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Lung mechanics, radiography and ^{67}Ga scintigraphy in experimental *Pneumocystis carinii* pneumonia

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Summary. Respiratory system pressure–volume (P–V) studies, ^{67}Ga-citrate scans, and chest radiographs were made in the corticosteroid-treated rat model of *Pneumocystis carinii* pneumonia. The steroid treatment used to provoke *Pneumocystis* infection in this model resulted in a reduction in body weight, lung weight and lung volumes compared to age-matched controls but no change in the normalized pressure–volume curve. *P. carinii* infection was associated with increased lung wet weight and flattening of the respiratory system P–V curve when compared to either age matched controls or steroid-treated animals on trimethoprim-sulfamethoxazole prophylaxis for *P. carinii*. Radiographs were interpreted as positive in only three of 11 animals with *P. carinii*, whereas 10 of 12 animals showed positive gallium-67 lung scans. We conclude that both gallium uptake and altered lung mechanics occur in the rat with *Pneumocystis carinii* and may reflect increased alveolar permeability and surfactant abnormalities noted in other studies.

Keywords: *Pneumocystis carinii*, rat, pneumonia, lung function, radiography, gallium

Pneumocystis carinii is a major cause of pneumonia in immunosuppressed hosts (Hughes 1978). The corticosteroid-treated rodent has proven to be a useful model for the investigation of this infection and considerable information has accumulated regarding the microbiology, immunology, and pathology of *P. carinii* in this model (Frenkel *et al.* 1966; Walzer *et al.* 1980; Yoneda & Walzer 1981; Walzer *et al.* 1984). There has been excellent correlation between findings in the rat model and disease occurring in man with *P. carinii*, such as the efficacy of trimethoprim-sulfamethoxazole treatment (Hughes *et al.* 1974).

Although severe respiratory distress is the hallmark of *Pneumocystis* pneumonia, there have been few previous studies of the physiological changes which occur with experimental *P. carinii* infection (Brun-Pascaud *et al.* 1985). We therefore made pressure-volume studies of the respiratory system in the rat and correlated these findings with lung histopathology for *P. carinii*.

Pneumocystis pneumonia in man characteristically causes a diffuse bilateral interstitial and alveolar pattern on chest radiographs (Burke & Good 1973). Positive scintiscans with gallium-67 (Ga-67), a radionuclide accumulating in sites of inflam-

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mation, have also been reported with *P. carinii* pneumonia (Levenson *et al.* 1976; Rhadapalli *et al.* 1977; Coleman *et al.* 1984). In order to determine whether these techniques could be applied in the animal model of *Pneumocystis*, we also studied the serial appearance of chest radiographs and Ga-67 lung activity in the rat.

Materials and methods

Male SPF CD rats (Charles River, Wilmington, MA) weighing 200–250 g upon arrival were used. Exogenous infection was minimized by utilizing filter crates and maintaining the animals in air-filtered cages. Rats were observed for 1 week in an isolated colony before being placed on one of three drug regimens administered in drinking water: Group 1 (control): tetracycline hydrochloride (E.R. Squibb and Sons, Princeton, NJ), 500 mg/liter; group 2: tetracycline, 500 mg/liter, and dexamethasone sodium phosphate (Elkins-Sinn, Inc., Cherry Hill, NJ), 1.0 mg/litre; Group 3 (steroid-TMP-SMZ): tetracycline, 500 mg/liter, dexamethasone, 1.0 mg/liter, and trimethoprim-sulfamethoxazole (Roche Laboratories, Nutley, NJ), 200 mg trimethoprim and 1.0 gram sulfamethoxazole/liter. Medications were well mixed in the drinking water and medicated water bottles changed every other day. Dexamthasone administered in this manner has been shown previously to reliably allow the development of *P. carinii* infection in rats. Tetracycline was administered to all animals to reduce bacterial superinfection. Group 3 animals were treated with trimethoprim-sulfamethoxazole to prevent *Pneumocystis carinii* infection in order for this group to serve as a control for possible effects of corticosteroid administration. Animals were maintained 3–5 per cage and fed standard laboratory chow *ad libitum*. Animals were removed from the filter cages only for weekly measurements of body weight until the time of study.

Pressure-volume studies. Animals at 0, 6, 8, 10 and 12–14 weeks after therapy were anesthetized with intraperitoneal pentobarbitol (Elkins-Sinn, Inc., Cherry Hill, NJ), 50 mg/kg. A tracheostomy was placed using a short polyethylene catheter (PE-100) secured tightly in the trachea with double silk ligatures. The abdominal cavity was then opened and the animal exsanguinated by aortic puncture. Immediately after cessation of spontaneous respirations, the tracheal cannula was connected to a lubricated metal three-way stopcock and the animal taken to minimal volume at an airway pressure of -20 cm H_2O. Respiratory system pressure-volume curves *in situ* were then obtained using a 20 ml syringe pump (Harvard Apparatus, Model 902, Dover, MA) connected to the cannula, beginning at minimal volume. Transpulmonary pressure was measured using a Statham PM 23 pressure transducer (range, -50 to $+300$ mm Hg, Gould, Inc., Cleveland, OH). An electrical volume signal was obtained by firm attachment of the plunger of the pump syringe to a linear potentiometer (Duncan Electronics, Costa Mesa, CA). Volume and pressure were displayed and photographed on an X–Y storage oscilloscope (Tektronix, Beaverton, OR) as well as recorded in time on a strip chart recorder (Gould, Inc., Cleveland, OH). The lungs were inflated to $+32.5$ cm H_2O, followed by return to -20 cm H_2O, and 3–4 further cycles to $+32.5$ cm H_2O. Cycling rate was a constant 0.4 cm^3/second. Air compressibility of the gas within the system (tubing, syringe, etc). was corrected by recording pressure and volume while advancing the plunger with the tracheal cannula clamped. Lung volume changes were then corrected for this compression artifact and expressed at ambient temperature and humidity. Leaks were avoided by careful attention to connector fit and continuous recordings of the oscilloscope tracings. Air trapping was minimal at the cycling rate selected but was occasionally seen in some control lungs (Frazer *et al.* 1979). The second and third pressure–volume curves were used for each animal although occasio-

nally a fourth curve was taken and the two best curves were averaged in volume at 2.5 cm H_2O pressure intervals. A maximal lung volume ('vital capacity') or V_{max} was calculated as the volume between +32.5 and −20 cm H_2O of the average curve. Percents of this maximal lung volume remaining at +5, +10, and 15 cm H_2O transpulmonary pressure on the deflation limb of the curve were calculated as an index of the shape of the deflation limb of the P–V curve (Mitzner *et al.* 1982). Respiratory system compliance in ml × cm H_2O^{-1} was also computed between the arbitrary points of +2.5 and +5.0 cm H_2O transpulmonary pressure on the steep linear portion of the deflation curve.

Histopathology. After the P–V curves were completed, a pneumothorax was introduced by carefully cutting the diaphragm. The lungs were dissected free of other tissues and weighed without the trachea. The deflated left lung was fixed in 10% formalin and sections stained with Gomori's methenamine silver nitrate stain. *P. carinii* infection was graded (0–4+) by a single observer (WTH) without prior knowledge of the treatment groups using the following criteria: 1+, isolated cysts seen, no significant inflammatory response; 2+, desquamation of alveolar cells, with increasing numbers of organisms; minimal or no inflammatory response in alveolar septa; 3+, extensive reactive, desquamative alveolopathy, large numbers of organisms; 4+, very large numbers of cysts seen in most alveoli, with reaction as above.

Hematoxylin and eosin-stained lung sections were also reviewed.

Chest radiographs. Prior to pressure–volume studies, magnification (2:1) posterior-anterior (PA) chest radiographs were performed on groups of animals at 8, 10, and 12–14 (12+) weeks after therapy using standard techniques. Light anesthesia was administered in a closed chamber with methoxyflurane (Abbott Laboratories, North Chicago, IL), and animals were positioned in the prone position. At the conclusion of the study, all films were interpreted by a radiologist (DG) without prior knowledge of the treatment groups. Films were read as negative, questionably positive, or definitely positive designating the area or areas involved with abnormal pulmonary opacities. Animals on treatment less than 8 weeks did not have radiographs or scans because earlier preliminary studies had not found positive radiographs at earlier time points.

Gallium-(67Ga) activity and images. Animals were injected with 100 μCi of Ga-67 citrate (carrier-free) via a tail vein at 8, 10, and 12+ weeks after starting drug therapy. Control animals reaching weights over 300 g received 150 μCi Ga-67. Forty-eight hours after injection, the animals were anesthetized with methoxyflurane and imaging was performed using a Medex 37-tube gamma camera with pinhole collimator interfaced to an Ohio-Nuclear 450 VIP computer. Images were photographed and also stored on magnetic tape. Animal (dorsum) to collimator distance was 5 cm and image collection time was 7 min. All scans were done with the animals in a prone position and with front extremities extended. Tissue samples (right lung, blood, spleen, liver, right kidney, heart, small intestine, and whole tibia) were collected after pressure–volume studies and exsanguination were completed. Surface blood was carefully removed by blotting and tissue Ga-67 activity was measured in a Beckman 1125 gamma counter and expressed as ct/min/gram wet tissue weight. Part of the left lung was also removed, weighed and then dried to constant weight in a microwave oven. The calculated wet/dry ratio was assumed to a constant for the whole lung and a dry lung weight calculated.

Statistical methods. Tests for significance were performed using the Wilcoxon's rank sum test for unpaired data.

Results

Histopathology

Histological semi-quantitative scores for *P.*

carinii infection for the animals included in this study at each time point after beginning therapy are indicated in Fig. 1. One Group 1 control animal was examined for *P. carinii* at each time except 12+ weeks, although a group of 3–5 control animals at each point was included in other results. These results are similar to previous studies in this model and demonstrate progressive infection with *P. carinii* in Group 2 steroid-treated animals and the efficacy of TMP-SMZ in preventing this infection in Group 3 steroid-treated animals.

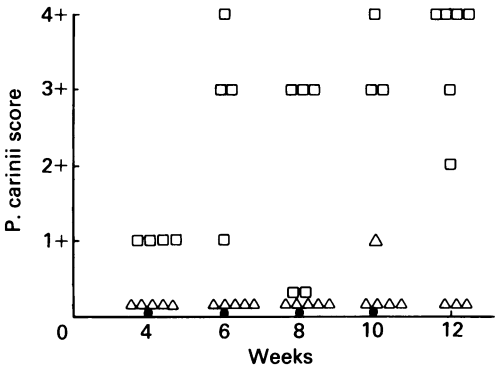

Fig. 1. Semi-quantitative histopathological score for *P. carinii* versus time on corticosteroids. ●, Group 1 (control); □, Group 2 (Steroid); △, Group 3 (steroid-TMP-SMZ). Only one Group 1 control (no treatment) animal was examined at each time point and none at 12+ weeks.

Two Group 2 steroid-treated animals with negative histopathology at 8 weeks for *P. carinii* and a single Group 3 animal with 1+ histopathology at 10 weeks were not included in the data for lung weight, pressure volume curves, or Ga-67 activity.

Body weight

The changes in body weights in the three groups of animals are shown in Fig. 2. Body weight decline compared to Group 1 controls was similar in the two steroid-treated groups (2 and 3) and was consistent with previous studies in this model using similar large dosages of steroids (Walzer *et al.* 1984).

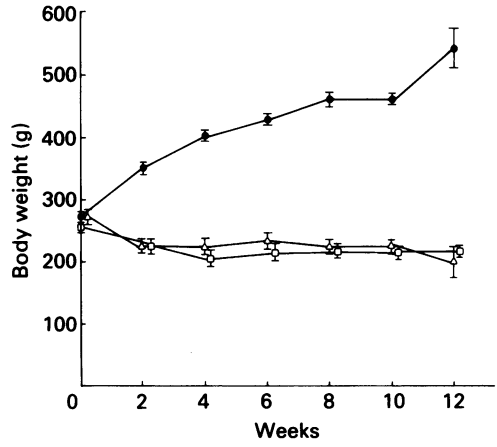

Fig. 2. Changes in body weight with time in the three groups. ●, Group 1 (control); □, Group 2 (steroid); and △, Group 3 (steroid-TMP-SMZ). Each point represents arithmetic mean, bars indicate 1 SE.

Difference in body weights between the two steroid-treated groups (2 and 3) were not significant at any time period.

Lung weights

Changes in lung weights and lung weight × 100/body weight ratios (LW/BW) are shown in Table 1.

Lung weights and LW/BW ratios for Group 1 control animals are similar to results published for male Spraque-Dawley rats in this weight range and show a plateau in lung weight with age and a decline in LW/BW ratio with increasing age and body weight (Brain & Frank 1968).

At 6 and 8 weeks, both steroid-treated groups had similar reductions in lung weights compared to control animals. Lung weights relative to body weight were increased in both due to the reduced BW, however. At 10 and 12+ weeks, the Group 2 animals with *P. carinii* had lung weights similar to Group 1 ratios. There was a trend toward lower lung weights and LW/BW ratios in the Group 3 animals without *P. carinii*, but these were not significantly different compared to Group 2. Dry weights were

Table 1. Changes in lung weight/body weight ratio

Weeks	Groups					
	1. Control		2. Steroid-P. carinii		3. Steroid-TMP-SMZ	
	Lung weight (gm) (LW)	LW × 100 body weight	Lung weight (LW)	LW × 100 body weight	Lung weight (LW)	LW × 100 body weight
0	1.42 (0.06)	0.53 (0.02)	—	—	—	—
6	1.91 (0.27)	0.44 (0.06)	1.18 (0.06)*	0.06 (0.03)	1.39 (0.09)*	0.63 (0.04)
8	2.10 (0.06)	0.49 (0.02)	1.69 (0.08)*	0.73 (0.04)‡	1.43 (0.06)*†	0.63 (0.08)*
10	1.73 (0.10)	0.38 (0.02)	2.15 (0.35)	1.15 (0.23)*	1.38 (0.16)	0.62 (0.09)*
12+	2.04 (0.09)	0.38 (0.02)	1.93 (0.17)	0.87 (0.05)*	1.46 (0.09)	0.74 (0.03)‡

Results expressed as arithmetic mean ± SE for 3–5 animals.
* Versus Group 1, $P<0.05$.
† Versus Group 2, $P<0.05$.
‡ $P=0.058$, *vs* Group 1.

similar in all three groups at all time points (data not shown). Wet to dry ratios were higher in the animals with *Pneumocystis* compared to Group 3 animals but the differences were not significant (2.13 ± 0.44 (SE) *vs* 1.74 ± 0.29 (SE) at 10 weeks and 2.43 ± 0.38 (SE) *vs* 1.79 ± 0.53 (SE) at 12 weeks).

Other organ weights

Other organ weights, like body weight, were significantly reduced in both steroid-treated animals at all time points. Unlike the increase in lung weights with time in the animals with *P. carinii*, other organ weights either remained constant (heart, right kidney) or declined slightly with increasing duration of steroid treatment (spleen, liver). Differences in other organ weights between the two steroid-treated groups were not significant.

Pressure-volume studies

Compared to the age-matched controls in Group 1, both the steroid and steroid-TMP-SMZ groups showed reduced lung volume, or V_{max} (17.5 ± 0.4 (SE) ml *vs* 13.6 ± 1.0 (SE) ml (Group 2) and 11.6 ± 0.8 (SE) ml (Group 3), at 8 weeks, $P<0.05$ for both groups). Since body, lung and other organ weights were also reduced, these reductions in lung volume must be interpreted with reference to the steroid effects on general somatic growth. Lung volumes per body weight were in fact increased in the two steroid groups compared to Group 1 (40.6 ± 2.0 (SE) *vs* 57.5 ± 7.0 (SE) and 50.8 ± 4.2 (SE), at 8 weeks), suggesting that steroid retardation of general body growth was greater than the effects on lung volume. Lung volumes normalized to the calculated dry lung weight, a better method for referencing lung volume changes to actual lung tissue mass (Mitzner *et al.* 1982), indicated that lung volumes/dry weight were not significantly different in any group from 6–12+ weeks (Table 2). Thus, although steroids resulted in reduced absolute lung volume, neither steroid therapy nor *P. carinii* infection significantly reduced volume per lung mass in this study.

Average pressure-volume curves for the three groups at 6, 8, 10 and 12+ weeks, with volume normalized as percentage of 'vital capacity' or V_{max}, are shown in Fig. 3. The major effect of *P. carinii* infection was a flattening of the pressure-volume curve at 8, 10 and 12 weeks but not at 6 weeks (despite histological evidence (1+ to 4+) of *P.*

Table 2. Changes in lung volume

	Groups		
Weeks	1. Control	2. Steroid-P. carinii	3. steroid-TMP-SMZ
6	12.2 (1.3)	18.4 (3.7)	16.6 (2.4)
8	13.9 (1.2)	18.4 (2.4)	13.2 (2.4)
10	12.7 (2.0)	12.0 (0.4)	13.8 (0.1)
12+	14.7 (2.0)*	13.4 (2.0)	12.4 (5.6)*

Results expressed as mean ± SE for V_{max} (ml)/dry lung weight (g) for groups of 3–5 animals.

* $n = 2$.

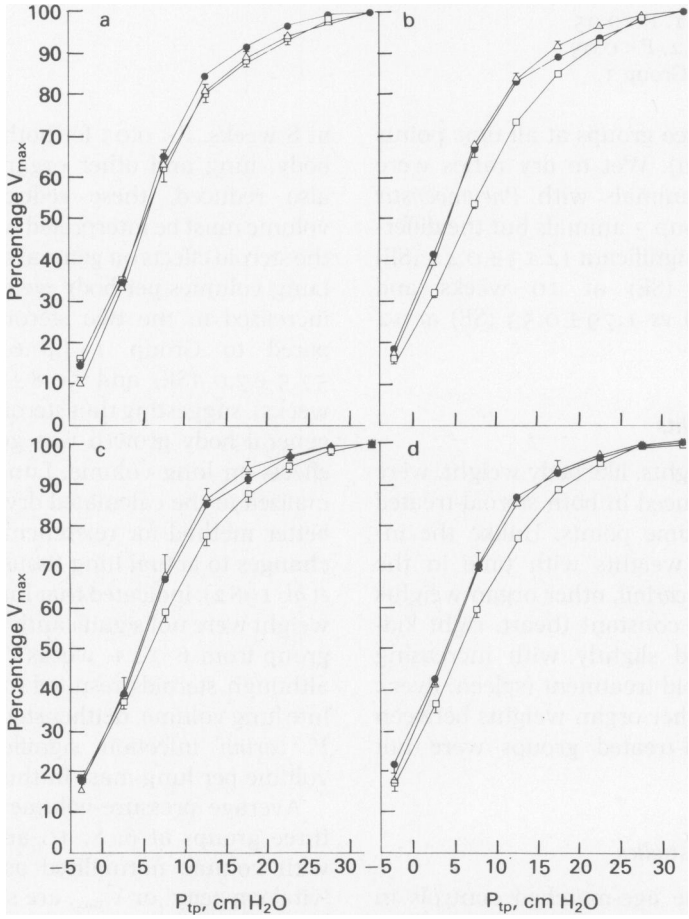

Fig. 3. Respiratory system pressure–volume (P–V) curves of all three groups of animals, from 6 to 12+ weeks after beginning steroids. *a*, 6 weeks; *b*, 8 weeks; *c*, 10 weeks; *d*, 12 weeks. Group 1 (control); □, Group 2 (steroid) with *P. carinii*; and △, Group 3 (steroid-TMP-SMZ). Symbols represent mean for 3–5 animals. Bars indicate 1 SE.

carinii, Fig. 2). Steroid treatment, although it resulted in reduced absolute lung volumes, did not appear in this study to alter the shape of the P–V curve of the Group 3 animals receiving prophylaxis for *P. carinii* compared to age-matched controls. The shape of the deflation limbs of the P–V curves is also indicated by the percentage of V_{max} remaining at different pressures during deflation from +32.5 cm H_2O. The percentages of V_{15}, 10 and 5 were significantly lower in the steroid-treated animals with *P. carinii* than controls from 8–12 weeks. Differences in percentage V_{10} were significant between the two steroid groups at 8, 10 and 12–14 weeks (Fig. 4). Only percentage V_{15} at 6 and 8 weeks were different in the TMP-SMZ animals compared to controls.

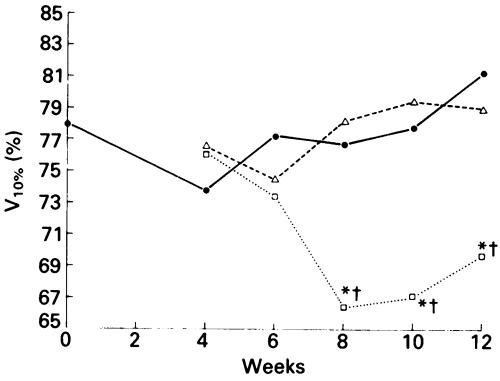

Fig. 4. Deflation volumes remaining at +10 cm H_2O as percent of V_{max} in the three groups. Symbols are for the same Groups as Fig. 4. * Significantly different from Group 1, $P<0.01$; † significantly different than Group 3, $P<0.01$.

Specific respiratory system compliances were calculated for the deflation curves between +2.5 and +5.0 cm H_2O and were lower in the two steroid groups compared to controls as expected because of the differences in absolute lung volumes. Differences in respiratory system compliance between the two steroid groups with and without *P. carinii* were not significant at any time period.

Chest radiographs, Ga-67 scans and activity: Only three of 11 animals with histological evidence of *P. carinii* were interpreted as showing positive radiographs without knowledge of the treatment groups. One of these animals had 3+ and two had 4+ histological grading. The radiographs of animals with

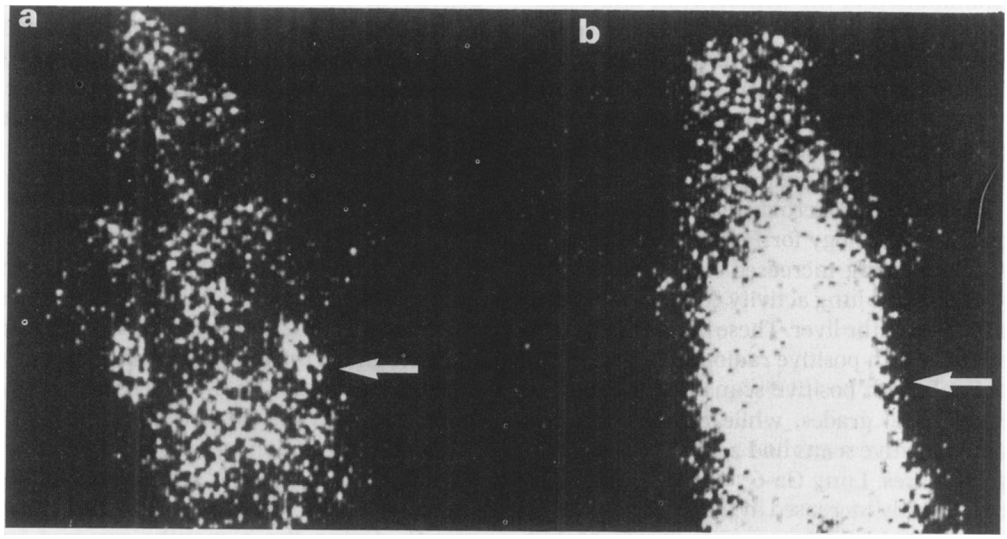

Fig. 5. Ga-67 scintiscans of a control animal (a) and a steroid-treated animal with 4+ *Pneumocystis carinii* (b), both at 10 weeks of study. The control scan shows maximal uptake in the liver and spleen and a clear difference between lung and liver at the level of the diaphragm (indicated by arrow). With *P. carinii*, there is marked increase in lung activity which cannot be separated from liver activity below the diaphragm.

Table 3. Gallium-67 activity

Time (weeks)	Group*	*P. carinii* Score		Lung
8	1-C	—	3	2.24 (1.30)
	2-S	3+,3+,3+	3	8.93 (3.78)
	3-TMP-SMZ	—	5	2.50 (0.67)
10	1-C	—	5	2.79 (1.06)
	2-S	3+,3+,4+,4+	4	4.30 (0.58)
	3-TMP-SMZ	—	3	3.13 (1.47)
12+	1-C	—	4	1.72 (0.47)
	2-S	2+,3+,4+,4+,4+	5	7.09 (6.23)
	3-TMP-SMZ		3	3.42 (1.27)

* 1-C: controls; 2-S: steroid-animals with P. carinii; 3-TMP-SMZ: steroid animals on trimethoprim-sulfamethoxazole prophylaxis.

Results expressed as arithmetic mean ± SE of

$$\frac{^{67}\text{Ga cpm per gram tissue wet weight}}{^{67}\text{Ga ct/min per ml whole blood}}$$

for groups of 3–5 animals.

P. carinii showed patchy infiltrates associated with a generalized increase in density in both lung fields which obscured the heart border. In Group 3 (steroid-TMP-SMZ), a single animal with a positive radiograph was seen, with negative histopathology for *P. carinii*. Examination of the hematoxylin and eosin-stained lung section on this animal revealed acute inflammatory changes. One animal in Group 3 also had evidence of low grade *P. carinii* infection (1+) but a negative chest radiograph and lung scan. No control animals had positive radiographs or scans.

Ten of the 12 steroid-treated animals with positive pathology for *P. carinii* had positive scans showing increased lung uptake (Fig. 5), defined as lung activity equal to or greater than that of the liver. These included all three animals with positive radiographs. All of the animals with positive scans had 3+ or 4+ histological grades, while the two animals with negative scans had 2+ and 3+ histological scores. Lung Ga-67 tissue activity was consistently increased in the animals with *P. carinii* compared to controls (Table 2), but there was no significant relationship between intensity of *P. carinii* infection (3+ versus 4+) and Ga-67 activity expressed as ct/min/gram wet or dry lung weight in this study but group sizes were small. Three of 12 of the scans of the animals on TMP-SMZ prophylaxis also showed slightly increased uptake, despite negative histopathology for *P. carinii*. Although the mean lung Ga-67 activity in the pneumocystis animals was consistently higher, the differences in mean activity between the two steroid-treated groups did not reach statistical significance, due to the variability in ^{67}Ga-activity despite similar intensity of *P. carinii* infection.

Discussion

Relatively little information is available on how specific infections alter lung mechanics (Somerson *et al.* 1971; Stokes 1985) and these studies in the rat model of *Pneumocystis carinii* provide new data on the lung injury associated with this organism.

The interpretation of respiratory system changes with *P. carinii* is complicated by the effects of both corticosteroids and lung growth during the 3 months required for provocation of the latent infection in this model. For this reason, both age-matched (Group 1) and steroid-treated animals

(Group 3) without *Pneumocystis* were included as controls.

We observed no significant changes in the shape of the normalized P–V curve from 0–12+ weeks of the study in the Group 1 animals, consistent with previous results in the older, growing rat (Nardell & Brody 1982). However, corticosteroid administration resulted in retardation of both lung and somatic growth. This led to smaller lung mass and absolute lung volumes in both steroid groups, independent of the effects of *P. carinii*. Pressure–volume curves of the Group 3 steroid animals without *P. carinii* resembled the control curves in shape when corrected for the volume differences and showed no significant change with increasing time on corticosteroids, in contrast as a previous study indicating slight lung recoil changes with chronic steroid administration in the rat (Picken *et al.* 1974).

P. carinii infection after 6 weeks on steroids was associated with flattening of the normalized P–V curve and decreased deflation stability (Figs 3 and 4). Although we did not separate the pressure–volume characteristics of the lungs and chest wall, the highly compliant chest wall makes only a small contribution to the total respiratory system P–V curve (Lai & Hildebrandt 1978) and these changes are consistent with increased lung recoil. Such a shift could result either from altered lung surfactant activity or altered tissue mechanical properties (Mitzner & Permutt 1981; Nardell & Brody 1982). The histology of *P. carinii* pneumonia in the rat shows an abundance of cysts, foamy debris, and inflammatory cells filling the alveolar spaces with minimal interstitial reaction (Walzer *et al.* 1980). This could disrupt the alveolar surface layer and contribute to changes in lung recoil. Bronchoalveolar lavage from rats with *P. carinii* also demonstrates a significant decrease in phospholipid content (Kernbaum *et al.* 1983), primarily in phosphotidylcholine, the major lipid component of surfactant (Sheehan *et al.* 1984). This decrease is particularly striking because chronic steroid administration results in a marked increase in lavage phospholipids in the absence of *P. carinii* infection (Sheehan *et al.* 1984). Whether this decrease in phospholipid reflects a decrease in surface active properties of surfactant is unknown but such a change could also explain the P–V changes we observed. Altered lung alveolar surface activity could also contribute to formation of oedema (Albert *et al.* 1979; Yoneda & Welzer 1981) in Pneumocystis pneumonia.

This study and previous clinical reports (Turbiner *et al.* 1978; Coleman *et al.* 1984) indicate that gallium-67 scintigraphy is a more sensitive method than radiography for detecting *P. carinii* pneumonitis, although both are nonspecific. Significant histopathological evidence of *P. carinii* was present in most animals from 8–12 weeks without definite radiological abnormality. In part, this is due to technical factors because subtle radiographic changes are difficult to recognize in magnification radiographs made at rapid respiratory rates in pneumonia. This also agrees with histological studies which indicate that the intensity of the host's inflammatory response (which presumably contributes to radiographical changes) lags behind the appearance of *P. carinii* organisms within the alveoli (Walzer *et al.* 1980).

Gallium-67 has not been used previously in the study of experimental lung infections. Ga-67 accumulates in inflammatory sites largely due to nonspecific factors, including altered vascular permeability and binding of Ga-67 to intracellular iron-binding proteins (eg. lactoferrin) elaborated at sites of inflammation (Tsan 1980; Tzen *et al.* 1980; Weiner *et al.* 1981). Thus, the positive Ga-67 scintiscans (as well as increased lung weights) are consistent with altered lung vascular permeability secondary to injury by *P. carinii*. Changes in permeability also were suggested by the histological observation of Yneda & Walzer (1980) who observed attachment of organisms to type I alveolar cells, followed by evidence of increased permeability of the alveolar-capillary membrane to horseradish peroxidase. It also is possible that *P. carinii*

induces release of iron-binding proteins by inflammatory cells, further contributing to increased ^{57}Ga tissue activity with this infection.

Although the numbers of animals were small in this study, there does not appear to be a clear correlation between the presence of *P. carinii* in the lung and Ga-67 activity. In AIDS patients, Coleman *et al.* (1984) have found significant numbers of organisms on bronchoalveolar specimens without lung gallium uptake. Further studies in the rat model may help clarify the factors that affect Ga-67 uptake in this infection.

Acknowledgements

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