Urine Excretion of Inhaled Technetium-99m-DTPA: An Alternative Method to Assess Lung Epithelial Transport

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Technetium-99m DTPA clearance (^{99m}Tc-DTPA) clearance measured by a gamma camera or a scintillation probe not only reflects epithelial transport, but is also influenced by an unknown amount of mucociliary clearance depending on particle size and aerosol deposition. This is confirmed by factor analysis of dynamic inhalation studies. Assessment of epithelial absorption by urinary excretion of inhaled ^{99m}Tc-DTPA is largely independent of aerosol lung deposition. Twenty-four-hour excretion reflects the amount of aerosol cleared by absorption, while two-hour excretion is a quantitative measure of the aerosol absorption rate from the epithelium into blood. Urinary ^{99m}Tc-DTPA excretion of two aerosols with different particle size correlated significantly ($p < 0.001$) with analysis of lung clearance curves. A very similar regression in the form of a cumulative exponential function was found with both aerosols. Two-hour urine values of nonsmokers differed significantly from those of smokers or patients with active interstitial or infectious lung disease. This alternative procedure is suited as a bedside test and holds promise for patient monitoring and follow-up.

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The alveolar and vascular spaces are separated by a tight barrier, the alveolar-capillary membrane, consisting of the alveolar epithelium, the capillary endothelium, and the interstitial space. However, the factor limiting the rate of solute diffusion is the epithelium rather than the endothelium, since the epithelium is ten times less permeable than the endothelium (*1,2*). Injury to this membrane may enhance movement of solutes across the respiratory epithelium or epithelial leakage (*3*). It is assumed that trans-epithelial transport of hydrophilic solutes takes place through intercellular junctions rather than through the cells.

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Increased pulmonary absorption rates were reported in association with a variety of lung diseases such as interstitial lung disorders (*4*), ARDS (*5*), or AIDS-related opportunistic pulmonary infections (*6*). Smoking (*7*) or physiologic factors such as inspiratory lung volume (*8*), posture (*9*), or exercise (*10*) also influence epithelial lung clearance. These physiologic alterations of epithelial transport may be caused by an increase in surface area for diffusion, an increase in permeability, changes in the thickness of the intervening membrane, changes in concentration gradient of the solute between epithelial surface and the blood, or an increase in exchange surface due to recruitment of capillaries (*8,10*).

Respiratory epithelial transport is commonly assessed by recording the absorptive clearance of aerosolized low-molecular-weight tracer solutes (^{99m}Tc-diethylene triaminepentaacetic acid (DTPA), molecular weight 492 daltons, approximate molecular radius 0.57 nm) from the lungs into the blood stream with a gamma camera or a scintillation probe (*11*). Penetration of the aerosol into the nonciliated respiratory units requires particles <1 μm, while particles >2 μm preferentially deposit on ciliated airways. Depending on aerosol size and breathing pattern, contribution of mucociliary clearance due to particle deposition on ciliated airways cannot be excluded. Scintillation probe and gamma camera register total lung clearance and cannot differentiate between clearance by mucus transport or trans-epithelial absorption. Only the camera provides information about initial aerosol deposition and regional lung clearance.

We have developed a simple, noninvasive method to measure the rate of epithelial absorption by way of the urinary excretion of inhaled ^{99m}Tc-DTPA, largely independent of its initial regional deposition.

MATERIALS AND METHODS

Theoretical Model of DTPA Clearance

Inhaled ^{99m}Tc-DTPA, which deposits on ciliated airways and is cleared via mucociliary transport (f1), moves from the lung periphery towards the pharynx to be swallowed or

coughed up and expectorated. From the literature (*12,13*) and from our own experiments (Köhn, unpublished data) we know that reabsorption of ^{99m}Tc-DTPA from the gut is negligible. In three healthy volunteers, radioactivity in urine collected over 24 hr after ingestion of 1.85 MBq (50 μCi) was <1%. Therefore, the activity measured in urine within 24 hr after inhalation must have been cleared from the lungs by epithelial absorption. Thus, the amount of 24-hr urinary ^{99m}Tc-DTPA excretion, expressed in percent of the initial lung deposition, reflects the total amount of radioaerosol cleared by absorption from the lungs into the circulating blood and filtered into urine by the kidneys (F2) (Fig. 1).

Theoretical computerized compartmental analysis of the compartments involved in the clearance of ^{99m}Tc-DTPA by epithelial absorption (lung, plasma, urine) was performed, varying the transfer rates and applying differential equations. These calculations demonstrate that, independent of ^{99m}Tc-DTPA lung absorption rates, the total amount of radioactivity cleared by absorption is found in the urine 24 hr after inhalation. For a normal half-time clearance of 100 min, 14.4 half-times have elapsed in 24 hr (Fig. 2). The cumulative 24-hr urinary ^{99m}Tc-DTPA excretion is an exact measure of the total amount of inhaled ^{99m}Tc-DTPA cleared by epithelial absorption.

While measurement of 24-hr urinary radioactivity offers information neither about the absorption rate of the radioaerosol from the epithelium into the blood nor about the severity of the respiratory epithelial defect, measurement of urinary activity 2–6 hr after inhalation is suitable to differentiate increased from normal epithelial membrane transport (Fig. 3). Measurement of urinary ^{99m}Tc-DTPA excretion two hours after inhalation was chosen for practical reasons since at that time sufficient urine is available without making the test too time-consuming.

The only limitation of this simple model is severe impairment of renal function (Fig. 4).

Measurement of Lung Epithelial Transport

Inhalation Procedure. In a first study, an ultrasonically (Pulmosonic, De Vilbiss Dietzenbach, FRG) generated ^{99m}Tc-DTPA aerosol was used (aerosol A). The droplet size was 2.8 μm mass median aerodynamic diameter (MMAD) (GSD 1.6). Larger droplets were eliminated by a settling bag. Patients inhaled through a mouthpiece with the nose clipped. Inhalation time was 3–5 min. Patients were instructed to inhale slowly with end-inspiratory breath holding pauses of 3–5 sec. Since this aerosol was not ideally suited for epithelial clearance studies, in a second study a dry aerosol of small particle size (0.5 μm MMAD, GSD 1.0) generated by a jet nebulizer was used (aerosol B). The inhalation device is a self-developed prototype (Mallinckrodt, Petten, Netherlands), which operates on the principle of reducing air humidity used for nebulization to 16%–18%, and adding pure ethanol to the saline-DTPA solution. A saline concentration of 0.09% was applied since with this concentration particle size was smaller than that with 0.9% NaCl (MMAD 0.5 μm versus 1.1 μm, respectively) (*14*). The inhalation procedure was the same as with the ultrasonic aerosol, but the inhalation time was markedly shorter because lung deposition efficiency with this device was 35%–40%. Lung clearance was recorded with a gamma camera (CGR,

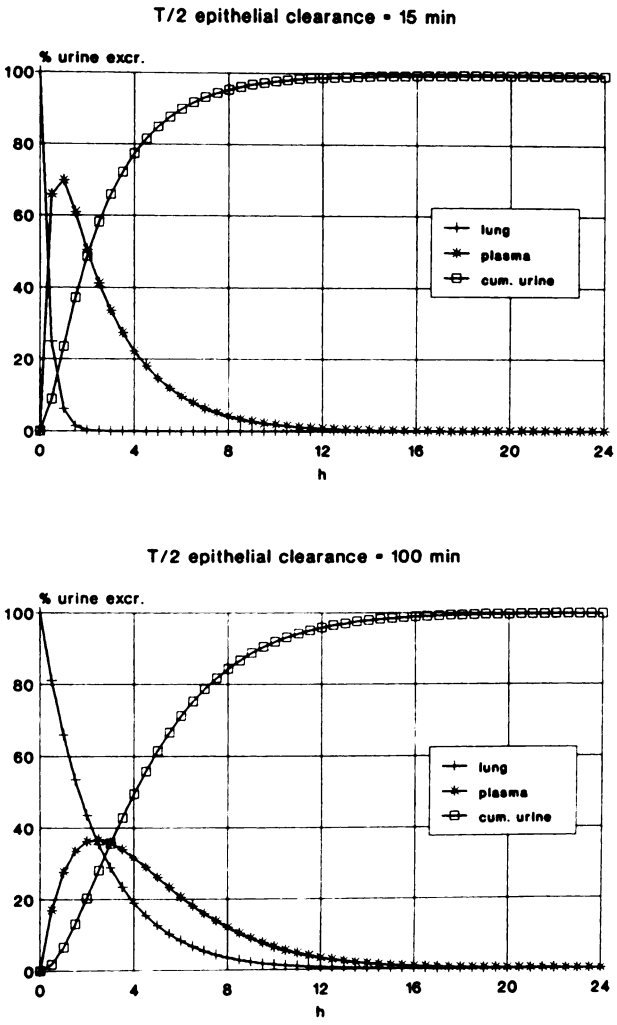


FIGURE 2
Computerized compartmental analysis of the influence of different ^{99m}Tc-DTPA absorption rates on cumulative urinary DTPA excretion. Top: increased epithelial clearance with T/2 15 min. Bottom: normal epithelial clearance with T/2 100 min.

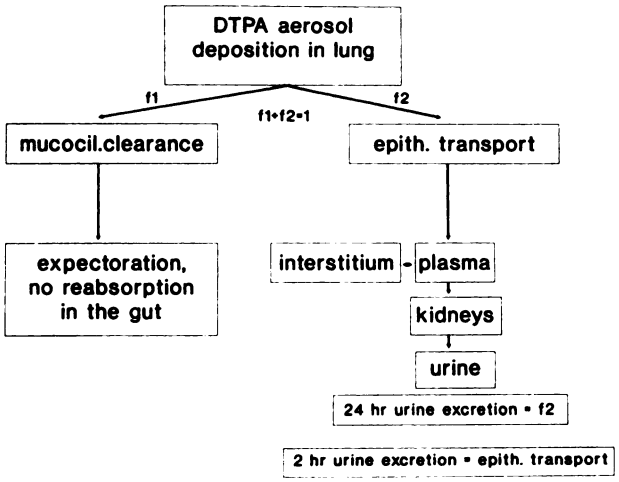


FIGURE 1
Model of aerosolized ^{99m}Tc-DTPA lung clearance.

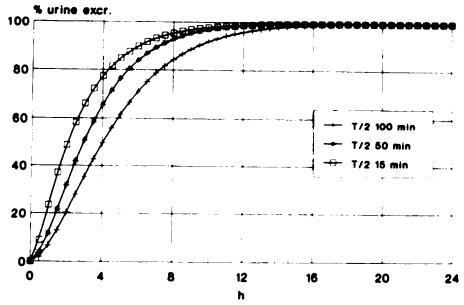


FIGURE 3
Influence of different ^{99m}Tc-DTPA absorption rates on urinary DTPA excretion: differentiation of increased from normal epithelial clearance is possible from urinary ^{99m}Tc-DTPA excretion measured in the first hours after inhalation. Measurement of 2-hr DTPA excretion was chosen for practical reasons.

Desmoulins, France) for 30 min with the patient in supine position.

Urinary Excretion of ^{99m}Tc-DTPA

For quantitative assessment of the respective contribution of both possible pathways (f1 and f2) to total lung clearance, quantification of the initial aerosol lung deposition is necessary. Therefore, the activity measured over the lungs has to be corrected for thoracic tissue absorption by an individual correction factor. This factor was measured by means of intravenously injected ^{99m}Tc-microspheres and calculated by the following equation:

$$\frac{\text{cpm injected dose (syringe before and after injection)}}{\text{cpm lung activity (geometric mean)}}. \quad (1)$$

The contribution of mucociliary transport (f1) and epithelial absorption (f2) to total lung clearance was assessed from the corrected initial lung activity and the 24-hr urinary ^{99m}Tc-DTPA excretion. The amount of aerosol cleared from the lungs via epithelial absorption (f2), is given by the following equation:

$$\frac{\text{cpm 24-hr urine}}{\text{cpm corrected lung activity}}. \quad (2)$$

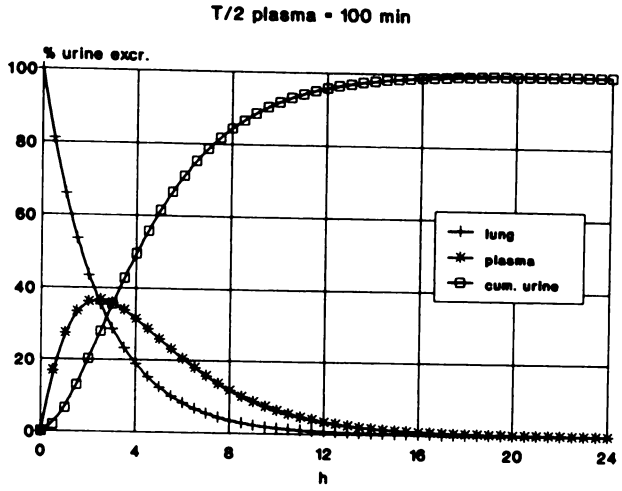
Radioactivity was measured in the urine at 2 and 24 hr after inhalation, correcting for decay and for the different measuring geometries of camera and well counter (sensitivity camera: counter = 1:5500). Correction for the physical decay of technetium was performed automatically using the minute zero of the day as time zero.

The 2-hr ^{99m}Tc-DTPA excretion in urine in percent of total ^{99m}Tc-DTPA cleared by absorption is then given by the equation:

$$\frac{\text{cpm 2-hr urine} * 100}{\text{cpm corrected lung activity}} * \frac{1}{f2}. \quad (3)$$

Equation 4 is obtained by substitution of f2 in Equation 3 by Equation 2:

$$\frac{\text{cpm 2-hr urine} * 100}{\text{cpm 24-hr urine}}. \quad (4)$$



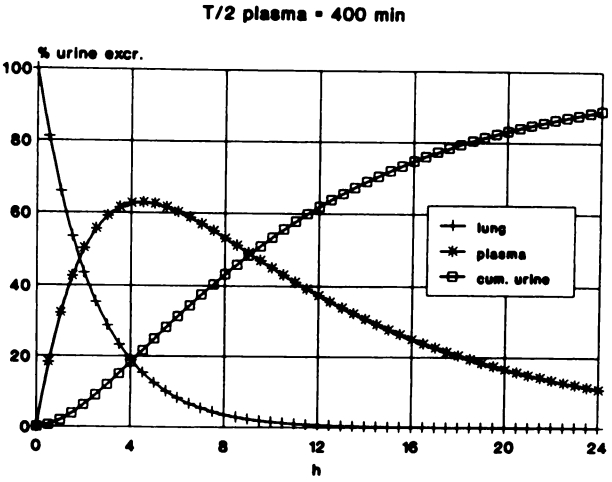


FIGURE 4
Computerized compartmental analysis of the influence of impaired renal function on cumulative ^{99m}Tc-DTPA excretion. Top: normal renal function. Bottom: severely impaired renal function.

Quality Control of ^{99m}Tc-DTPA

Since chemical breakdown of ^{99m}Tc-DTPA during ultrasonic nebulization has been reported (*15*), we studied a possible influence of our nebulization device on the stability of the generated ^{99m}Tc-DTPA aerosol. Radiochemical purity of the stock solution, the ultrasonically produced aerosol, and of urine samples collected at 2 and 24 hr following aerosol inhalation was determined by thin-layer chromatography. Chemical impurities such as free ^{99m}TcO4$^-$ or reduced hydrolyzed technetium were <1%, suggesting that the ^{99m}Tc-DTPA molecule was neither destroyed by the ultrasonic nebulizer used in this study, nor during its movement from lung to urine.

Lung Clearance of ^{99m}Tc-DTPA Measured by Gamma Camera

In addition to the measurement of ^{99m}Tc-DTPA excretion in urine, total and regional lung clearance curves were recorded over a period of 30 min using a gamma camera (CGR),

and were then analyzed by monoexponential fitting. Lung clearance results were expressed as the clearance half-time (T/2) in minutes or as the slope (k) in %/min calculated over the first 15 min. Parametric images of the monoexponential slopes also were computed. Regions of interest over the lungs were drawn by hand, utilizing the patient's individual ^{99m}Tc-microspheres perfusion lung scan.

We did not correct for radioactivity in the pulmonary circulation and chest wall using a calibration dose of i.v. ^{99m}Tc-DTPA (*7*), since the contribution is negligible and correction changes clearance values in the same direction (*8*, *16*).

Factor Analysis of ^{99m}Tc-DTPA Lung Inhalation Studies

Factor analysis according to Šamal et al. (*17*) was applied to dynamic inhalation studies with both types of aerosol to demonstrate that there is no time lag between the onset of epithelial and mucociliary clearance and that both mechanisms always operate simultaneously.

Factor analysis of dynamic radionuclide studies provides decomposition of data variance into images and time-activity curves, corresponding to the underlying dynamic structures. The method is based on the analysis of study variance and on subsequent imaging of its principal components in a simplified factor space. Thus, physiologic factors can be derived corresponding to the different temporal behavior of specific anatomical structures even if these structures overlap, as is the case in the lung. A "factor image" displays the spatial distribution of the extracted factors. The method also permits quantification of the percent contribution of each factor to the total information of the study. Twenty-three studies of aerosol A and 17 studies of aerosol B were available for factor analysis.

Patients

Forty-four unselected consecutive patients with various pulmonary disorders, and ten nonsmokers, and seven smokers without lung disease were investigated with the ultrasonic aerosol (aerosol A).

Of the 44 patients, 11 had interstitial lung disease, 7 COLD, 3 bronchial asthma, 5 pneumonia, 4 pulmonary embolism, 2 bronchogenic carcinoma, 3 tuberculosis, 1 mesothelioma, 1 M. Hodgkin, 1 non-Hodgkin lymphoma, 1 sleep-apnea syndrome, 3 viral infections, and 2 *pneumocystis carinii pneumonia.*

A second group of 20 consecutive patients (12 patients with interstitial lung disease—mostly sarcoidosis—and 8 with mild obstructive lung disease) were studied using the dry aerosol of small particle size (aerosol B) to evaluate the reliability of the urinary excretion method.

In all patients, epithelial transport was assessed by both the clearance half-time or slope measured over the lungs and the urinary ^{99m}Tc-DTPA excretion method.

RESULTS

In 59 patients, the mean correction factor for tissue absorption was 2.3 ± 0.5 (mean ± s.d.). The ^{99m}Tc-DTPA aerosol used in the first study was generated by an ultrasonic nebulizer delivering particles of 2.8 μm MMAD (GSD 1.6). For this particle size, there was a wide range of the amount of aerosol cleared by absorption (f2) (66.9% ± 24.4%). The assumption that the aerosol is preferentially cleared via mucociliary transport (f1) when deposited more centrally and via absorption through the epithelium (f2) when deposited more peripherally is supported by a highly significant inverse correlation between the f2 and a penetration index (ratio inner/outer lung zone) ($r_s = -0.71$, $p < 0.001$) (Fig. 5).

Aerosol clearance measured over the lungs correlated significantly with epithelial clearance measured by urinary ^{99m}Tc-DTPA excretion. As expected, a cumulative exponential function ($A(t) = A\infty(1-\exp(-kt))$) rather than a linear regression described the correlation best, since no more than 100% of the activity deposited in the lung can be cleared into the urine. Both methods revealed a very similar regression with both types of aerosol (aerosol A: $r = 0.75$, $p < 0.001$, $n = 61$, % 2-hr urine excretion = 88.4 (1-exp(-0.351 * k%/min(lung))) and aerosol B: $r = 0.96$, $p < 0.001$, $n = 20$, % 2-hr urine excretion = 73.1 (1-exp(-0.378 * k%/min (lung))), respectively) (Fig. 6).

The results of factor analysis with both types of aerosol are shown in Table 1. Total extractable "communality" (= the extent of the original input data explained by extracted factors) was 79.5% ± 8.8% with aerosol A and 98% ± 0.9% with aerosol B ($p < 0.001$). Contribution to factor 1 (related to epithelial absorption) was 22.4% ± 12.6% for aerosol A and 31.9% ± 7.5% for aerosol B, respectively ($p < 0.01$). The respective values for factor 2 (related to mucociliary transport)

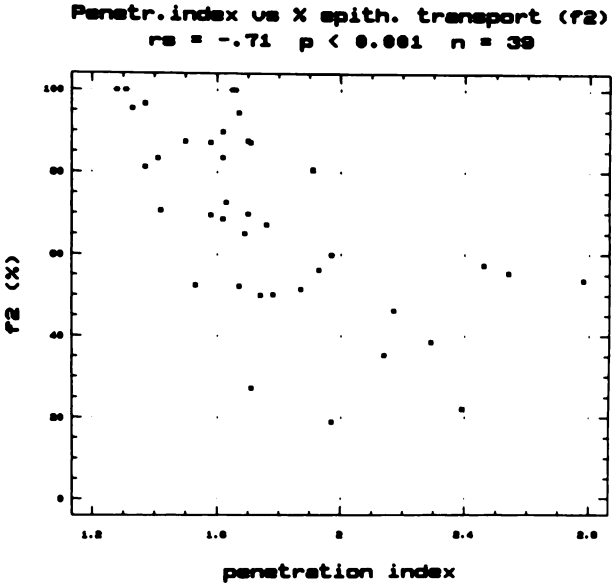
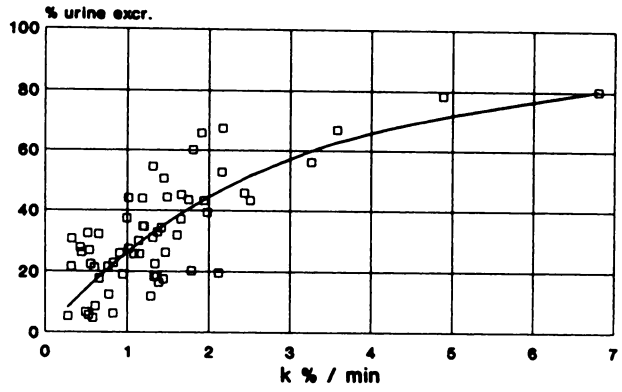


FIGURE 5
Relationship between penetration index (ratio of counts inner/outer lung zone) and amount of aerosol cleared by absorption (f2) ($r_s = -0.71$, $p < 0.001$). More centrally deposited aerosol is cleared preferentially via mucociliary transport, while peripherally deposited aerosol is cleared by epithelial transport.



Aerosol B r = 0.961 n = 20
y = 73.1(1-exp(-0.38*k))

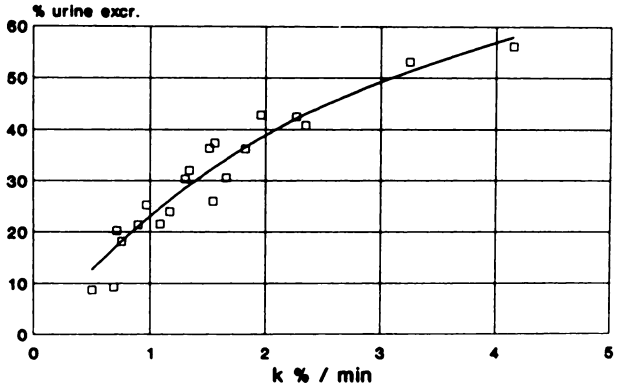


FIGURE 6
Correlation between lung clearance (%/min.) and 2-hr urinary ^{99m}Tc-DTPA excretion. Top: ultrasonically produced aerosol (aerosol A): n = 61, r = 0.75, p < 0.001; regression in the form of a cumulative exponential function (% 2-hr urine excretion = 88.4 (1-exp(−0.351 * k% /min)). Bottom: dry aerosol of small particle size (aerosol B): n = 20, r = 0.96, p < 0.001; very similar regression (% 2-hr urine excretion = 73.1 (1-exp(−0.378 * k%/min)).

were 13.5% ± 8.7% and 35.3% ± 8.2% (p < 0.001). The background contribution of aerosol A was significantly higher (p < 0.001) than that of aerosol B (65.4% ± 14.3% versus 32.3% ± 9.0%, respectively). Factor analysis always revealed two factors with opposite temporal behavior; one was mainly localized peripherally and had the form of a descending curve, the other was mainly localized centrally and had the form of an ascending curve, indicating that both mechanisms of lung clearance operate simultaneously during the observation period.

Two typical "factor images" of aerosol A and aerosol B are shown in Figure 7.

A loose but significant inverse correlation was found between two-hr urinary ^{99m}Tc-DTPA excretion and serum creatinine values (r_s = −0.37, p < 0.01, n = 51) (Fig. 8).

TABLE 1
Results of Factor Analysis of Dynamic Inhalation Studies with Two Different Types of Aerosol

	Aerosol A* (n = 23)	Aerosol B† (n = 17)	p
TCM (%)	79.5 ± 8.8	98 ± 0.9	<0.001
RCF_1 (%)	22.4 ± 12.6	31.9 ± 7.5	<0.01
RCF_2 (%)	13.5 ± 8.7	35.3 ± 8.2	<0.001
RCB (%)	65.4 ± 14.3	32.3 ± 9.0	<0.001

* Aerosol A: ultrasonic aerosol of rather large particles (MMAD 2.8 μm).
† Aerosol B: dry aerosol of small particle size (MMAD 0.5 μm).
TCM = total extractable communality (information); RCF_1 = factor 1 (related to epithelial transport); RCF_2 = factor 2 (related to mucociliary transport); and RCB = background.

Of the patients studied with aerosol A, several subgroups with different pulmonary disorders were selected. Results obtained with the urinary excretion method were compared with those of nonsmokers or smokers without pulmonary disease.

Epithelial clearance assessed by two-hour urinary ^{99m}Tc-DTPA excretion in nonsmokers was significantly different from that of smokers without lung disease (Fig. 9), or from patients with various lung diseases (Fig. 10).

DISCUSSION

Assessment of lung epithelial transport by a gamma camera requires soluble tracer solutes of small particle size (< 1 μm) to ensure deposition distal to the ciliated airway surfaces. However, in the clinical setting considerable variability of regional deposition is likely to occur. Factors accounting for this variability such as particle size, hygroscopicity, breathing pattern, lung volume, preparation of ^{99m}Tc-DTPA, have recently been discussed (*18*).

Clearance measured over the lungs, therefore, always consists of different components with different temporal behavior according to regional deposition of particles on different types of pulmonary epithelium.

There are two possible pathways for deposited particles to leave the lung: (1) trans-epithelial absorption (alveolar and possibly bronchial) into the blood, and (2) mucociliary transport along the surface of the airways.

Cheema et al. (*13*) have shown that ^{99m}Tc-DTPA is bound to the mucus with high affinity and therefore unlikely to cross mucus layers of physiologic thickness. This activity is cleared very slowly by mucus transport. On the other hand, Oberdörster et al. (*18*) in dogs, and, very recently, Bennett and Ilowite (*19*) in man have provided evidence of ^{99m}Tc-DTPA clearance through the bronchial epithelium. However, this occurs at a much slower rate than from the alveolar epithelium

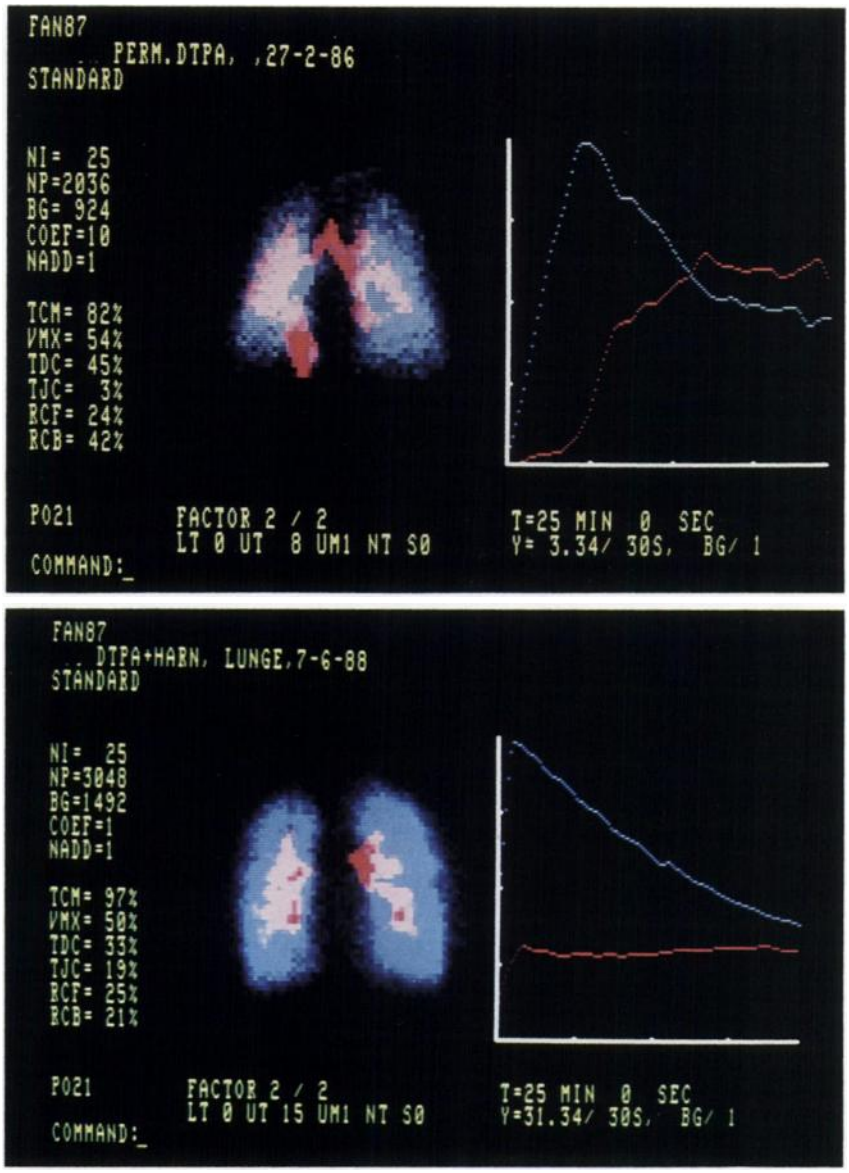


FIGURE 7
Typical "factor images" and time-activity curves of principal components derived by factor analysis of dynamic inhalation studies. (Top panel) Ultrasonically generated aerosol (aerosol A): Total communality (as a portion of total study variability explained by the extracted factors) = 82%. Contribution of factor 1 (blue),—located more peripherally and related to epithelial absorption = 34%; that of factor 2 (red), located more centrally and related to mucociliary transport = 24%. High background activity of 42%. (Bottom panel) Aerosol with small particle size (aerosol B): Total communality = 97%; contribution of factor 1 (blue), related to epithelial absorption, is markedly higher than that of factor 2 (red), related to mucociliary transport (54% vs. 25%). Background is only 21%.

and the mucus pathway is the primary one accounting for most of the clearance from bronchial airways (*19*).

Factor analysis of dynamic inhalation studies permits extraction of principal components with different temporal behavior corresponding to specific anatomical structures with different clearance rates, even if these anatomical structures overlap, as is the case in the lung. Dynamic inhalation studies with both types of aerosol always demonstrated two factors with opposite temporal behavior, one related to epithelial transport by absorption, and one related to mucociliary transport along the surfaces of the airways, operating simultaneously during the observation period. According to the type of aerosol used and to the deposition pattern achieved, the contribution of the mucus pathway varies significantly and thus influences the results of epithelial clearance when measured over the lungs.

The gamma camera provides information about regional aerosol distribution and regional lung clearance. External detection methods other than factor analysis cannot discriminate between the rate of aerosol cleared by mucociliary transport or by epithelial absorption.

Although a settling bag was used, the rather large particle size of the ultrasonically generated aerosol (aerosol A) used in the first study caused significant deposition of the aerosol on ciliated airways. Even selection of peripheral lung areas for clearance curve analysis could not eliminate the contribution of mucociliary transport. Therefore, when measuring clearance by epithelial absorption over the lungs, the mucus pathway for ^{99m}Tc-DTPA clearance has to be considered.

Measurement of epithelial clearance from urinary ^{99m}Tc-DTPA excretion permits assessment of transepithelial absorption without any interference by mucociliary transport.

Aerosol cleared via the mucus transport route and

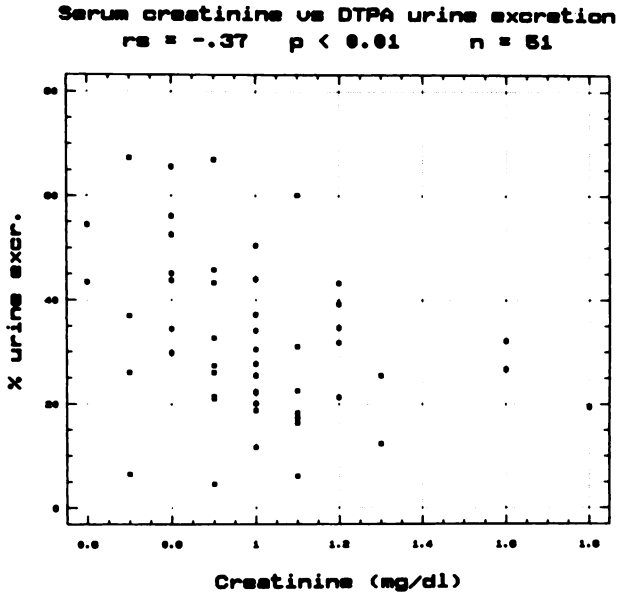


FIGURE 8
Significant inverse correlation between serum[s] creatinine values and 2-hr urinary ^{99m}Tc-DTPA excretion ($r_s = -0.37$, $p < 0.01$, $n = 51$).

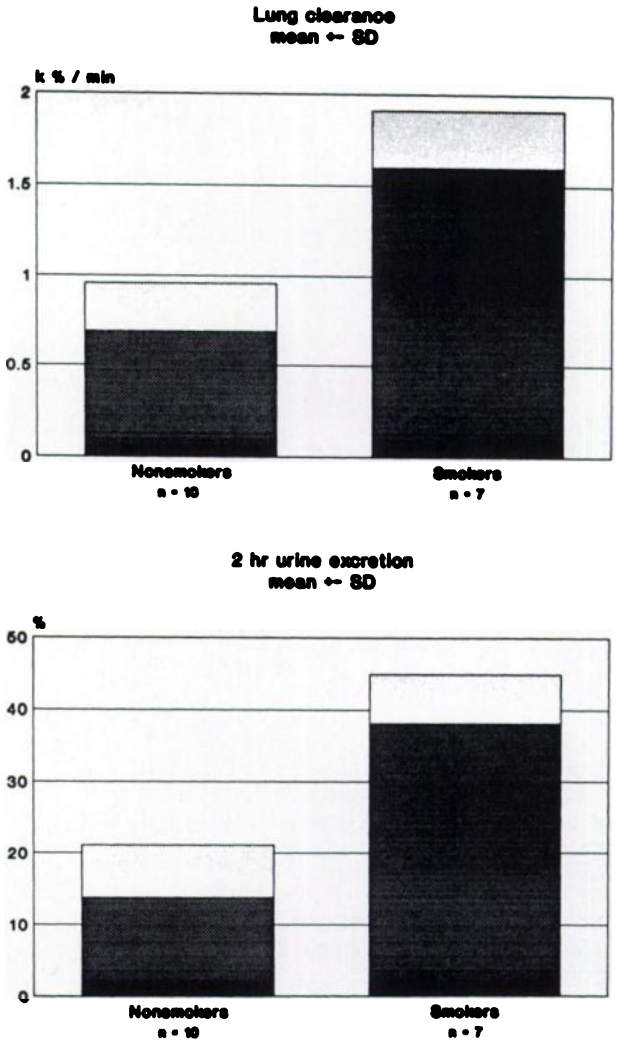


FIGURE 9
Influence of smoking on epithelial clearance as assessed by the gamma camera (top) and by 2-hr urinary ^{99m}Tc-DTPA excretion (bottom): significantly increased values in smokers compared to nonsmokers.

swallowed is not reabsorbed from the gut (*12,13*). Therefore, only ^{99m}Tc-DTPA cleared by epithelial absorption into the blood is excreted in the urine. With our proposed method, particle size and initial lung deposition of the aerosol are not so crucial since the clearance rate expressed as the ratio of the 2-hr to 24-hr ^{99m}Tc-DTPA excretion is not influenced by the quality of the aerosol.

Nevertheless, in vivo stability of the ^{99m}Tc-DTPA complex is pivotal, as intestinal absorption of free technetium is known to be significant (*12*). We found that radioactivity in urine collected over 24 hr after ingestion of ^{99m}Tc-DTPA was <1%. This is confirmed by reports stating that absorption of swallowed ^{99m}Tc-DTPA from the gut is so poor and slow (probably due to binding to gastric and intestinal mucus) that recirculation of gastrointestinal activity does not substantially influence pulmonary clearance measurements (*12,13*). In addition, chromatography of the ^{99m}Tc-DTPA stock solution, the generated aerosol as well as of urine samples taken 2 and 24 hr after inhalation revealed <1% of free or reduced hydrolyzed technetium. These findings provide evidence that the ^{99m}Tc-DTPA preparation used in this study remained stable in vitro before and after nebulization as well as in vivo, and was not reabsorbed from the gut.

For urine sampling good patient compliance is required and severe impairment of renal function is a limiting factor. The expected significant inverse correlation ($p < 0.01$) between two-hour urine excretion of ^{99m}Tc-DTPA and serum creatinine values in our patients confirms this assumption. However, the exact limitations of renal impairment remain to be established.

In normals, a wide range of epithelial lung clearance half-times has been reported. Although Fiorica et al. (*20*) found intra-patient variability to be too great to allow the method to be clinically useful, our own experience (Köhn, unpublished data) and that of others (*19,21,22*) does not concur with this conclusion. We and others found intra-individual variation of the epithelial absorption rate expressed in %/min to be ~10%.

The correlation between lung clearance and urinary DTPA excretion was highly significant ($p < 0.001$) with both the ultrasonic aerosol (aerosol A) and the aerosol of small particle size (aerosol B). The very similar regression between these methods expressed by the cu-

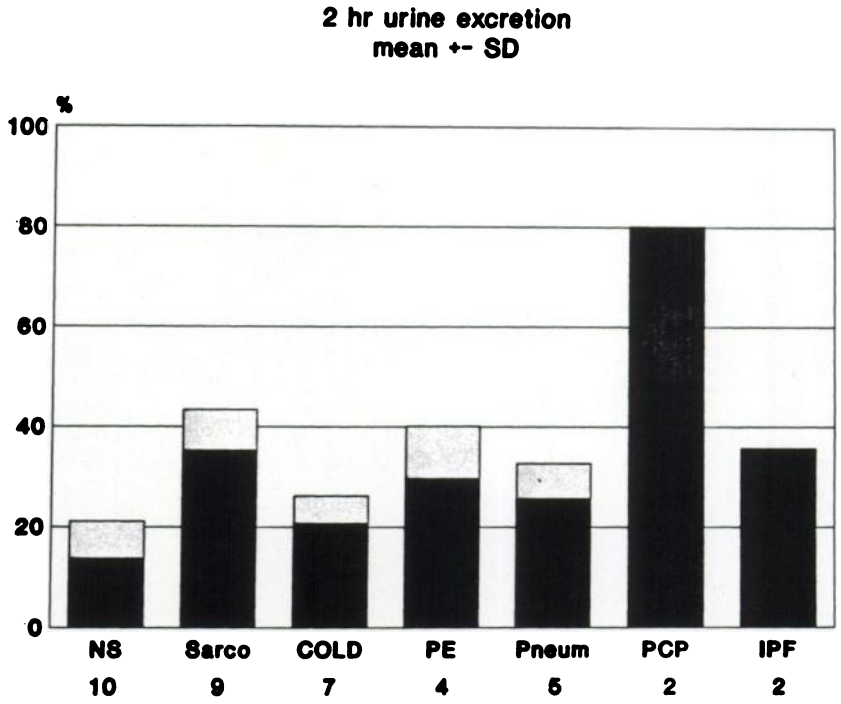


FIGURE 10
Clinical results of the urinary ^{99m}Tc-DTPA excretion method in selected patients with various lung diseases (The respective means and s.d. are listed). (NS = nonsmokers, Sarco = sarcoidosis, COLD = chronic obstructive lung diseases, PE = pulmonary embolism, Pneum = pneumonia, PCP = Pneumocystis carinii pneumonia, and IPF = idiopathic pulmonary fibrosis.

mulative exponential function found with both types of aerosol suggests that with the urinary excretion method aerosol particle size is not so crucial.

Increased absorption rates of inhaled ^{99m}Tc-DTPA from the lung were reported in various pulmonary disorders such as sarcoidosis (*4*), ILF (*4*), ARDS (*5*), or opportunistic lung infections in AIDS patients (*6*). Lung clearance is also significantly increased in cigarette smokers (*7*) and influenced by physiologic factors such as lung volume (*8*), posture (*9*), or exercise (*10*).

The priority of this study was to establish an alternative method to clearance measurement over the lungs rather than to perform a large-scale clinical investigation. The preliminary results suggest that this alternative technique might be of clinical usefulness. Cigarette smokers or patients with active interstitial or inflammatory lung disease had significantly increased lung epithelial clearance compared to nonsmokers without lung disease. In two patients with the acquired immunodeficiency syndrome and *Pneumocystis carinii* pneumonia, epithelial clearance was extremely high in terms of two-hour urinary ^{99m}Tc-DTPA excretion and clearance measured over the lungs.

The presented method permits quantitative assessment of the rate of tracer transfer across the epithelium into the blood and of the percentage of deposited aerosolized ^{99m}Tc-DTPA cleared by mucociliary transport. Only an inhalation device and a well counter to measure urine radioactivity are required, and the method is, therefore, well suited as a bedside test.

This simple procedure can be performed as an alternative method outside nuclear medicine departments and might be useful for monitoring critically ill patients with ARDS, for assessment of disease activity in interstitial lung disease, for early detection of AIDS-related opportunistic lung infections and for close follow-up of these patients after therapy.

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