information is related to possible damaging stresses and may be an important factor in assessing clearance of particles deposited on the moving mucus sheath.]

The remaining two sessions bore the common title, Gas Flow and Particle Transport. Doctor S. Goren, University of California at Berkeley, was chairman of the Monday afternoon session. The first paper in this session was given by Professor P. G. Saffman, California Institute of Technology, on the subject Gas Dynamics with Emphasis on Periodic Flow. In recognition of the accepted anatomical data indicating that the cross sectional area of the airways increases from about 2.5 cm^2 in the trachea to 11,000 cm^2 in the alveolar sacs, the speaker suggested a mechanical model based on a conical cylinder filled with a porous medium and a flexible piston capable of conforming to the walls. Saffman did not pursue this model further but then went on to a consideration of oscillatory flow. Referring to the work of Sexl [Th. Sexl, Zeits. für Physik 61, p. 349 (1930)], he introduced the Navier-Stokes equations and Sexl's assumption that the pressure gradient in the flow direction $\left(\frac{\partial P}{\partial x}\right)$ is a periodic function of time, thus

$$\frac{\partial P}{\partial x} = P_p \cos \omega t.$$

Employing an order of magnitude argument he demonstrated the emergence of a frequency parameter as an important nondimensional index to the relative significance of the periodicity. The frequency parameter is given by

$$F = \frac{\omega d^2}{\nu};$$

where

ω = frequency of the flow oscillations
d = conduit diameter
ν = kinematic viscosity.

It was shown by Sexl that Poiseuille (laminar) flow is a bad assumption unless $F \ll 1$. For $F \gg 1$ the velocity is 90° out of phase with the pressure and the velocity distribution is almost uniform across the conduit, the velocity gradient being confined to a layer on the order of $\sqrt{\frac{\nu}{\omega}}$ thick. Saffman noted that, assuming 12 respirations per minute, the frequency parameter is approximately 30* in the trachea and 0.05 in the smaller airways. Thus, the periodic nature of the flow cannot be ignored in the trachea but becomes insignificant in the small airways. While steady Poiseuille flow can develop (sustain) instabilities at Reynolds numbers (Re) around 2000, this is completely irrelevant with respect to pulsatile flow. Unfortunately, the stability of Sexl's result under the influence of small perturbations cannot yet be determined theoretically; however, it appears that instabilities occur for $Re(F)^{-\frac{1}{2}} \approx 10$, "but it may be that this turbulence is confined to the wall region." Saffman also pointed out the problems associated with the finite length of the various segments of the airways. For steady Poiseuille flow there is a finite entry length (approximately 0.03 dRe) required to establish the characteristic parabolic velocity profile: Hatterbeck and Chang found a change in the entrance length for oscillating steady flow (no back flow). The effect of curvature of the conduit on steady Poiseuille flow was studied by Dean [W.R. Dean, Phil. Mag. 4, p. 208 (1927) and 5, p. 673 (1928)]: an additional pressure drop on the order

$$Re\left(\frac{d}{\text{radius of curvature}}\right)^{\frac{1}{2}}$$

is noted and the curvature has the effect of making the flow more unsteady. In addition, curvature leads to the formation of secondary flows transverse to the main direction of flow and directed so that the radial component of velocity at the center of the pipe is toward the outside of the bend with return flow along the walls. The flexible character of the walls is another complicating factor which, at the very least, can introduce a narrowing of an airway because of the Bernoulli effect. This narrowing reduces the cross sectional area and, for a given volume flow rate, leads to a higher velocity resulting in more narrowing, etc. [The process of Bernoulli narrowing will continue until the volume flow rate decreases, or until the structural strength of the wall can successfully resist further changes. This may be a major factor in some of the manifestations of emphysema in which certain airways completely collapse during exhalation.]

*Saffman appears to be in error by a factor of about 10 (see Appendix C).

Finally, Saffman commented on some of the peculiarities of branching flow. Although it may be possible to obtain some qualitative ideas about the flow structure by theoretical means, the experimental approach should be much more promising. It is important to keep in mind the necessity of observing the two scaling laws and to keep the frequency parameters constant as well as the Reynolds numbers. Qualitatively, during the inspiratory phase one might expect the possibility of separation and eddy formation along the outside wall at a bifurcation, whereas, during expiration separation may occur at the point where the two streams join at the intersection of the branching tubes. In response to a question about the effect of wall roughness, Saffman commented that this probably has little effect on Poiseuille flow (in the smaller airways) and not much more effect on turbulent flow, but the formation of eddies at bifurcations may depend critically on the nature of the surface.

Second speaker on the afternoon program was Doctor Kenneth T. Whitby, Department of Mechanical Engineering, University of Minnesota, whose subject was Aerosol Generation and Measurement. Whitby's group has developed a unique series of instruments for the generation and measurement of aerosol particles and the application of their measurement techniques to atmospheric aerosols has produced some very interesting and useful data. In the size range from 0.05 to about 10 microns radius the normal atmospheric particle size frequency distribution is given approximately by

$$\frac{dN}{dr} = 2.5\,\Phi\, r^{-4}\ ;$$

where Φ = volume fraction (cubic microns/cm^3),

and r = particle radius (microns).

The maximum total number concentration is about 10^6 particles/cm^3 in the environment and particles less than about 0.03 microns radius are lost rapidly and do not contribute significantly to the atmospheric aerosol unless there is a continuous source generating particles of this or smaller size. Whitby also commented that there is a growing conviction, although as yet unsubstantiated in the literature, that most atmospheric particles smaller than a few tenths micron diameter are liquid droplets. He went on to describe

various means of generating a monodisperse aerosol, which he defined, for practical purposes, as an aerosol having a narrow distribution of sizes such that the geometric standard deviation (σ_g) is less than 1.2. [This means that 68.3% of the particles lie in the size range between 83% and 120% of the median size.] Fuchs [N.A. Fuchs, Mechanics of Aerosols, Pergamon Press, New York, 1964] suggests $\sigma_g < 1.6$ in this regard. Atmospheric aerosols have broader size distributions, for which $\sigma_g \gtrsim 2.5$. There are three major methods for generating monodisperse aerosols. One of the most popular methods is the dispersion of presized particles such as the polystyrene particles [Dow Chemical Company, Midland, Michigan] which are available in the size range 0.08 to 2.7 microns diameter and $\sigma_g \approx 1.05$ (max. concentration $< 10^3/cm^3$). A second method is the controlled condensation of vapors onto selected nuclei: a device developed by Whitby is capable of producing droplet aerosols in the size range 0.01 to 3 microns diameter with geometric standard deviations in the range 1.15 to 1.5. Finally, nearly uniform droplets can be generated by an atomization-impaction technique (0.01 to 2 microns diameter: σ_g from 1.3 to 2), or by means of a high speed spinning disk (liquid drops 10 to 150 microns diameter can be dried to produce solid particles 0.5 to 50 micron diameter : $\sigma_g > 1.1$). Another significant area of research of Whitby's group is the behavoir of airborne aggregates of solid particles. He reported that the fluid drag on an aggregate is nearly independent of the shape when the size is comparable to the mean free path of the fluid, and the drag on a long chain aggregate is approximately equal to that of a sphere of equal volume. The amount of electrical charge transferred to a chain-like aggregate is somewhat greater than to an equal volume sphere.

The final speaker on Monday afternoon was Doctor Sheldon K. Friedlander, W.M. Keck Engineering Laboratories, California Institute of Technology, one of the major organizers of the conference. Professor Friedlander spoke on Aerosol Transport Mechanisms. In order to place the engineering problem in its proper perspective, the speaker pointed out a number of relevant classical engineering problems that have been solved, at least to some extent -- oscillatory flows in long tubes, longitudinal dispersion in conduit flow, and mass transport in the boundary layer. Although a detailed knowledge of flow structure, eddy formation, separation, etc., is largely unavailable, there is a fair chance to guess

at local deposition rates in the conducting airways. One problem is particle deposition at the branch points. Consider the first puff of cigarette smoke -- as the slug of contaminated air goes down the respiratory tree, each branch point is confronted with a high concentration of particulates. In a qualitative analogy with the heat transfer to a nose cone, we would expect higher mass transfer at the stagnation point. The relevant dimensionless quantity in the heat transfer case is the Peclet number, given by

$$\text{Pe} = \text{Re} \times \text{Prandtl number} = \frac{\ell v}{\alpha} ;$$

where ℓ = a characteristic length,

v = fluid velocity,

α = thermal diffusivity.

Assuming complete analogy between heat and mass transfer we take α to be the same as the diffusivity (brownian motion) of the airborne particle. For example, the diffusion constant for a 0.2 micron diameter particle is 2.2×10^{-6} cm^2 sec^{-1}, and taking $\ell = 1$ cm and $v = 60$ cm sec^{-1} the modified Peclet number is approximately 3×10^7, which is very large indeed. Thus, we would expect convective movement of the particles downstream to predominate over particle diffusion to the walls. The number concentration of particles in the flow stream must satisfy the following equation:

$$\frac{\partial n}{\partial t} + y f(t) \frac{\partial n}{\partial x} = D \frac{\partial^2 n}{\partial x^2}.$$

Friedlander and his associate, Professor Wang, have made a first approximation by treating the development of the boundary layer on a flat plate, but still retaining a variation with time, simulating a portion of the inspiratory phase. They chose to use

$$f(t) = \frac{b}{(c - 2t)^{\frac{3}{2}}} = \text{velocity}.$$

Assuming the similarity parameter

$$\eta = \left[\frac{f(t)}{9x}\right]^{\frac{1}{3}} y,$$

and choosing b = 71.9 and c = 11.7 to approximate the known velocity function, Friedlander indicated that there appears to be an asymptotic solution which is a function of x and η. It takes on the order of 0.3 seconds to form a particle diffusion boundary layer which for a 0.2 micron particle becomes approximately 25 microns thick. For a branch airway immediately following the 6th bifurcation (Appendix A), assuming a tidal volume of 450 cm^3 [factor of 2 too low] and if the particle concentration is 10^8 per cm^3 [probably about right, or perhaps a factor of 5 too low, for cigarette smoke], Friedlander and Wang have calculated the deposition rate to be 2.86×10^5 particles cm^2 per puff of cigarette smoke. [Wang indicated to me that he does not yet have calculations for the other orders of branching but is planning to complete the study as soon as he can and will publish.] In summary, Professor Friedlander drew up a series of particle transport problems and related each of these to possible solutions of simplified, but solvable, problems. The problem of convective diffusion can be related to the similarity solution of the unsteady boundary layer on a flat plate (as above). Impaction of particles at bifurcations can be approached by use of a rather "simple minded" wedge model. However, the problem of eddy transport is intractable without experimental data on flow patterns, and would be very difficult even if we knew the flow structure. In addition to detailed modeling of sedimentation and diffusion of particles in the pulmonary region, Friedlander, like Saffman, stressed the need for experimentation on the fluid dynamical problems as well as on mass transfer in branching systems.

Professor Morton Corn, School of Public Health, University of Pittsburgh, was chairman of the last formal session, Gas Flow and Particle Transport - II (Tuesday morning, January 23). The first speaker was W. D. Rannie, California Institute of Technology, who discussed Longitudinal Dispersion in Tubes. Professor Rannie suggested the relation of the longitudinal dispersion of particles and vapors in a conduit to the smearing out of a heat pulse in pipe flow, a problem studied by Nusselt and others in 1927. Starting with a pulse of heat, generated at time $t = 0$ in a thin transverse slice of the flowing fluid, and assuming a wall of finite thickness and heat capacity and insulated on the outside, there will be a gradual widening of the heat pulse and a decrease in the maximum temperature as the pulse moves down the conduit with the flowing fluid. The pulse width is proportional to, and the maximum temperature is inversely proportional to $\sqrt{t}$. In 1954 Taylor solved the heat flux equation, giving the result (far downstream)

$$\theta = \frac{\theta_o}{2\sqrt{\pi D_o t}} \exp - \left(\frac{(x - \bar{u}t)^2}{4 D_o t}\right);$$

where θ_o = temperature of initial pulse

x = distance downstream

$\bar{u}$ = average velocity of fluid

and $$D_o = \alpha + \frac{\bar{u}^2 a^2}{48\alpha} = \alpha\left(1 + \frac{Re^2 Pr^2}{192}\right);$$

where a = conduit radius

α = thermal diffusivity of the fluid

Re = Reynolds number

Pr = Prandtl number.

The mass transfer analog of this solution would require replacing the Prandtl number with the Schmidt number

$$Sc = \frac{\nu}{D};$$

where ν = kinematic viscosity of the fluid

and D = mass diffusivity (e.g., particle diffusion constant).

According to Rannie this solution is good for

$$x > 0.03\, a\, Re,$$

[Laufer says 0.0285 a Re].

[For many gases in air $Sc \approx 1$, in which case the first term (diffusion) predominates for Re < about 10 and convective transport (second term of D_o) begins to become dominant for Re > 10 which is the case for the first 12 or 13 generations of the airways. In the case of particles the diffusion constant is quite low (high Schmidt number), hence convective transport will dominate the longitudinal dispersion of particles much deeper into the airways than the 12th generation, e.g., in the case of particles larger than about 0.01 microns diameter convective transport will predominate even in generation 22, where the Reynolds number is about 0.04.] Rannie suggests that, for gases, the portion that is unabsorbed can be assumed to be uniformly distributed across the cross section. He suggests that experimental work will be needed to understand mass transfer in the trachea and, possibly, also in the major bronchi; however, calculation should be adequate for the deeper airways.

The next speaker, Dr. Bernard Altshuler, Institute of Environmental Medicine, New York University, presented a paper on Gas Diffusion in Lung Spaces. He discussed the phenomenological model of gas mixing in the lung which he has described previously in the literature [see e.g., B. Altshuler, et al, p. 47, Inhaled Particles and Vapours, ed. by C. N. Davies, Pergamon Press, Oxford, 1961]. The general idea is that in each respiratory cycle a finite fraction of the tidal volume mixes into and becomes part of the functional residual volume and vice verse. Thus, in addition to the particles and vapors retained by deposition, upon exhalation the volume of gas remaining in the lungs includes a small fraction of gas from the previous inspired volume along with its associated content of undeposited particles and vapors. Altshuler and his associates at NYU have studied the inhalation of monodisperse particles by human volunteers and he showed slides of retention as a function of the number of breaths. For 0.4 micron diameter particles of triphenyl phosphate the fraction retained changed with each breath, reaching equilibrium after four breaths at about 87% for two of the human subjects and about 70% for another. He described a new valve designed to expose a subject to a known concentration of aerosol in the form of a single puff or "bolus." In operation, the subject inhales through a valve leading directly to a pneumotachograph or other flow measuring device. The valve consists of two flexible tubes of similar dimensions and positioned so that they cross at 90° without intersecting. While the subject is inhaling through one tube, the aerosol is being pumped through the other to a concentration monitor (e.g., a tyndallometer). At the desired point in the inspiratory cycle the valve is rotated 90° and the tube containing a known concentration and known volume of aerosol is introduced into the airstream to be inhaled. Altshuler also points out that people who have attempted to calculate particle deposition in the pulmonary region have neglected to consider that alveolar ducts are, after all, alveoli also. That is, their walls are alveolated and can in no sense be treated as smooth tubes. He did not offer a remedy to this problem; however, in his paper at the 2nd International Conference on Inhaled Particles and Vapours [Altshuler, et al, p. 323, Inhaled Particles and Vapours II, ed. by C. N. Davies, Pergamon Press, Oxford, 1967], he suggested an empirical approach in which experimental data on total retention and computed values for tracheo-bronchial retention may be used to produce an estimate of the pulmonary deposition as a function of particle size.

The third speaker on Tuesday morning was Prof. E. D. Palmes, also of New University. Professor Palmes discussed the Deposition of Monodisperse Particles in the Lung beginning with the theoretical work of Findeisen [Germany, 1935], and the experimental studies of LaMer , Brown and Hatch, and Altshuler [in U.S.A], and Muir and Davies [London]. He showed a curve of deposition in the mouth as a function of particle size extracted from data of Lippman and Albert [NYU: paper presented orally at the American Industrial Hygiene Association National Meeting, 1967: to appear in AIHA Journal in 1968: I have a preprint]. [In order to compare with a report in the literature which indicates 66% retention of cigarette smoke particles in the mouth from one puff, I noted that according to Lippman's data, unit density particles must be as large as 7 to 12 microns diameter to give 66% retention in the mouth.] Next the speaker reviewed some results which he, Altshuler and Norton Nelson obtained in studies of particle retention during breath holding [p. 339, Inhaled Particles and Vapours II]. He pointed out that the fraction exhaled decreases as an exponential function of time as predicted by H. D. Landahl [Bull. Math. Biophys. 12, p. 43, 1950]. The prediction equation is based on a model which assumes a tubular filter bed having uniform diameter tubes; consequently, fitting the parameters of the exponential derived from the observed data to the tubular filter bed model yields an effective diameter. This effective diameter of the airways is observed to change faster than the cube root of the total lung volume [varying tidal volume], and possibly indicates that the dominant region of the lung [with respect to deposition] depends upon tidal volume. These results, along with the bolus inhalation valve described by Altshuler, suggest a possible application to the assessment of the effective airway diameter as a function of depth of penetration for an individual. This could develop into an important technique, allowing the lung physiologists to estimate the location and degree of obstruction or constriction in certain disease states.

The final speaker on the program was Dr. Mary O. Amdur, Harvard University, who described her extensive studies on the Joint Action of Particles and Gases. Doctor Amdur's work has been directed toward defining an objective means to measure lung response to an irritant gas. She has been able to demonstrate a direct relationship

between the change in pulmonary resistance and the exposure level to the gas and, in the work described, refers to the per cent increase in pulmonary resistance as a basic parameter for comparison with the concentration of gas. The pulmonary resistance is defined as the ratio of the maximum intrapulmonary pressure to the maximum rate of change of lung volume, both measured during exhalation. When guinea pigs were exposed to an approximately constant level of about 2.2 parts per million (ppm) of sulfur dioxide (SO_2) the per cent change in pulmonary resistance was 20 for SO_2 alone, increased to 50 in the presence of an added sodium chloride (NaCl) aerosol, was 65 with potassium chloride (KCl) particulates plus SO_2, and was observed to be 100 for SO_2 plus an ammonium thiocyanate (NH_4SCN) aerosol. A detailed plot of change in pulmonary resistance as a function of ppm SO_2 showed two distinct patterns of response. In the presence of poorly soluble oxides such as manganese dioxide (MnO_2) and iron oxide (Fe_2O_3) the observed response was similar to that seen for SO_2 alone; however, the response was increased significantly when soluble particles of the same cations were used, e.g., manganese chloride (MnCL) and ferric sulfate ($Fe_2(SO_4)_3$). Doctor Amdur suggests that the synergistic effects of particles and SO_2 are related to solubility rather than straight adsorption on the particle surface.

SUMMARY OF CONFERENCE

This conference reemphasized a number of the inadequacies in our knowledge of gas and particle movement in the respiratory tract, but it also served to stimulate the thinking of the engineers and physiologists who should be able to contribute heavily in the near future to this somewhat lagging field. Among the engineers there appears to be a concensus regarding the need for applying the experimental approach to understanding gas flow and mass transfer in the proximal airways, and there was general agreement that simplified models probably can be applied successfully to estimating theoretically the parameters of gas flow and particle deposition in the deeper transitory airways.

Although not exhaustive by any means, the following represent some of the more significant questions and inadequacies in our understanding of gas and particle transport in the lungs:

1. An adequate anatomical model of the airways is still lacking. This is despite the fact that numerous persons have worked on this problem since Findeisen's work in 1935. The latest and most thorough study was done by Weibel [loc.cit.] but his work, although valuable and highly competent, is sadly lacking in that his model is based primarily on measurements made on only one human lung. Considering the known variability in size and kind of structure of the airways, it is presumptious indeed to place much confidence in a "one-lung" model. Ideally, one would want a statistical model including mean dimensions and estimates of variance for identifiable groups of the population, i.e., male, female, child, youth, adult, etc. The techniques applied by Weibel are available and all that is necessary is to support and encourage some competent group to expand on his original work.

2. Where are the deposition hot spots in the lung and how are they affected by particle size and respiratory parameters?

3. What is the flow resistance and shear stress on the walls of flexible tubes carrying oscillatory flows and under what conditions do they collapse?

4. Is there knowledge already or what studies can be done that will allow us to detect, prevent, remedy or cure emphysema?

5. What is the significance of particle-gas interactions in the respiratory tract?

6. Not mentioned in the conference, but implicit in much that was said, is the complete lack of a model to predict local sites of absorption of slightly soluble gases in the lungs. Such a model might go a long way toward explaining particle-gas synergism as observed by Amdur and others.

7. Also not mentioned is the subject of clearance of particles and partially soluble gases via the moving mucus lining, the so-called mucus escalator. The rheological properties of the mucus layer, changes induced by inhaled gases and soluble particles, and the resulting effects on clearance and on the local elastic characteristics are amenable to engineering research and their understanding may well help to clarify other significant questions.

Professor Friedlander outlined some of the problems which he feels that engineers and physiologists may be able to solve in the reasonably near future:

1. Determine the elastic characteristics of lung tissues and structures;
2. Understand the stability properties of oscillatory flow in tubes;
3. Observe the eddy structure (separation) of the flow at a simple branch;
4. Determine local patterns of particle deposition at a branch;
5. Estimate the rate at which a contaminant reaches the alveoli if the time history of its concentration downstream of the trachea is known;
6. Develop microinstrumentation for *in vivo* measurements.

On the whole, I found the conference to be very stimulating and I am convinced that it has served a valuable purpose. It must surely not have been the first time engineers with their unit operations approach have mutually confronted physiologists accustomed to a general systems viewpoint, still the dichotomy became most evident at times. Nevertheless, the exchange of views led to many lively conversations during coffee breaks and luncheons. Undoubtedly the three organizers of the conference, Dr. Norton Nelson, NYU; Dr. Jerry Mead, Harvard; and Dr. Sheldon Friedlander, Cal. Tech; have worked hard and accomplished much toward motivating needed research in this increasingly important area.

I have included some travel information regarding transportation and lodging in the area near the Cal Tech campus as Appendix B.

1/18/68

ARCHITECTURE OF THE LUNG.

Weibel's simplest model: Model A: regular dichotomy.

recalculated from his data, rounded after calculation.
*** Weibel's Data (Morphometry of Human Lung, Academic Press, 1963) X

		gener -ation ***	num -ber ***	diam mm ***	len -gth mm ***	cum length mm	area[1] cm^2	vol. ml	cum.[2] vol. ml	At flow 1000 ml / sec: speed cm/sec	time msec	cum. time msec	press. diff.[3] microns H_2O	cum. press. diff.[3] microns H_2O	Reyn -olds No.[4]	volume supplied ml	diam if spherical cm
	Trachea	0	1	18	120	120.0	2.6	31	31	393	30.5	31	87	87	4350	4800	20.9
	Main bronchus	1	2	12.2	47.6	167.6	2.3	11	42	427	11.1	41	82	169	3210	2400	16.6
	Lobar bronchus	2	4	8.3	19	186.6	2.2	4	46	462	4.11	45	76	246	2390	1200	13.2
		3	8	5.6	7.6	194.2	2.0	1	47	507	1.50	47	73	320	1720	600	10.5
	Segmental bronchus	4	16	4.5	12.7	206.9	2.6	3	51	392	3.23	50	147	467	1110	300	8.3
		5	32	3.5	10.7	217.6	3.1	3	54	325	3.29	53	170	638	690	150	6.6
	Bronchi with	6	64	2.8	9.0	226.6	4.0	4	57	254	3.55	57	174	812	434	75	5.2
	Cartilage in wall	7	128	2.3	7.6	234.2	5.3	4	61	188	4.04	61	162	974	277	37.5	4.1
		8	256	1.86	6.4	240.6	7.0	4	66	144	4.45	65	160	1134	164	18.8	3.3
		9	512	1.54	5.4	246.0	9.6	5	71	105	5.15	80	143	1277	99	9.4	2.6
		10	1.02K	1.3	4.6	250.6	14	6	77	73.6	6.25	77	120	1397	60	4.7	2.1
	Terminal bronchus	11	2.05K	1.09	3.9	254.5	19	7	85	52.3	7.45	85	103	1500	34	2.34	1.64
		12	4.10K	.95	3.3	257.8	29	10	94	34.4	9.58	94	75	1576	20	1.17	1.3
2ndy lobule	Bronchioles with	13	8.19K	.82	2.7	260.5	43	12	106	23.1	11.7	106	55	1632	11	.586	1.03
	muscle in wall	14	16.4 K	.74	2.3	262.8	72	16	122	14.1	16.2	122	35	1667	6.5	.292	.823
		15	32.8 K	.66	2.0	264.8	112	22	144	8.92	22.4	144	24	1692	3.6	.146	.654
primary lobule or acinus	Terminal bronchiole	16	65.5 K	.60	1.65	266.5	185	36	175*	5.40	30.6	175	14	1707	2.0	.0732	.519
	resp. bronchiole	17	131 K	.54	1.41	267.9	300	42	217	3.33	42.3	217	10	1716	1.1	.0366	.412
	resp. bronchiole	18	262 K	.50	1.17	269.0	514	60	278	1.94	60.2	277	5	1722	.57	.0183	.327
	resp. bronchiole	19	524 K	.47	.99	270.0	909	90	367	1.10	90.0	368	3	1725	.31	.0092	.259
	alveolar duct	20	1.05M	.45	.83	270.9	1.7K	138	506	0.60	138	506	1.4	1726	.17	.0046	.205
	alveolar duct	21	2.10M	.43	.70	271.6	3.0K	213	719	0.32	213	719	.74	1727	.08	.0022	.163
	alveolar duct	22	4.19M	.41	.59	272.1	5.5K	326	1045	0.18	326	1047	.37	1727	.04	.0011	.129
	alveolar sac	23	8.39M	.41	.50	272.6	11K	553	1599	0.09	553	1602	.16	1728	-	.0006	.102
	alveoli, 21 per duct		300 M	.28	.23	272.9		3200	4800								
									175*)								

(* Dead Space - 40 ml for mouth.

(1) Area = Total Area (2) cum. = cumulative. (3) pressure difference from mouth if flow were laminar

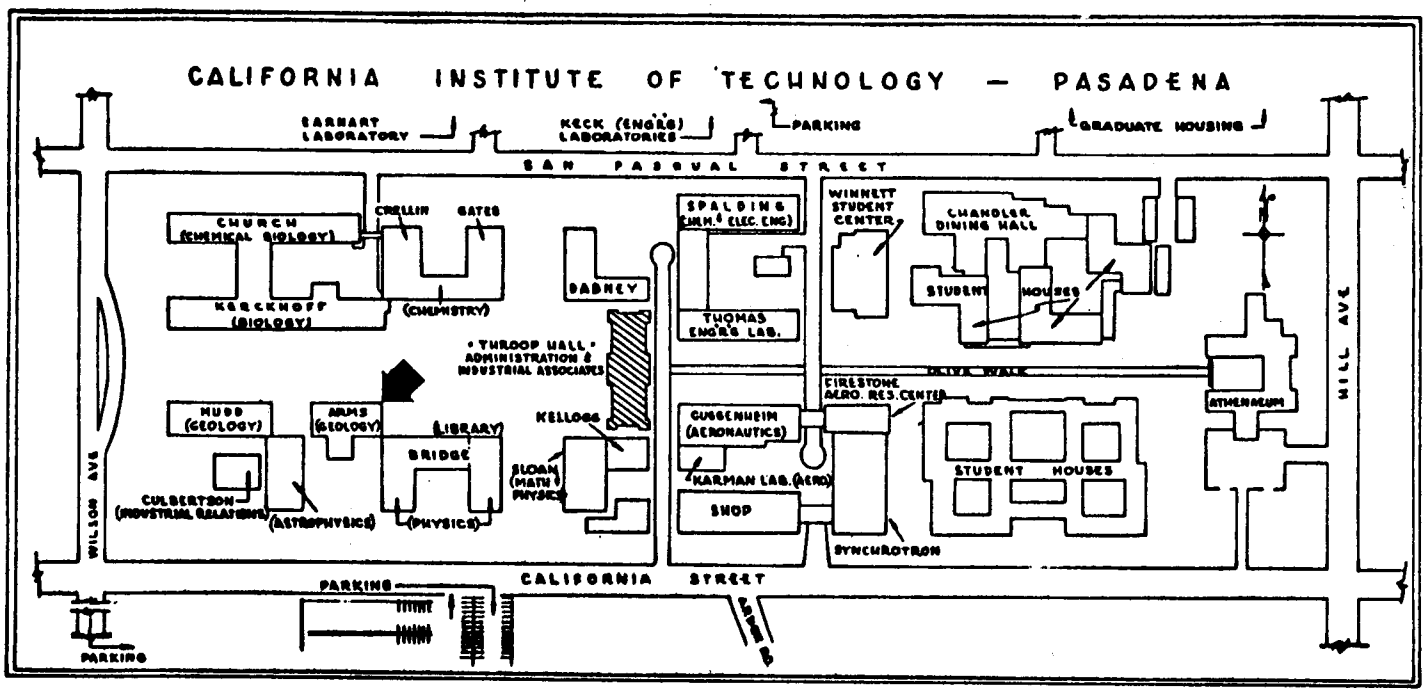
(4) Added by B. Altshuler $K = 10^3$ $M = 10^6$

X Dr. Briscoe's reference is in error. The publisher is Springer-Verlag, Berlin.

APPENDIX B

TRAVEL INFORMATION: California Institute of Technology, Pasadena.

Airport limousines (buses) leave the Los Angeles International Airport at approximately one hour intervals for Pasadena. Riders are deposited at the Huntington-Sheraton Hotel which is a very nice hotel but not within convenient walking distance of the Cal Tech campus. Probably the closest place to stay off campus is the Imperial 400 Motel which is clean, reasonable in price, entirely adequate and within about 5 blocks of the campus. This motel is located on East Colorado Blvd. which parallels San Pasqual Street about 5 blocks along Michigan (arrow pointing to Earhart Laboratory). It is necessary to take a taxi back to the Huntington-Sheraton to catch the return bus which leaves there for the airport at 20 minutes after the hour. The bus trip requires approximately 30 minutes depending on traffic. Food at the Athenaeum (faculty club) was very good, imaginative and well prepared.



APPENDIX C

PULSATILE FLOW IN A CYLINDRICAL CONDUIT

S. Uchida [Zeits. angew. Math. Physik. VII, p. 403-422 (1956)] has shown that in the case of fully developed, viscous oscillatory flow, the periodical nature of the velocity distribution is characterized by the parameter

$$F' = R\left(\frac{\omega}{\nu}\right)^{\frac{1}{2}} = \left(\frac{\omega d^2}{4\nu}\right)^{\frac{1}{2}}.$$

The velocity profile can be obtained from the asymptotic expansions of the Bessel function, the particular form depending upon whether F' is very small or very large.

If the kinematic viscosity of air in the lung is assumed to be 0.15 stokes (room temperature value) the Saffman frequency parameter F = 27, corresponding approximately to the value 30 mentioned in his talk. However, assuming $\nu = 0.17$ (air at 37° C) the frequency parameter of Uchida is F' = 2.5. Although F' is not very much greater than 1.0, it can be shown that the fully-developed root-mean-square velocity profile is more nearly that of slug flow than of parabolic flow [for F' = 5, see H. Schlichting, Boundary Layer Theory, (McGraw-Hill, New York, 1968), 6th edition, Chapter 15, p. 421, Figure 15.11]. Thus, Saffman's conclusion remains valid: the periodic nature of the flow should not be ignored in the trachea but can be neglected in the deeper airways.

The true picture is even much more complex than indicated here. Although there are other factors involved it will suffice to point out the fact that the narrow, compliant, opening of the glottis acts as a turbulence promoter, the trachea has more of a U-shape than a circular cross section, and, even if we could assume laminar flow, the full length of the trachea is within the entrance length, hence the requirement of fully-developed flow obviates the use of the Sexl-Uchida-Saffman treatment. It seems clear that the often voiced opinion in favor of an experimental approach is well founded.

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