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Comparison of the Pulmonary Bactericidal Capacity of Mice and Rats Against Strains of *Pseudomonas aeruginosa*[1]

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After aerosol deposition of *Pseudomonas aeruginosa* strains in mice and rats, completely different patterns of pulmonary bacterial clearance were observed in each animal species.

Hospital-acquired respiratory infections are important factors contributing to morbidity and mortality of many patients admitted to general medical services (1, 7). Gram-negative bacilli, particularly *Pseudomonas aeruginosa*, have been responsible for increasing numbers of such infections (6, 8, 11). Studies to elucidate the pathogenesis of this problem were performed in several laboratories (4, 5, 9). One experimental approach has been to assess patterns of pulmonary bactericidal capacity (pulmonary clearance) of various gram-negative bacilli after their aerosol deposition in lungs of laboratory animals. Such studies were usually performed in a single animal species, with resulting data being considered representative of most laboratory animals. The present studies point out limitations to this hypothesis and require that clinical application be made only with the utmost caution.

Throughout the study normal 18- to 20-g white Swiss mice and 100- to 120-g Sprague-Dawley rats were used. A modified Henderson aerosol apparatus (3) was used to expose animals to the *P. aeruginosa* strains tested (hereafter designated *Pseudomonas* 16 and *Pseudomonas* 22). Animals were exposed to bacterial aerosols by methods we previously described (10). They were killed at predetermined intervals after exposure; their lungs were weighed and cultured quantitatively, with results expressed as organisms per gram of lung. Representative segments of lung from each interval were studied histologically. Pulmonary bactericidal capacity was calculated as the number of organisms remaining at each time interval divided by the number of organisms deposited (time zero animals) and expressed as a per cent.

Results in studies with rats (Table 1) disclosed that pulmonary bacterial clearance of both *Pseudomonas* 16 and *Pseudomonas* 22 was progressive after deposition, with 46 and 42%, respectively, remaining after 1 hr; 4.9% and 5.5%, respectively, at 4 hr. By contrast, two distinct patterns of pulmonary bactericidal activity were observed after aerosol exposure of mice to the same *Pseudomonas* strains (Table 2). *Pseudomonas* 16 multiplied in murine lung during the first hour after nebulization, but was thereafter progressively cleared. On the other hand, *Pseudomonas* 22 persisted at relatively unchanged

TABLE 1. *Clearance of viable Pseudomonas aeruginosa from normal rat lungs*[a]

Strain	Time (hr) after nebulization	No. of rats per time interval	Per cent of deposited bacteria remaining
Pseudomonas 16	Time 0	80	100[b]
	1	20	46
	4	20	4.9
Pseudomonas 22	Time 0	80	100[c]
	1	24	42
	4	20	5.5

[a] Mean bacterial count per milliliter of aerosol suspension: 7.6×10^9 (*Pseudomonas* 16); 8.3×10^9 (*Pseudomonas* 22).

[b] Mean bacterial count per gram of lung (± standard error of mean): 1.95×10^6 (±0.23).

[c] Mean bacterial count per gram of lung (± standard error of mean): 4.01×10^6 (± 0.72).

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TABLE 2. *Clearance of viable Pseudomonas aeruginosa from normal mouse lungs*[a]

Strain	Time (hr) after nebulization	No. of mice per time interval	Per cent of deposited bacteria remaining
Pseudomonas 16	Time 0	22	100[b]
	1	21	140
	4	21	13
Pseudomonas 22	Time 0	22	100[c]
	1	21	127
	4	20	97

[a] Mean bacterial count/ml of aerosol suspension: 6.45×10^8 (*Pseudomonas* 16); 1.715×10^9 (*Pseudomonas* 22).

[b] Mean bacterial count/g lung (± standard error of mean): 1.85×10^5 (± 0.27).

[c] Mean bacterial count/g lung (± standard error of mean): 2.65×10^5 (± 0.52).

numbers in mouse lungs 4 hr after deposition. Histological changes produced in lungs of all animals were similar and of minor degree, consisting of occasional moderate pulmonary edema and bronchiolar exudate without mucosal damage.

Previous studies (2, 4, 9) suggested that each bacterial species may have its own characteristic rate of clearance from normal animals. We also demonstrated in mice that with numerous strains of *Pseudomonas* there are even strain differences within the same bacterial species (9*a*). The data reported in the present study suggest that, even with the same strains of *P. aeruginosa*, different patterns of pulmonary bactericidal activity can be demonstrated in at least two separate animal species. Thus, studies of pulmonary bacterial clearance performed in one animal species must be interpreted cautiously when comparing them with similar observations in other laboratory animals. Even greater circumspection must be exercised in applying such data in a clinical context.

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