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A statistical description of aerosol deposition in nose and mouth for inspiration and expiration has been presented based upon a comprehensive analysis of pertinent experimental data reported in the literature. Due to inherent intersubject and intrasubject variabilities, randomness exists in the deposition data. This randomness has been accounted for in developing predictive relationships for deposition.

## Statistical analysis of aerosol deposition in nose and mouth

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### introduction

Inhaled particles will deposit along the air passages between the point of entry at lips or nares and larynx. The amount of particles entering the lung thus depends upon the route of entry in the head. Normally, the nasal route collects more particles than the oral because it has nasal hairs and more complex air passages.

Information on nasal deposition has been obtained mostly from experimental work. The usual technique for measuring inspiratory deposition is to draw the aerosol through the nose and out of the mouth while the subject holds his breath.<sup>(1-6)</sup> The aerosol concentration is measured before it enters the nose and after it leaves the mouth. Neglecting mouth deposition during expiration, inspiratory nasal deposition can be calculated from the concentration difference.

Experimental data show that inspiratory nasal efficiency is best described as a function of the parameter ( $\rho d^2 Q$ ) where  $\rho$  is the particle mass density,  $d$  the particle diameter and  $Q$  the air flow rate. Since this parameter is equivalent to the particle Stokes number, deposition is largely contributed by particle inertia.

Using the data of Landahl and Black,<sup>(1)</sup> Landahl and Tracewell<sup>(2)</sup> and Pattle,<sup>(3)</sup> an empirical relationship was adopted by the Task Group on Lung Dynamics<sup>(7)</sup> to calculate the inspiratory nasal deposition. This relationship is

$$\eta_{NI} = -1.200 + 0.475 \log \frac{\rho d^2 Q}{(g \mu m^2 \text{ sec}^{-1})} \quad (1)$$

Later data obtained by Lippmann<sup>(6)</sup> using radioactive aerosols also support this relationship. However, relatively scattered and lower nasal depositions were reported by Hounam *et al.*<sup>(4,5)</sup> using the similar inspiration technique. Hounam's results further show that inspiratory nasal efficiency fits better using a new parameter ( $\rho d^2 \Delta P$ ), where  $\Delta P$  is the pressure difference across the nose and mouth. Hounam's relationship is

$$\eta_{NI} = 4.331 + 0.660 \log \frac{\rho d^2 \Delta P}{(kg \text{ m}^{-1} \text{ Pa})} \quad (2)$$

Inhalation through nose and out of mouth with breath-holding cannot be regarded as normal breathing. A different breathing method to measure nasal deposition was employed

by Giacomelli-Maltoni *et al.*<sup>(8,9)</sup> and improved by Heyder and Rudolf.<sup>(10,11)</sup> In this method, the lung (tracheobronchial tree and pulmonary region) is also considered a part of the experimental system. The deposition of particles in the nose is calculated from total deposition of particles in the entire respiratory tract for mouth, nose, mouth-nose and nose-mouth breathing. Because mouth deposition is not significant under the experimental condition, this method allows the determination of nasal deposition for both inspiration and expiration. The experimental correlations of Heyder and Rudolf are as follows:

$$\eta_{NI} = -1.15 + 0.47 \log \frac{\rho d^2 Q}{(g \mu m^2 \text{ sec}^{-1})} \quad (3)$$

for inspiration, and

$$\eta_{NE} = -1.01 + 0.43 \log \frac{\rho d^2 Q}{(g \mu m^2 \text{ sec}^{-1})} \quad (4)$$

for expiration.

Fry<sup>(12)</sup> measured nasal deposition of 4.06  $\mu\text{m}$  particles using the methods and apparatus developed by Hounam *et al.* The particle carries on the average 62 unit charges as produced and 11 unit charges as the particle passing through a bipolar ion field for charge reduction. It was found that the difference between average particle charge has no effect on nasal deposition.

There are very limited amounts of data available for mouth deposition. Deposition in the mouth for expiration is normally assumed to be negligible under the experimental condition. For inspiration, deposition of particles in the mouth was measured by Lippmann,<sup>(13)</sup> Foord *et al.*,<sup>(14)</sup> Stahlhofen *et al.*<sup>(15)</sup> and Chan and Lippmann<sup>(16)</sup> using radioactive aerosols. In these experiments, the subject breathes through a large bore tube in the mouth. The amount of deposition is obtained from the difference of activity measurements, one immediately after the exposure and the other after the deposited particles are removed with mouthwash or by other means. Using their own data, Foord *et al.* obtained a relationship for inspiratory mouth deposition in the form

$$\eta_{MI} = -0.651 + 0.2 \log \frac{\rho d^2 Q}{(g \mu m^2 \text{ sec}^{-1})} \quad (5)$$

However, a different relationship was derived by Chan and Lippmann based upon the data of Lippmann, Stahlhofen *et al.* and Chan and Lippmann. It gives

$$\eta_{MI} = 4.14 \times 10^{-2} + 1.02 \times 10^{-5} \frac{\rho d^2 Q}{(g \mu m^2 sec^{-1})} \quad (6)$$

For  $\rho d^2 Q > 1.3 \times 10^4 g \mu m^2 sec^{-1}$ , equation (6) has a higher deposition than that given by equation (5).

Deposition experiment in the mouth by natural mouth breathing without using a mouth-piece was conducted by Dennis.<sup>(17)</sup> His data was calculated by the Task Group on Lung Dynamics as a linear function of  $\log \rho d^2 Q$ . Comparison of this result with equation (6) shows that natural breathing has a much greater mouth deposition than breathing through a tube. However, as pointed out by the Task Group, mouth deposition by natural breathing is quite sensitive to the degree to which the mouth is opened, it is

inadvisable to apply Dennis' result to mouth deposition in general.

Equations (1)(3)-(6) imply that deposition in the nose and mouth is mainly caused by impaction, since  $\rho d^2 Q$  corresponds to the particle Stokes number which is a measure of particle inertia. For small particles at low flowrate, dependence on other parameters is possible. But this has not been studied experimentally.

Theoretical deposition studies in the nose and mouth are scarce because our present knowledge on the anatomical structure and flow field is limited. There have been only two studies on nasal deposition for inspiration. Landahl<sup>(18)</sup> used a four-region model to calculate deposition by considering inertial and settling effect of particles. His results show less deposition than the experimental data. Scott *et al.*<sup>(19)</sup> adopted a more accurate nose model consisting of five regions: (I) the region filled with nasal hair, (II) the nasal valve, (III) the expansion region, (IV) the turbinate region,

**TABLE I**  
**Source of Deposition Data in Nose and Mouth**

Source	Aerosol	Particle Diameter ( $\mu m$ )	Flowrate Q (Lpm)	Number of Subjects	Type of Breathing
<b>Inspiratory Nasal Deposition</b>					
Landahl & Black (1947)	polydisperse clouds (sampled by Cascade Impactor)				
Landahl & Tracewell (1949)	methylene blue, bismuth subcarbonate, tyrosine, corn oil, Na <sub>2</sub> SO <sub>4</sub> , NaHCO <sub>3</sub> , Ca <sub>3</sub> (PO <sub>4</sub> ) <sub>2</sub>	aerodynamic dia. (0.5 - 23)	constant Q (17.4 - 17.8)	5	nose-in mouth-out with breath holding
Pattle (1961)	monodisperse methylene blue	geometric dia. (1.0 - 9.0)	constant Q (10, 20, 30)	1	
Hounam <i>et al.</i> (1969, 1971)	monodisperse radioactive polystyrene	aerodynamic (1.78 - 7.96)	constant Q (5 - 37)	3	
Lippmann (1970)	monodisperse Fe <sub>2</sub> O <sub>3</sub> (sizable charged)	geometric dia. (0.8 - 2.4)	average Q (20 - 30)	2	
Giacomelli-Maltoni (1972)	monodisperse Carnuba wax	aerodynamic dia. (0.25 - 1.8)	average Q (~ 24)	15	nose-in mouth-out vs mouth-in mouth-out
Martens & Jacobi (1974)	monidisperse polystyrene latex	geometric dia. (0.3 - 1.9)	average Q (~ 30)	1	
Hyder & Rudolf (1974, 1977)	monodisperse di-2-ethyl-hexyl sebacate	geometric dia. (0.5 - 3.5)	constant Q (5 - 37)	4	
<b>Expiratory Nasal Deposition</b>					
Hyder & Rudolf (1974, 1977)	monodisperse di-2-ethyl-hexyl sebacate	geometric dia. (0.5 - 3.5)	constant Q (5 - 37)	4	mouth-in nose-out vs mouth-in mouth-out
<b>Inspiratory Mouth Deposition</b>					
Lippmann (1977)	monodisperse radioactive Fe <sub>2</sub> O <sub>3</sub>	aerodynamic dia. (2 - 10)	average Q (22 - 39)	22	mouth breathing through a tube
Foord <i>et al.</i> (1978)	monodisperse polystyrene labelled with 99m <sub>TC</sub>	aerodynamic dia. (2.5 - 7.5)	average Q (15 - 60)	19	
Chan & Lippmann (1980)	monodisperse radioactive Fe <sub>2</sub> O <sub>3</sub>	aerodynamic dia. (0.2 - 7)	average Q (~ 28)	26	
Stahlhofen <i>et al.</i> (1980)	monodisperse radioactive Fe <sub>2</sub> O <sub>3</sub>	aerodynamic dia. (1 - 10)	constant Q (45)	3	

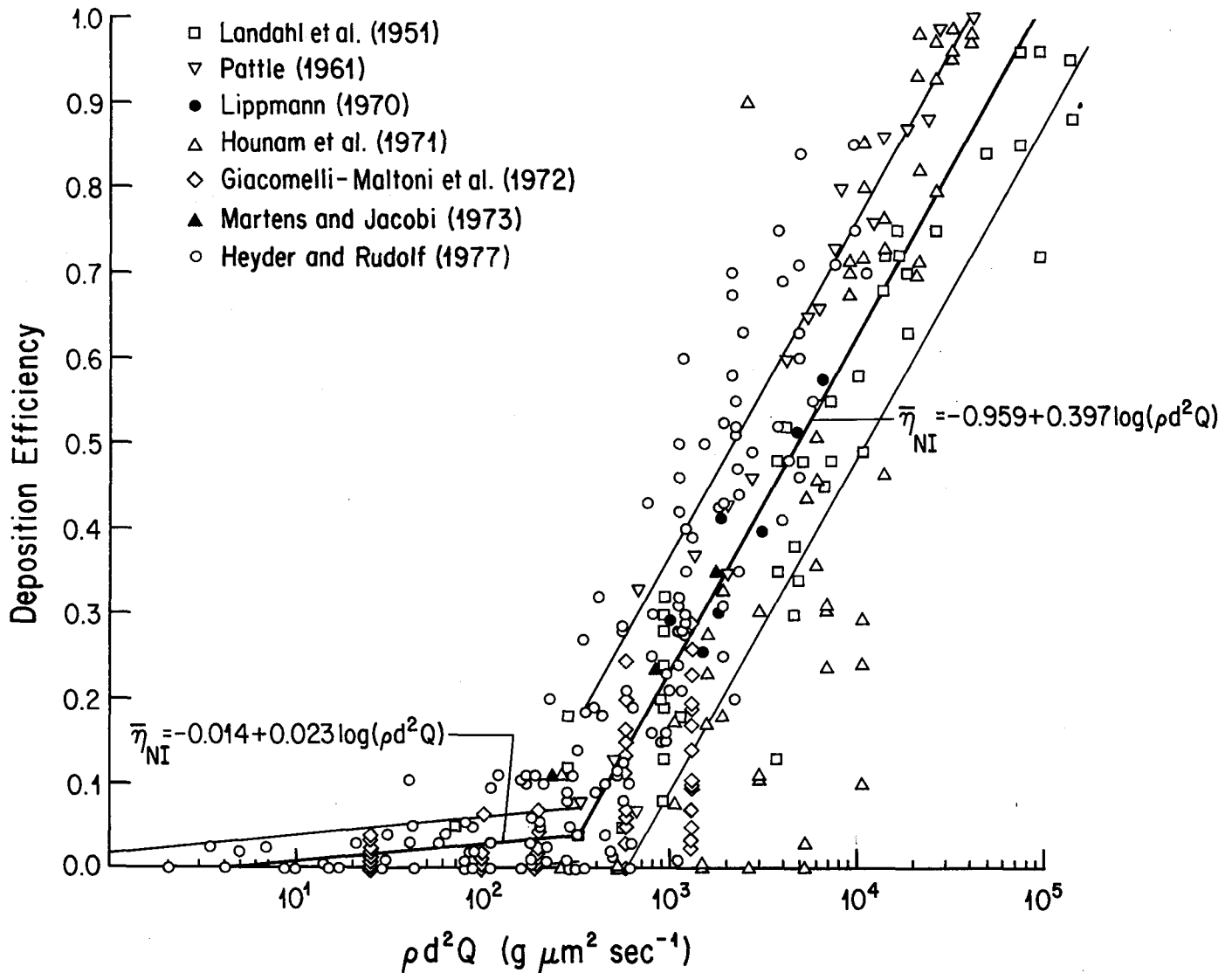


Figure 1 — Deposition of particles in the head for nasal inspiration as a function of  $\rho d^2 Q$ . The equations of  $\bar{\eta}_{NI}$  and their  $\sigma_{NI}$  are given by solid lines.

and (V) the posterior bend. Additional to direct impaction, they considered deposition due to secondary flows in the expansion region. This secondary flow is thought to be generated by the air jet from the nasal valve. Calculated depositions using this model show reasonably good agreement with data for both total and regional deposition in the nose.

Deposition data in the nose and mouth by various workers that we previously reported always exhibit a very large amount of scatter. In addition to uncertainties in measurement technique, one major source of this scatter comes from intersubject and intrasubject variabilities. The intersubject variability may arise from the difference in anatomical structure and dimensions, number of nasal hair, breathing pattern, etc. while the intrasubject may be caused partly by the nasal cycle in which flow may be distributed equally side to side or as much as 80% -20%.

The empirical relationships (1) to (6) and the theoretical results by Landahl and Scott *et al.* do not provide the statistical characteristics of deposition. This information is

important in the consideration of establishing exposure standards. Furthermore, deposition variabilities in the tracheobronchial and alveolar regions of the lung are known to exist.<sup>(13)</sup> Because inhaled aerosols reach these regions after they pass through the nose or mouth, it is possible that deposition variations in the tracheobronchial and alveolar region are caused by those which occur in the nose or mouth.

In this paper, a statistical analysis is performed on the deposition data in order to derive more consistent formulas for predicting nasal and mouth deposition at inspiration and expiration. Their associated statistical properties are also presented.

#### data collection and analysis

The experimental work that we have reviewed above provides accurate and reliable deposition data for nose and mouth to date. These data are used as the basis of our analysis. Table I lists the sources of all experimental data that we used in our analysis together with other pertinent

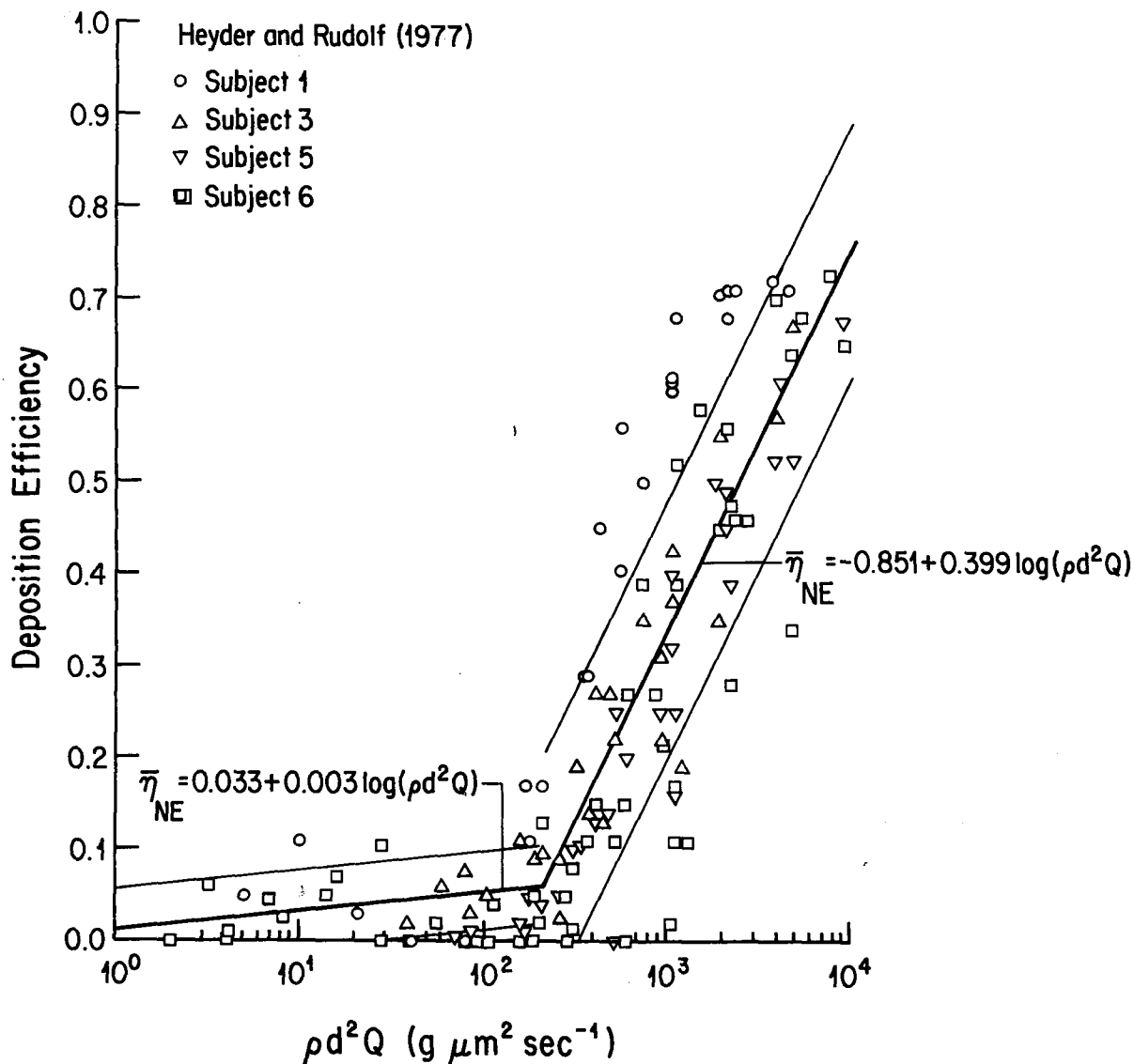


Figure 2 — Deposition of particles in the head for nasal expiration as a function of  $\rho d^2 Q$ . The equations of  $\bar{\eta}_{NE}$  and their  $\sigma_{NE}$  are given by solid lines.

information concerning the experiments. These data are presented in Figures 1 to 3 for the cases of inspiratory nasal deposition, expiratory nasal deposition and inspiratory mouth deposition respectively. All data points with negative efficiency in the nasal deposition experiment of Heyder and Rudolf have been replaced by zero deposition.

An observation of Figures 1 and 2 shows that the data points can fit well into two linear relationships in terms of  $\log \rho d^2 Q$ , one for small  $\rho d^2 Q$  and the other for large  $\rho d^2 Q$ , with a smaller slope for small  $\rho d^2 Q$ . This is expected on physical grounds that small  $\rho d^2 Q$  in the experiment corresponds to submicron particles, for which diffusional effect becomes increasingly important, resulting in a weaker dependence on particle inertia. The breakpoint of these two relationships is found in the following manner. We first chose a breakpoint for the deposition data at  $\rho d^2 Q = 250 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$ . Two linear regressions were derived separately from the data for  $\rho d^2 Q < 250 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$  and  $\rho d^2 Q > 250 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$ . The two linear regressions meet at a new break-

point which was used as the breakpoint of our formulae. The linear relationships for nasal deposition we obtained are as follows:

Inspiratory nasal mean efficiency

$$\bar{\eta}_{NI} = -0.014 + 0.023 \log \frac{\rho d^2 Q}{(\text{g } \mu\text{m}^2 \text{sec}^{-1})} \quad (7a)$$

for  $\rho d^2 Q < 337 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$

and

$$\bar{\eta}_{NI} = -0.959 + 0.397 \log \frac{\rho d^2 Q}{(\text{g } \mu\text{m}^2 \text{sec}^{-1})} \quad (7b)$$

for  $\rho d^2 Q > 337 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$

Expiratory nasal mean efficiency

$$\bar{\eta}_{NE} = 0.033 + 0.003 \log \frac{\rho d^2 Q}{(\text{g } \mu\text{m}^2 \text{sec}^{-1})} \quad (8a)$$

for  $\rho d^2 Q < 215 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$

and

$$\bar{\eta}_{NE} = -0.851 + 0.399 \log \frac{\rho d^2 Q}{(\text{g } \mu\text{m}^2 \text{sec}^{-1})} \quad (8b)$$

for  $\rho d^2 Q > 215 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$

For mouth deposition, Figure 3 shows that all data points for  $\rho d^2 Q < 1000 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$  are nearly zero. We, therefore, neglected these points in the calculation. For  $\rho d^2 Q > 1000 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$ , a single relationship was derived from the data. The result is

$$\bar{\eta}_{MI} = -1.117 + 0.324 \log \frac{\rho d^2 Q}{(\text{g } \mu\text{m}^2 \text{sec}^{-1})} \quad (9a)$$

for  $\rho d^2 Q > 3000 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$

and

$$\bar{\eta}_{MI} = 0 \quad (9b)$$

for  $\rho d^2 Q < 3000 \text{ g } \mu\text{m}^2 \text{sec}^{-1}$

Equations (7)-(9) are plotted in Figures 1 to 3 for the use of predicting mean depositions. To account for intersubject and intrasubject variabilities, we may write, for a given  $\rho d^2 Q$ ,

$$\eta_i = E(\eta_i) + \epsilon_i = \bar{\eta}_i + \epsilon_i \quad (10)$$

where  $\eta_i$  is the deposition efficiency for occurrence  $i$ ,  $E(\eta_i)$  is the expected value of  $\eta_i$ , and  $\epsilon_i$  is a random variable such that

$$E(\epsilon_i) = 0 \quad (11)$$

An observation of the data in Figures 1 to 3 shows that  $\epsilon_i$  does not vary significantly with  $\rho d^2 Q$ . The variance of  $\epsilon_i$  is therefore assumed to be constant for each case. Thus,

$$\text{Var}(\epsilon_i) = E(\epsilon_i^2) = \sigma^2 \quad (12)$$

where  $\sigma$  is the standard deviation. Based on the data points, the values of  $\sigma$  are obtained for nose and mouth deposition in various ranges of  $\rho d^2 Q$ . The results are tabulated in Table II.

It is natural to assume that the distribution of  $\epsilon_i$  in equation (9) is normal due to the fact that many random sources exist in problems of this type. To check the validity of this assumption, Chi-square tests were performed based upon the data points for inspiratory nasal, expiratory nasal and inspiratory mouth depositions. In all cases the assumed distributions are accepted at 5% significance level. The validity of the normal distribution for each  $\epsilon_i$  was also verified

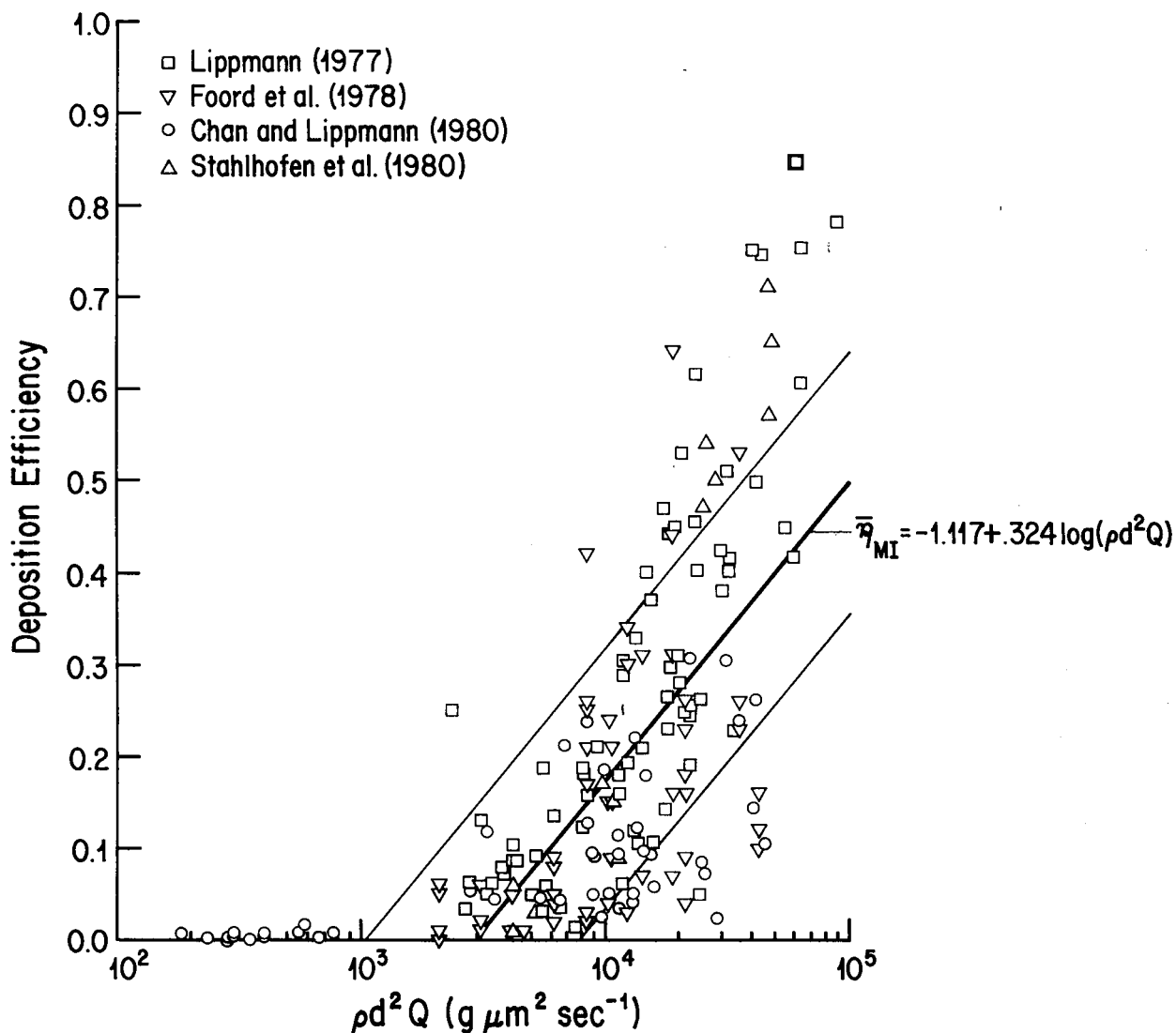


Figure 3 — Deposition of particles in the head for mouth inspiration as a function of  $\rho d^2 Q$ . The equation of  $\bar{\eta}_{MI}$  and its  $\sigma_{MI}$  is given by solid lines.

**TABLE II**  
Values of  $\sigma_{NI}$ ,  $\sigma_{NE}$  and  $\sigma_{MI}$

	$\rho d^2 Q < 337 \text{ g } \mu\text{m}^2\text{sec}^{-1}$	$\rho d^2 Q > 337 \text{ g } \mu\text{m}^2\text{sec}^{-1}$
Inspiratory nasal efficiency		
$\sigma_{NI}$	0.034	0.145
Expiratory nasal efficiency		
$\sigma_{NE}$	0.046	0.140
Inspiratory mouth efficiency		
$\sigma_{MI}$	0	0.144

using normal probability papers, and these are presented in Figures 4 to 6. It is seen that cumulative relative frequencies provided by the data closely follow straight lines in all cases.

### combined nose and mouth breathing

Normal breathing is usually accomplished by a combination of nose and mouth breathing, though the exact proportion of air breathed through the nose and the mouth is not well established. Some measurements have recently been made by Camner and Bakke.<sup>(20)</sup> Let the fraction of air breathed through the nose be  $\alpha_I$  for inspiration and  $\alpha_E$  for expiration. Then particle deposition in the head may be written in the form.

$$\eta_{HI} = \alpha_I \eta_{NI} + (1-\alpha_I) \eta_{MI} \quad (13)$$

for inspiration, and

$$\eta_{HE} = \alpha_E \eta_{NE} \quad (14)$$

for expiration.

Assuming  $\alpha_I$  and  $\alpha_E$  are deterministic, the mean and variance of the combined breathing are given by

$$\bar{\eta}_{HI} = \alpha_I \bar{\eta}_{NI} + (1-\alpha_I) \bar{\eta}_{MI} \quad (15)$$

$$\bar{\eta}_{HE} = \alpha_E \bar{\eta}_{NE} \quad (16)$$

$$\text{Var}(\eta_{HI}) = \alpha_I^2 \text{Var}(\eta_{NI}) + (1-\alpha_I)^2 \text{Var}(\eta_{MI}) = \alpha_I^2 \sigma_{NI}^2 + (1-\alpha_I)^2 \sigma_{MI}^2 \quad (17)$$

and

$$\text{Var}(\eta_{HE}) = \alpha_E^2 \text{Var}(\eta_{NE}) = \alpha_E^2 \sigma_{NE}^2 \quad (18)$$

If  $\alpha_I$  and  $\alpha_E$  are probabilistic, with their mean values equal to  $\bar{\alpha}_I$  and  $\bar{\alpha}_E$  and standard deviations to be  $\sigma_i$  and  $\sigma_e$  respectively, we may obtain

$$\bar{\eta}_{HI} = \bar{\alpha}_I \bar{\eta}_{NI} + (1-\bar{\alpha}_I) \bar{\eta}_{MI} \quad (19)$$

$$\bar{\eta}_{HE} = \bar{\alpha}_E \bar{\eta}_{NE} \quad (20)$$

$$\text{Var}(\eta_{HI}) = \sigma_i^2 [\sigma_{NI}^2 + \sigma_{MI}^2 + (\bar{\eta}_{NI} - \bar{\eta}_{MI})^2] + (1-\bar{\alpha}_I)^2 \sigma_{MI}^2 + \bar{\alpha}_I^2 \sigma_{NI}^2 \quad (21)$$

and

$$\text{Var}(\eta_{HE}) = \sigma_e^2 \sigma_{NE}^2 + \sigma_e^2 \bar{\eta}_{NE}^2 + \sigma_{NE}^2 \bar{\alpha}_E^2 \quad (22)$$

In the derivation of above equations, it is assumed that  $\eta_{NI}$ ,  $\eta_{MI}$ ,  $\alpha_I$  and  $\alpha_E$  are statistically independent.

### concluding remarks

A statistical description of aerosol deposition in nose and mouth has been presented based upon a comprehensive analysis of pertinent experimental data available. Due to inherent intersubject and intrasubject variabilities, randomness exists in the deposition relationships and the results presented here permit one to make probabilistic statements concerning aerosol deposition in various regions. Equations (7)-(9), which give the mean deposition information, together with standard deviations given in Table II and normal distribution results, completely characterize the statistical behavior of deposition efficiencies, and various probabilities of interest can be easily calculated.

By way of illustration, consider  $\eta_{NI}$ , inspiratory nasal efficiency, at  $\rho d^2 Q = 500 \text{ g } \mu\text{m}^2\text{sec}^{-1}$ . Equation (7b) and Table II show that it is a normally distributed random variable with mean  $\bar{\eta}_{NI} = 0.113$  and standard deviation  $\sigma_{NI} = 0.145$ . The probability of  $\eta_{NI}$  taking values in an arbitrary interval (a,b) is then given by (see, for example, Soong<sup>(21)</sup>)

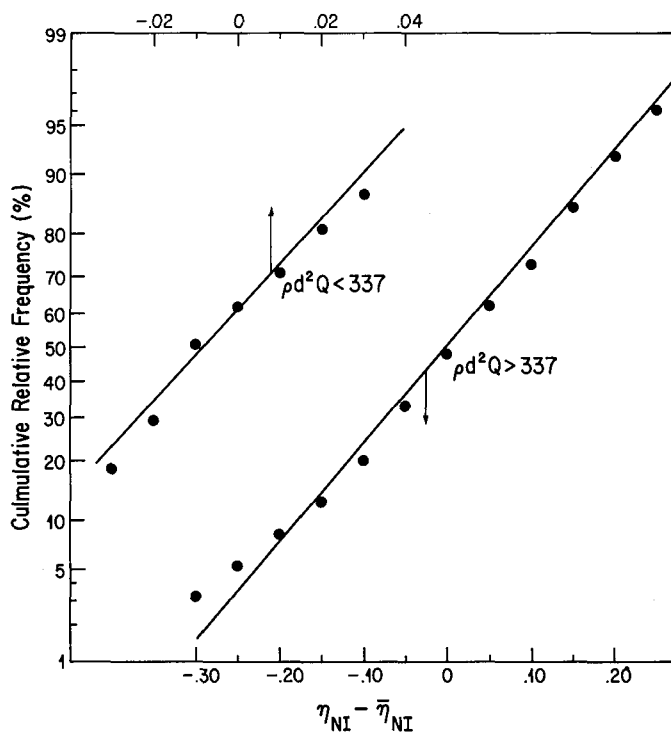


Figure 4 — Cumulative relative frequency diagram for  $(\eta_{NI} - \bar{\eta}_{NI})$ .

$$P(a \leq \eta_{NI} \leq b) = F_U\left(\frac{b - 0.113}{0.145}\right) - F_U\left(\frac{a - 0.113}{0.145}\right) \quad (23)$$

where  $F_U(u)$  is the probability distribution function of the standardized normal random variable, i.e., a normal random variable with zero mean and unit standard deviation, and is widely tabulated. Let  $a = 0.2$  and  $b = 0.4$ , for example. Table A.3 in Soong<sup>(21)</sup> gives

$$P(0.2 \leq \eta_{NI} \leq 0.4) = F_U(1.98) - F_U(0.60) = 0.976 - 0.726 = 0.25 \quad (24)$$

If  $a = 0.2$  and  $b = +\infty$ ,

$$P(\eta_{NI} \geq 0.2) = F_U(1) - F_U(0.60) = 1 - 0.726 = 0.274. \quad (25)$$

Similar calculations can be made for  $\eta_{NI}$  at other values of  $\rho d^2 Q$  and for efficiencies in other regions. It is noted that, as represented by Equations (13) and (14), the combined efficiencies  $\eta_{HI}$  and  $\eta_{HE}$  (with  $\alpha_I$  and  $\alpha_E$  being deterministic), being linear combinations of normal random variables, are also normal. Same types of calculations can also be performed with respect to these quantities.

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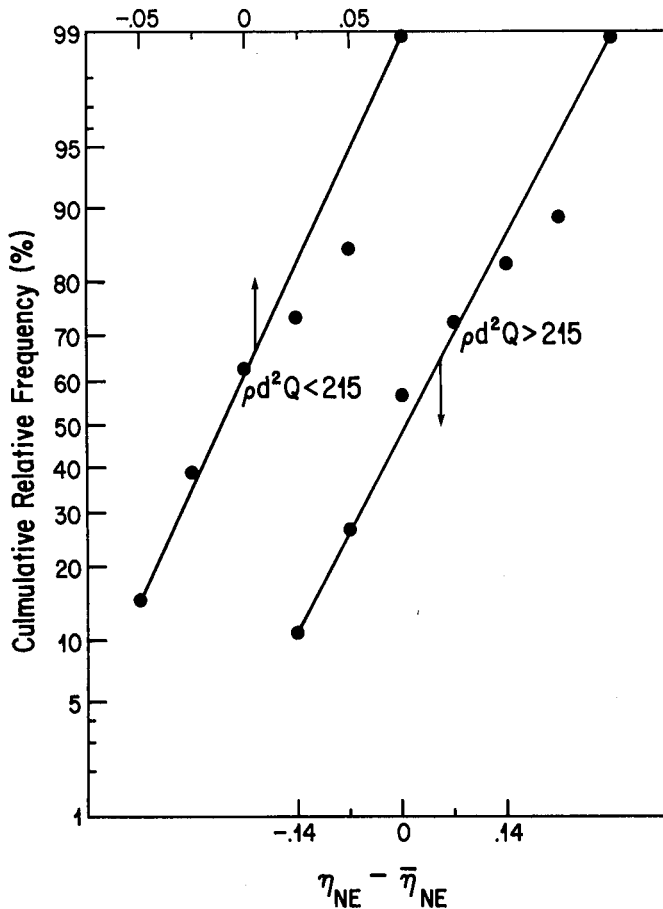


Figure 5 — Cumulative relative frequency diagram for  $(\eta_{NE} - \bar{\eta}_{NE})$ .

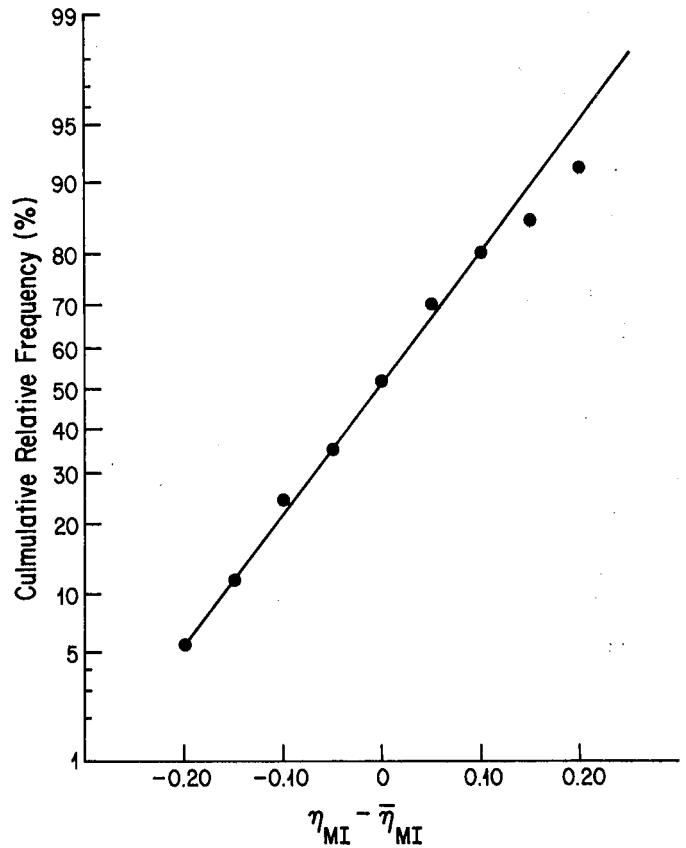


Figure 6 — Cumulative relative frequency diagram for  $(\eta_{MI} - \bar{\eta}_{MI})$ .

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NIOSH CURRENT INTELLIGENCE BULLETIN: #35

## Ethylene Oxide (EtO): Evidence of Carcinogenicity

May 22, 1981

The National Institute for Occupational Safety and Health (NIOSH) recommends that ethylene oxide be regarded in the workplace as a potential occupational carcinogen, and that appropriate controls be used to reduce worker exposure. These recommendations are based primarily on an industry-sponsored study demonstrating that ethylene oxide is carcinogenic in experimental animals. In this study, ethylene oxide was associated with increases in leukemia in female rats and peritoneal mesotheliomas (malignant tumors) in male rats. There has been widespread recognition of the mutagenic potential of ethylene oxide, and recent evidence demonstrates adverse reproductive effects in mammals, which also are of public health concern. In addition, limited epidemiologic investigations at two worksites provide evidence that excess risk of

cancer mortality may exist for the ethylene oxide workers studied. Some workers are on occasion exposed to relatively high concentrations of ethylene oxide, particularly where it is used for fumigation and sterilization. On the basis of this information, NIOSH requests that producers, distributors, and users of ethylene oxide, and of substances and materials containing ethylene oxide, give information to their workers and customers, and that professional and trade associations and unions inform their members.

CIB #35 is available from the U.S. Department of Health and Human Services, Public Health Service Centers for Disease Control, National Institute for Occupational Safety and Health, Robert A. Taft Laboratories, 4676 Columbia Parkway, Cincinnati, OH 45226.