COMPARISON OF A CONVECTIVE MIXING MODEL'S PREDICTIONS TO EMPIRICAL RESULTS FOR AEROSOL DISPERSION IN THE HUMAN LUNG

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INTRODUCTION

Recent modelling work has attempted to use axial diffusion to explain the observed dispersion of an aerosol bolus in transit through the lung (Edwards, 1994). This type of modelling attempts to derive from first principles the underlying mechanism of aerosol dispersion. An alternative approach has used mixing theory derived from reactor vessels to surmount problems encountered in small-scale mixing (McCawley *et al.*, 1988). Noting that Ultman (1985) had used an approach that is mathematically similar in applying network theory to this problem, it was decided to try to relate the number of vessels in series to the number of bifurcated generations in the lung.

METHODS

Aerosol dispersion data from humans were collected as previously described (Khandare, *et al.*, 1994). In brief, the apparatus consisted of an aerosol generation and detection system linked with a volume measurement system (Fig. 1). The subject was able to control both flow and volume for the breathing cycles. The subject used was an asymptomatic, white male, aged 45 who had never smoked. Data on aerosol concentration and breathing volume were collected and stored digitally at a rate of 60 Hz for the duration of the subject's test. A 0.5 µm corn oil aerosol was used. The input was normalised to a dirac delta function by a deconvolution of the input and output pulses.

THEORY

For the purposes of this theory the lung is conceived as a series of mixing tanks, in each of which complete mixing occurs. Based on the empirical data of Scherer *et al.* (1975) for a five generation glass lung, the best fit occurs when the ith generation of the lung corresponds to 2^i identical tanks. Because significant mixing is assumed to occur at the bifurcation, the generations/mixing tanks were divided so as to contain the bifurcation at the center of the mixing tank. Thus the zeroth generation begins halfway down the trachea. Other assumptions are that the transit time, t_i,
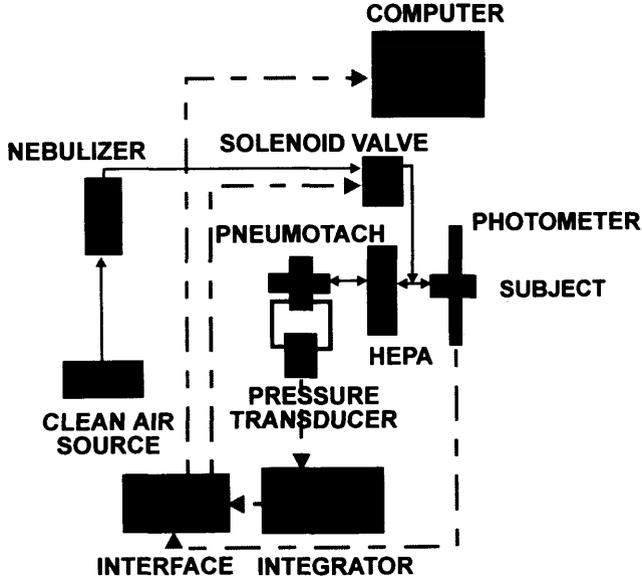
Fig. 1. Aerosol dispersion apparatus used for collecting experimental data cited in this paper.

through any generation is independent of the previous generation's; during unidirectional flow (either inspiration or expiration) any given particle makes only one entrance from the previous generation and one exit to the next generation.

Complete mixing, assumed for each mixing tank, means that all particles have the same probability of leaving the tank as stated above. The corresponding density function for t_i is

$$f(t) = (1/\bar{t_i}) \exp(-t/\bar{t_i})$$ (1)

where $\bar{t_i}$ is the expected residence time.

One can then define equations for the first and second moments of the output probability function of a single completely mixed tank (having an exponential output), the first moment being $\bar{t}$, the expected mean residence time, and the second moment defined as the variance,

$$\sigma_v^2 = \bar{t}^2.$$ (2)

An important property of the variance is that for unidirectional flow, statistically independent tanks in series have additive variances. Statistically independent means that the history of a particle (the residence time in previous tanks) has no bearing on the residence time in the current tank. This then reduces mixing in the lung to a series of statistically independent tanks. For a given volume of penetration v_p, the lung is divided into M statistically independent mixing tanks. The total variance for a complete breathing cycle, viewed as unidirectional flow through this symmetrical lung, can then be expressed as

$$\sigma_v^2 = \sum_{i=0}^{2M-1} (\bar{t_i})^2.$$ (3)

In this form it can be seen that the model has no dependence on flow rate when the output is given in terms of volume exhaled. Because it is more common to express the output in terms of time (Wen and Fan, 1974) and since the residence time in any generation is equal to the total volume of tanks in that generation, v_i^T, divided by the total flow rate, Q, equation (3) can be re-written as,

$$\sigma_v^2 = \sum_{i=0}^{2M-1} (v_i^T/Q)^2. \tag{4}$$

However, many of the published models use empirical data that express the dispersion in terms of the half-width (σ_H), which is a shortened form of the term "full width at half maximum" and is defined as the width of the expired aerosol pulse at half the maximum concentration, written as a function of expired volume. Therefore, it may be convenient to have an expression for converting the variance to the half-width. Multiplying the square root of the variance by $2Q$ gives an approximation of σ_H (designated σ_{H^*}). For a normal distribution a closer approximation can be calculated for

$$\sigma_H = (2\ln2)^{1/2} (2Q\sigma) \text{ or}$$

$$\sigma_H = \sqrt{2\ln2} \cdot 2 \sqrt{2} \left[\sum_{i=0}^{M-1} (v_i^T)^2 \right]^{1/2} \tag{5}$$

where the volume of penetration is

$$\sum_{i=0}^{M-1} v_i^T.$$

The conversation factor relating variance to half width is dependent on the shape of the exhaled aerosol distribution and could vary from as low a value as 0.87 to approaching $(2\ln2)^{1/2}$, that is, 1.18.

One criticism of the approach used in the statistical model above is the need for a symmetrical lung with a first-in, first-out arrangement for flow. Alternatively it is possible to again model the ith generation of the lung as 2^i identical complete mixing tanks. For each volume of penetration, v_p, all volumes are fixed, corresponding, of course, to the lung volume for that generation as specified by Weibel's Model A for regular dichotomy (Weibel, 1963). The exception to that is the last generation which expands and contracts to accommodate the changing air volume of the breathing cycle. Thus it is possible to achieve a first-in, last-out (FILO) arrangement for the aerosol flow. Because the flow is not unidirectional, equation (3) is no longer true and it is easiest to numerically solve the system of equations to find the concentration in tank T_i, over some time span, dt such that the output for the FILO Model is

$$\frac{dq_i}{dt} = \frac{r_i q_{i-1}}{v_i} - \frac{(s_i + 2r_{i+1}) q_i}{v_i} + \frac{2s_{i+1} q_{i+1}}{v_i} , (i = 0, \ldots, 23) \tag{6}$$

where the flow rate during inspiration into the trachea is a constant Q. The flow rate during inspiration into each of the tanks making up the ith generation is r_i, $2r_{i+1} = r_i$ and $s_i = 0$. During expiration the flow rate out of each of the tanks is s_i when $s_0 = Q$, $2s_{i+1} = s_i$ and $r_i = 0$. If this equation (6) is rearranged to give the
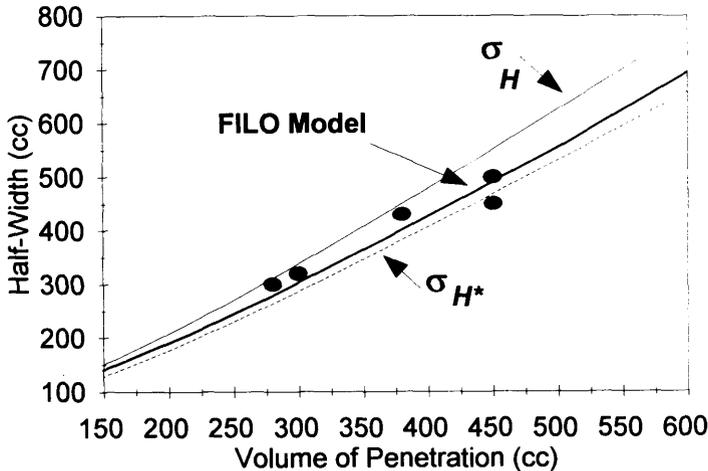
Fig. 2. Comparison of model and experimental results for a flow rate of 500 ccs^{-1}, tidal volume of 1000 cc and a bolus volume of 100 cc, for a single, typical, asymptomatic, male subject, age—44 years, height—175 cm. The values for σ_{H^*} are calculated as specified in the text, multiplying equation (4) by $2Q$; the values for σ_H are from equation (5); and the values for the FILO Model are derived from equation (6).

change in concentration with a change in volume than the FILO Model becomes independent of flow rate as was the case with the statistical model [equation (3)].

RESULTS

The output of the different approaches to half-width calculation are shown in Fig. 2. These were then compared to the data of an individual analyzed as previously noted. At penetration volumes above 400 cc, deposition loss was measureable, though less than 10%. No measurements were made above this volume since deposition losses are not accounted for by this current theory.

DISCUSSION

There is not a substantial difference in the values calculated by the different approaches taken in Fig. 2 deriving a relationship between aerosol dispersion measured by the half-width of the expired pulse and volume of penetration of the inhaled pulse. In fact, the normal distribution approximation is similar to the approach taken by Scherer *et al.* (1975) in analyzing their five generation glass model. By using only the top 10% of the output concentration they approximated a normal distribution from what was obviously a gamma distribution similar to that found in human aerosol dispersion data (McCawley *et al.*, 1988). Like Scherer we also concluded that there should be no dependence of dispersion on flow rate based on either of our model approaches. This condition is pointed to by Edwards (1994) as being a necessary model feature for agreement with data from a number of published studies.

The statistical approach taken in the first model presented in the paper used a

first-in, first out sequence which is also similar to Edwards (1994). However, it has long been known (Altshuler *et al.*, 1959) that the filling and emptying sequence for aerosols cycled through the lungs is first-in, last-out. The FILO model approach also allows the model to be adjusted on a specific generation level to try to mimic changes that might occur in disease by changing the volume of any bifurcation (tank) or the flow rate through that bifurcation (tank).

One interpretation of the comparability of empirical and model results might be that the uniform residence times derived from using the regular dichotomy of Model A represent the uniformity of ventilation long recognised to occur in healthy lungs. The time constants would then be the product of the resistance and compliance of the various pathways. Therefore, the statistically significant differences between healthy subject and those with presumed mild obstruction first noted by McCawley and Lippmann (1984) and later confirmed by other authors (Blanchard, 1996) may be due to changes in the ventilation patterns due to obstruction.

CONCLUSIONS

Two separate models were derived based on Weibel's regular dichotomy for the lung. Both models were able to predict experimental results for the change in half-width with a change in penetration of an aerosol bolus. The two models also show dispersion to be independent of flow rate, in agreement with published data. One of the models uses a first-in, last-out approach and both models can be altered to mimic potential changes in the lung during obstruction. There is also no requirement to derive the flow profile in the airways since the assumed complete mixing adequately describes the empirical data.

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