ACUTE EFFECTS OF BREATHING INERT DUST PARTICLES AND OF CARBACHOL AEROSOL ON THE MECHANICAL CHARACTERISTICS OF THE LUNGS IN MAN. CHANGES IN RESPONSE AFTER INHALING SYMPATHOMIMETIC AEROSOLS [1]

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(Submitted for publication June 3, 1957; accepted July 24, 1958)

Some acute physiological effects of inhaling fine particulate matter on respiration have been previously described (1–11). In those studies, comparisons were made between some respiratory responses to dust particles and carbachol aerosol. The response-preventive effect of sympathomimetic aerosols was pointed out. However, an analysis of the effect of these agents on pulmonary mechanics was not possible because suitable methods were not available at that time.

The present study is an attempt to characterize, using a limited number of subjects, the nature of the response of the lungs to inhalation of fine inert particles by using methods of measurement which have been recently developed, some in this laboratory. The effects upon the mechanical characteristics of the lungs, in man, of inhaling dust particles and carbachol aerosol, and the effects after sympathomimetic aerosols, have been investigated during the present study. We did not have an opportunity to use an electron microscope for study of particle size, and did not expose large numbers of subjects to inhalation of particulate matter.

Because some of the methods are quite new, information regarding spontaneous variation, or response to a pharmacologically inactive aerosol, such as distilled water, has not yet been published. The current status of these control measurements will be mentioned in the section on results.

[1] This investigation was supported in part by a research grant (RG-5085) from the National Institutes of Health, United States Public Health Service.

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METHODS

All measurements were made with the subject sitting. The plethysmographic method was used for determination of airway resistance (12), and thoracic gas volume at resting level (13, 14). Lung compliance and total pulmonary resistance were determined using the esophageal pressure method (15). Photographic records of these factors in response to inhalation of charcoal powder are shown in Figures 2 and 3. Pulmonary tissue resistance was determined by subtracting airway resistance determined plethysmographically from pulmonary resistance determined by the esophageal pressure method (16, 17). The arrangement of apparatus and accuracy of measurement are described (16, 17). Lung volumes were measured by means of a recording spirometer (18), and corrected to body temperature, pressure and saturation (BTPS).

Aerosols were administered using a small laboratory aerosol generator, D 30[1], which normally produces particles having a mean diameter of 0.04 μ, and maximal diameter of 0.5 μ (19). Powders were dispersed by a slow air stream passing through a three flask elutriator system (Figure 1) and breathed from a long glass tube directed into the mouth. Carbachol (Merck) solution (20) was used. The sympathomimetic drug used was a mixture of isoproterenol, cyclopentamine, and procaine in 80 per cent propylene glycol (Aerolone Compound®, Lilly). The fine particles which were breathed were of relatively insoluble material: Those which consisted of carbon particles were coal dust, activated charcoal (U.S.P., Merck), and India ink, diluted one to one, filtered three times, and aerosolized. Calcium carbonate particles (precipitated powder, U.S.P., Baker) were delivered from an aqueous suspension by an aerosol generator or from a dry flask by elutriation. Aluminum powder (McIntyre) of the type inhaled to prevent silicosis was used. Particles in the air stream were not seen by ordinary room light, but were visible by the Tyndall effect. In two cases, the amount of dust administered was measured by comparing the receptacle's weight before and after the experiment. The amount of coal dust inhaled was found to be approximately 10 mg. and of calcium carbonate 5 mg. for each two minute period of inhalation.

Physiological measurements were recorded in each of five successive states: *A.* during a control period; *B.* after breathing carbachol aerosol or a dust; *C.* after a period of waiting to determine the duration of response, or after a repetition of dust exposure to enhance the effect, or instead, immediate progression without delay to *D;* *D.* after breathing a sympathomimetic aerosol; *E.* after again breathing the previous carbachol aerosol or dust particles at the same concentration and for the same number of breaths.

To obtain accuracy and reproducibility, each physiological measurement was repeated several times. The rate at which the series of procedures could be carried out on any given subject was limited by the large number of measurements, requiring about 20 minutes for completion in each of the five successive states, rather than by any attempt to follow a rigid time schedule. The way in which the experiment progressed was as follows: *A.* Control measurements were made. *B.* The duration of dust exposure, 10 to 20 breaths, required about one to three minutes. Lung compliance and pulmonary resistance during quiet breathing were measured. The body plethysmograph was closed, and airway and tissue resistance and thoracic gas volume measurements (panting) were made at a mean time of eight minutes after exposure. Thoracic gas volume was then measured at resting respiratory level (functional residual capacity). The plethysmograph was reopened at a mean time of 13 minutes after exposure, and spirometer recordings made. Series C, D and E each required corresponding amounts of time (about 20 minutes) for inhalation and measurement.

RESULTS

Some physical characteristics of the subjects are listed in Table I. Measurements on these subjects of lung volumes, alveolar gas uniformity, and pulmonary mechanics prior to dust exposure were within normal limits. The first experiments (Subjects L.D. and A.D.) were performed with low concentrations of carbachol, aerosolized. A few breaths were given, followed by measurements of airway resistance and thoracic gas volume, then more breaths. Finally a 2 per cent solution was adopted for use (Subjects L.D., P.K. and R.A.), and measurements were begun of subdivisions of lung volume, lung compliance and pulmonary tissue resistance. The mean values obtained on each subject are listed in Table II. After the series of experiments with carbachol was completed, a series of experiments with inert dust particles was begun. The results of these experiments are listed in Table III.

TABLE I

Some physical characteristics of the subjects

Subject	Age	Sex	Height	Weight
	yrs.		*cm.*	*Kg.*
A. D.	33	M	189	91
R. A.	32	M	166	73
P. K.	32	M	177	74
R. J.	30	M	183	75
L. D.	63	M	179	86

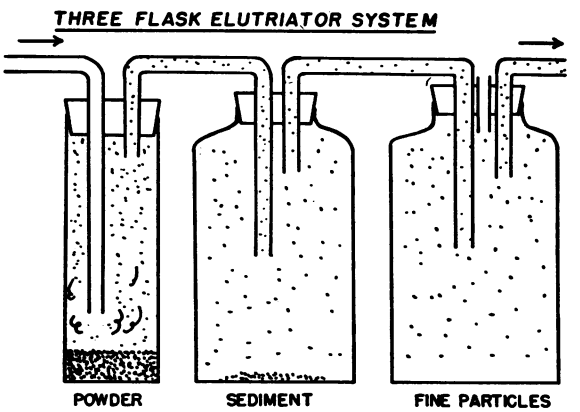

FIG. 1. METHOD OF DELIVERING DRY POWDERS FOR INHALATION FROM A SYSTEM OF FLASKS

The larger particles are allowed to settle out before inhalation.

To evaluate the significance of an apparent change, one must take into consideration not only the mean values, listed in the tables, but also the variation of individual measurements from the mean, variations of response in individual subjects on different occasions, some knowledge of the past history of the subject, his day to day variations of airway resistance, the amount of variation to expect spontaneously or from the mere procedures themselves on similar subjects, and any factors that may systematically change the results.

Normal subjects in this laboratory have shown no significant spontaneous trend of airway resistance measured at 20 minute intervals over periods of two hours, although control values vary slightly from day to day for unknown reasons. Such subjects do not show changes after inhaling water aerosol from a hand nebulizer or after doing vital capacity maneuvers. They show a slight decrease of resistance after receiving recognized "bronchodilator" drugs, or a slight or moderate increase of airway resistance after inhaling considerable doses of histamine aerosol (this must be

TABLE II

Changes in the mechanical characteristics and subdivisions of lung volume after breathing carbachol (CCh) aerosol before and after sympathomimetic aerosol (dilator) *

Subject	Condition	Breaths	Time†	C_L	R_L	R_A	R_{tis}	FRC	ERV	RV	IC	VC	TLC
		no.	*min.*	*L./cm. H_2O*	*cm. H_2O / L./sec.*	*cm. H_2O / L./sec.*	*cm. H_2O / L./sec.*	*L.*	*L.*	*L.*	*L.*	*L.*	*L.*
L. D.	Control					1.33		4.10					
	CCh ½%‡	6	0			1.92§		4.30					
		6	8			2.35§		4.02					
	Dilator	10	18			1.09§		4.10					
	CCh ½%	6	28			1.20		3.98					
L. D.	Control					1.62		4.21					
	CCh 1%	10	0			1.82		4.31					
		10	13			2.12§		4.43					
		10	21			2.56§		3.89					
		10	32			3.07§		3.70					
	Dilator	12	40			1.21§		4.61					
		12	48			1.37		4.73					
	CCh 1%	12	58			1.48§		4.61					
			70			1.58		4.80					
			225			1.54		4.68					
A. D.	Control			0.21		0.90		3.93	2.28	1.65	4.21	6.43	8.14
	CCh 1%	10	0	0.18		0.76§		3.80					
		10	21			0.84		3.95					
		10	43			0.79		4.04	2.20	1.84	4.05	6.15	8.09
	Dilator	10	57	0.22		0.46§		4.10					
		10	68	0.24		0.34§		4.20	2.12	2.08	4.40	6.49	8.60
	CCh 1%	10	87	0.36		0.32§		4.30					
L. D.	Control			0.19	2.16	1.77		5.21	1.86	3.35	2.77	4.76	7.98
	CCh 2%	10	0	0.14	2.52	2.05§		5.00	1.80	3.20	2.42	3.84	7.42
		20	12	0.17	3.30	2.50§							
		20	25										
	Dilator	20	38	0.34	1.27	1.16§		5.49	1.86	3.64	2.35	4.78	7.84
		10	56	0.33									
	CCh 2%	10	71	0.30	1.62	1.57§		5.85					

* Abbreviations are as follows: C_L, dynamic compliance of the lungs; R_L, pulmonary resistance; R_A, airway resistance; R_{tis}, pulmonary tissue resistance ($R_L - R_A$).

Thoracic gas volume subdivisions are abbreviated as follows: FRC, functional residual capacity; ERV, expiratory reserve volume; RV, residual volume; IC, inspiratory capacity; VC, vital capacity; TLC, total lung capacity.

Resistances were measured over the range from zero to one-half liter per second of inspiratory airflow while the subject was panting. All readings were from films, except for Subjects A. D. and L. D., where values for CCh 1 per cent and CCh ½ per cent were read from direct scales.

† Elapsed time after the onset of the first inhalation.

‡ Per cent concentration of CCh in distilled water.

§ Airway resistance values which were significantly greater or less than the control value ($p < 0.05$).

done with caution). Airway resistance values in normal subjects are inversely related to the lung volume at which they are measured. In these studies, the lung volume did not change during the procedure.

A detailed analysis of physiological measurements, particularly airway resistance, made on Subject R.A. will serve to illustrate spontaneous variation of individual values, statistical variation about the mean, variation of values after exposure to dust, day to day variations of resistance, variations of responsiveness of the subject on different days, and the relative degree of change of the various physiological factors under different circumstances.

Subject R.A. changed from control values of airway resistance 1.65, 1.06, 0.68, 1.35 and 0.82 (mean, 1.11) to values of 3.83, 2.69, 2.90 and 3.18 (mean, 3.15) immediately after exposure to carbachol 20, 10 and 10 breaths over 6 minutes. In this case the mean difference, 2.04, was significant ($p = 0.0000002$). A slight change of lung compliance (from 0.20 to 0.14) was found. No significant change occurred of the subdivision of thoracic gas volume. After 40 breaths of sympathomimetic aerosol, the airway resistance values were

TABLE II—*Continued*

Subject	Condition	Breaths	Time†	C_L	R_L	R_A	R_{tis}	FRC	ERV	RV	IC	VC	TLC
		no.	*min.*	*L./cm. H_2O*	*cm. H_2O / L./sec.*	*cm. H_2O / L./sec.*	*cm. H_2O / L./sec.*	*L.*	*L.*	*L.*	*L.*	*L.*	*L.*
R. A.	Control			0.20	1.41	1.11	0.30	3.05	1.34	1.72	3.71	4.68	6.76
	CCh 2%	20	0										
		10	3										
		10	6	0.14	3.39	3.15§	0.22	3.00	1.14	1.86	3.06	4.56	6.06
	Dilator	40	28	0.16	1.95	1.64§	0.31	3.03	1.19	1.73	3.46	4.53	6.49
		10	53										
	CCh 2%	20	63	0.20	1.20	1.25	−0.05	2.66	1.37	1.29	3.45	4.72	6.11
P. K.	Control			0.19	2.59	2.09	0.50	3.39	1.95	1.45	3.16	4.77	6.55
	CCh 2%	10	0										
		10	6										
		10	11	0.18	3.35	2.62§	0.73	3.76					
		10	21	0.16	3.62	2.61§	1.01	3.90	1.79	2.11	3.06	4.80	6.96
	Dilator	15	41										
		15	47	0.16									
		10	54	0.20	1.66	1.73	−0.07	3.48	1.92	1.56	3.23	4.80	6.71
			70	0.23									
	CCh 2%	30	73	0.21	1.93	1.60§	0.33	3.60	1.92	1.68	3.06	4.80	6.66
			82	0.22									
R. A.	Control			0.16	1.90	1.56	0.34	3.03					
	CCh 2%	10	0	0.17									
		20	3										
		20	8	0.14	2.35	1.88	0.47	2.96	1.39	1.58	3.34	4.73	6.30
	Dilator	20	36	0.14									
		20	44	0.17	1.54	1.32	0.22	2.74					
		20	65	0.17	1.60	1.19	0.41	2.75	1.41	1.33	3.49	4.82	6.24
	CCh 2%	20	93										
		20	97	0.16	1.63	1.19	0.44	2.97	1.37	1.60	3.49	4.86	6.46

1.18, 1.59, 1.93, 1.48 and 2.03 (mean, 1.64). The difference from the control values was small but probably significant ($p = 0.02$). After carbachol, 20 breaths, the airway resistance was 1.74, 0.96, 0.89, 0.92 and 1.72 (mean, 1.25). The difference from the control values was not significant. The compliance, tissue resistance, and subdivisions of thoracic gas volume showed no change or slight changes which were probably not significant. Excursions of total pulmonary resistance followed airway resistance closely. Two days later, the same subject showed no significant increase of airway resistance after 10, 20 and 20 breaths of carbachol (mean airway resistance before carbachol, 1.56; after carbachol, 1.88; $p = 0.27$).

This same subject, R.A., was exposed on a different day to activated charcoal powder in the inspired air stream. Photographic records of airway resistance, pulmonary resistance, lung compliance and thoracic gas volume at resting level (FRC) are shown in Figures 2 and 3. The control airway resistance values were 0.99, 1.65, 1.38, 1.76 and 1.63 (mean, 1.48). After inhaling 15 breaths of activated charcoal powder, a maximum value of pulmonary resistance of 13.7 was obtained. The plethysmograph was then closed, and the airway resistance values were 4.58, 7.80, 4.76, 3.21 and 3.99 (mean, 4.87). The difference from control values was highly significant ($p = 0.0007$).[4] There were changes of compliance, vital capacity and pulmonary tissue resistance as well (Table III).

At the time when the resistance value was highest, the subject had tightness of the chest, dyspnea, cough and wheeze but no stridor audible at the throat. The subjective symptoms improved rapidly. Yet 26 minutes after exposure, airway resistance values were 2.83, 2.62, 3.94, 2.79 and 1.67 (mean, 2.77), and the difference from the control values was still significant ($p = 0.00001$). After 30 breaths of sympathomimetic aerosol his airway re-

[4] Another subject, A.D., was subsequently exposed to inhalation of charcoal powder, and airway resistance was found to change from 1.00 ± S.E. 0.061 to 1.43 ± S.E. 0.058 immediately after exposure. Twenty minutes later, the airway resistance was 1.29 ± S.E. 0.060. These changes were not as great as those of R.A., but were statistically significant and in the same direction.

TABLE III

Changes in the mechanical characteristics and subdivisions of lung volume after breathing dust particles before and after dilator aerosols *

Subject	Condition	Breaths	Time	C_L	R_L	R_A	R_{tis}	FRC	ERV	RV	IC	VC	TLC
		no.	*min.*	*L./cm. H_2O*	*cm. H_2O / L./sec.*	*cm. H_2O / L./sec.*	*cm. H_2O / L./sec.*	*L.*	*L.*	*L.*	*L.*	*L.*	*L.*
L. D.	Control			0.20	1.69	1.45	0.24	4.85	1.80	3.05	2.44	4.31	7.29
	India ink	25	0	0.21	4.06	2.82‡	1.24	4.32					
			23	0.19	3.06	2.52‡	0.54	4.44	2.05	2.39	2.28	4.41	6.72
			43	0.16									
	Dilator	25	63	0.19	1.33	0.95‡	0.38	5.27	2.19	3.09	2.48	4.59	7.75
	India ink	25	123	0.18	1.90	1.56	0.34	5.20	2.09	3.11	2.53	4.82	7.73
R. J.	Control			0.21	1.85	1.16	0.69	3.84	1.88	1.96	3.75	5.54	7.59
	$CaCO_3$†	10	0	0.19	1.93	1.29	0.64	3.89					
		10	19	0.16	3.17	2.29‡	0.88	3.89	1.83	2.08	3.71	5.46	7.60
	Dilator	20	49	0.22	1.30	1.27	0.03						
		10	69	0.27				3.66	1.86	1.80	3.89	5.68	7.55
	$CaCO_3$†	10	89	0.21	1.29	1.28	0.01	3.89	1.91	1.89	3.84	5.61	7.73
R. A.	Control			0.22	2.19	1.48	0.71	2.73	1.24	1.49	3.71	4.70	6.44
	Charcoal†	15	0	0.14	6.72	4.87‡	1.85	2.93					
			26	0.14	2.88	2.77‡	0.11	2.80	0.90	1.90	2.37	3.70	5.17
	Dilator	15	34	0.18									
		15	45	0.16	1.44	1.34	0.10	2.62	1.37	1.25	3.74	4.71	6.36
	Charcoal†	15	59	0.21	1.67	1.38	0.29	2.77	1.33	1.45	3.06	4.37	5.83
A. D.	Control				0.82	0.84		3.59	2.12	1.47	4.10	6.12	7.69
	Coal dust†	30	0		1.19	1.29‡		3.75	2.22	1.53	4.04	6.26	7.79
		10	30		1.26	1.44‡							
	Dilator	10	45		0.72	0.76							
		10	58		0.63	0.65‡		3.58	2.22	1.36	4.23	6.22	7.81
		10	83		0.43	0.64		3.60					
	Coal dust†	10	134		0.91	0.86		3.59	2.22	1.37	4.21	6.20	7.80
R. A.	Control			0.18	1.59	1.37	0.22	2.88	1.28	1.54	3.26	4.63	6.08
	$CaCO_3$	20	0	0.18	2.18	1.96‡	0.22						
		20	15	0.18	2.13	1.92‡	0.21	2.58					
		20	28	0.19	2.57	2.53‡	0.04	2.87	1.05	1.82	3.40	4.60	6.27
	Dilator	20	50										
		20	84	0.24	1.36	1.50	−0.14	2.62					
		20	128	0.19	1.21	0.72‡	0.49	2.72	1.29	1.44	3.44	4.55	6.16
	$CaCO_3$	20	138	0.24	1.12	1.03	0.09	2.66	1.25	1.41	2.91	4.35	5.57
L. D.	Control			0.19	2.81	2.45	0.36	4.61					
	Water	20		0.25	2.29	2.02	0.28	5.15					
	Saline	20		0.21	2.56	1.92‡	0.64	5.23					
	Aluminum†	6	0	0.20	4.19	3.10‡	1.10	4.91					
		3	14	0.16	5.14	4.17‡	0.97	5.57	1.98	3.59	1.76	4.18	7.33
			58		5.60	3.88‡	1.72	4.87					
	Dilator	20	67	0.26	1.93	1.27‡	0.66	5.01	1.98	3.03	2.43	4.66	7.44
	Aluminum†	6	99	0.21	1.27	1.12‡	0.15	5.31	2.14	3.17	2.50	4.55	7.81

* The abbreviations are the same as those in Table II. All readings are from films except for Subject A. D. (from direct scales).

† Aerosol produced from elutriator flasks containing dry powder, yielding particles less than 5 μ diameter. Remaining aerosols were produced from a liquid suspension to yield only fine particles, less than 0.5 μ diameter.

‡ Values significantly greater or less than control value ($p < 0.05$).

sistance values were 1.49, 1.12, 1.69, 1.17 and 1.24 (mean, 1.34). Following repetition of 15 breaths of charcoal powder, his airway resistance was 1.12, 1.41, 1.98, 1.07, 1.37 and 1.35 (mean, 1.38), and lung volumes and compliance were within the range of control values.

When the same subject was exposed to a different powder, $CaCO_3$, two days later, his control airway resistance values were 1.56, 1.53, 1.42, 1.27 and 1.09 (mean, 1.37), and values after $CaCO_3$ were 2.25, 1.97, 2.70, 1.41 and 1.46 (mean, 1.96). The difference is probably significant ($p = 0.02$). Repeated inhalation of $CaCO_3$ yielded a mean airway resistance of 1.92 and when repeated again it was 2.53. All values after $CaCO_3$, when averaged, yielded a mean of 2.15, which was significantly dif-

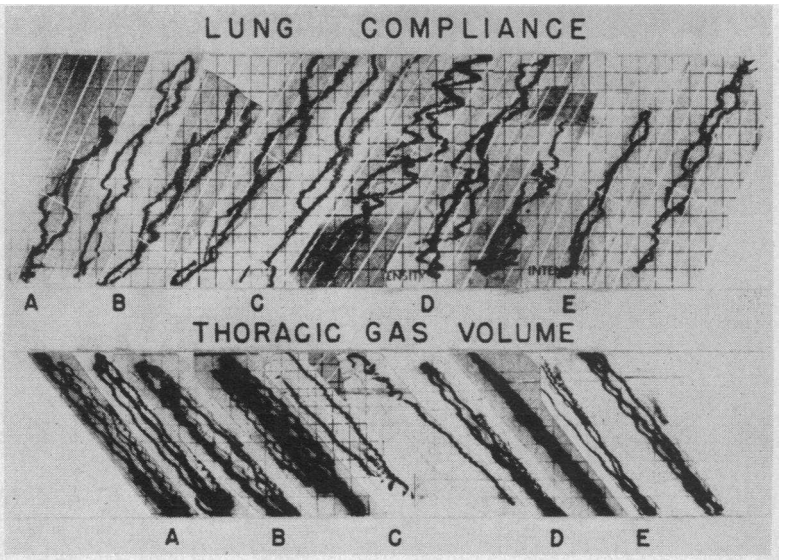

FIG. 2. PHOTOGRAPHS OF CATHODE RAY OSCILLOGRAPH IMAGES, MOUNTED SIDE BY SIDE, SHOWING LUNG COMPLIANCE (ESOPHAGEAL PRESSURE METHOD) AND THORACIC GAS VOLUME AT RESTING EXPIRATORY LEVEL (PLETHYSMOGRAPHIC METHOD) FOR SUBJECT R.A.

Two measurements of each taken during *A.* control period, *B.* after 15 inhalations of activated charcoal powder, *C.* after waiting 26 minutes, *D.* after inhalation of sympathomimetic aerosol, and *E.* after again breathing 15 breaths of the same powder.

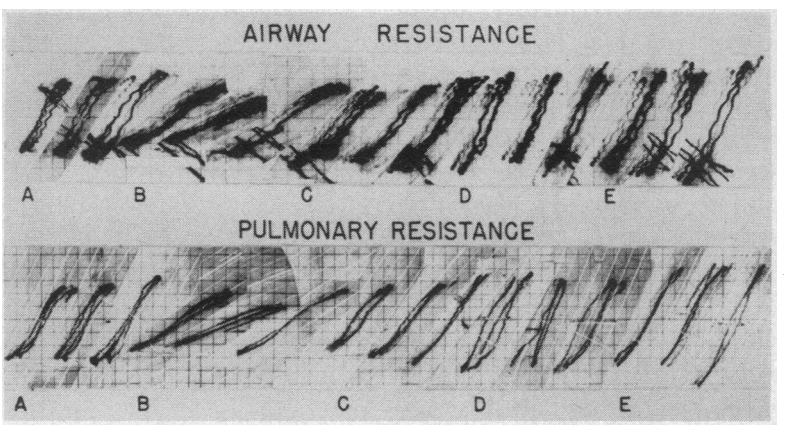

FIG. 3. AIRWAY RESISTANCE (PLETHYSMOGRAPHIC METHOD) AND PULMONARY RESISTANCE (ESOPHAGEAL PRESSURE METHOD) IN SUBJECT R. A.

Three photographs within each period during the same experiment described in Figure 2. There is a pronounced increase in resistance by both methods following inhalation of dust, some spontaneous decrease with time, complete remission after dilator aerosol, and very little effect from administration of dust following the dilator aerosol.

ferent from the control value of 1.37 ($p = 0.000001$).

Thus, a response was obtained on Subject R.A. after carbachol, activated charcoal powder or calcium carbonate particles and consisted principally of an increase in airway resistance. When marked, this was accompanied by increased tissue resistance, decreased vital capacity and decreased

TABLE IV

Group mean values showing the average result of breathing carbachol and different inert dusts before and after sympathomimetic aerosols *

Condition	C_L	R_L	R_A	R_{tis}	FRC	ERV	RV	IC	VC	TLC
	L./cm. H_2O	*cm. H_2O / L./sec.*	*cm. H_2O / L./sec.*	*cm. H_2O / L./sec.*	*L.*	*L.*	*L.*	*L.*	*L.*	*L.*
Control	0.19	1.99	1.41	0.38	3.86	1.86	2.04	3.46	5.13	7.36
Carbachol	0.16	2.80	2.26	0.62	3.92	1.66	2.07	3.19	4.81	6.92
Dilator	0.24	1.42	1.15	0.18	3.92	1.70	2.07	3.39	5.08	7.18
Carbachol repeated	0.24	1.35	1.30	0.14	4.26	1.75	2.05	3.33	5.16	7.11
Control	0.20	1.83	1.46	0.37	3.74	1.69	2.09	3.28	4.93	7.06
All dust	0.17	3.29	2.63	0.66	3.90	1.67	2.22	2.93	4.77	6.81
Dilator	0.21	1.17	1.03	0.13	3.64	1.82	1.99	3.37	5.07	7.18
Dust repeated	0.21	1.36	1.21	0.15	3.90	1.82	2.07	3.18	4.98	7.08

* Values on individual subjects and abbreviations of the headings are listed in Tables II and III.

compliance. After sympathomimetic aerosol, these effects were gone and were not elicited on re-exposure to the original agent.

Other subjects exposed to carbachol were P.K., L. D. and A.D. The other subjects exposed to various types of dust were L.D. (aluminum powder on two different days and India ink aerosol), R.J. (calcium carbonate powder) and A.D. (common coal dust powder and later charcoal powder). One of these subjects, L.D., was given water aerosol and then normal saline aerosol but these failed to produce a response. The mean values of film readings before and after exposure, and after sympathomimetic aerosol and then re-exposure to the agent, are given in Tables II and III. Variations of individual readings from the mean were similar in these subjects to those described above for Subject R.A. Changes of airway resistance statistically different from the control values in individual subjects ($p < 0.05$) are starred. It can be seen that the type of response to these different agents is quite similar in different subjects, although the degree of exposure and magnitude of response varied considerably. The average values for the group are listed in Table IV and Figure 4, and the statistical changes of the group in Table V and Figure 4. The response was characterized by a statistically significant increase of airway resistance and total pulmonary resistance, with possibly significant increase of pulmonary tissue resistance after dust.

Aluminum powder was administered to L.D. (Table VI) resulting in increased airway resistance. A long period was allowed for spontaneous recovery (Figure 5) and then the exposure to aluminum powder was repeated. The initial increase of airway resistance, which had returned almost to normal spontaneously, was reproduced on second exposure. This experiment was done to see whether tachyphylaxis occurred spontaneously after first exposure, thereby preventing response to a later dosage. Tachyphylaxis

TABLE V

Group statistics *

Condition		Changes from control values									
		C_L	R_L	R_A	R_{tis}	FRC	ERV	RV	IC	VC	TLC
CCh	Mean	−0.030	0.76	0.70	0.17	0.02	−0.12	0.21	−0.25	−0.32	−0.23
	S.D.	0.021	0.73	0.67	0.60	0.24	0.07	0.33	0.37	0.42	0.51
	S.E.	0.009	0.37	0.25	0.30	0.09	0.03	0.17	0.19	0.21	0.26
Dust	Mean	−0.024	1.76	1.21	0.56	−0.03	−0.05	0.04	−0.27	−0.15	−0.31
	S.D.	0.036	1.56	1.19	0.56	0.21	0.24	0.42	0.62	0.47	0.62
	S.E.	0.016	0.64	0.49	0.25	0.09	0.11	0.19	0.28	0.21	0.28

* The response of a given subject on a given day was averaged, weighted once, and the change from the control value of the subject determined. These changes were averaged for the group (mean), and standard deviation from the mean (S.D.) and standard error of the mean (S.E.) were computed.

did not occur in this experiment. The data in the tables show that a response to dust inhalation could be brought about again within 10 minutes, 2 hours, or 24 hours after a previous exposure.

DISCUSSION

The factor which changed to the greatest degree after exposure to the agents, carbachol, dust particles or sympathomimetic aerosols, was the airway resistance. Changes of compliance when present were relatively slight and may be attributable to inequal distribution of resistance in different regions of the lung (21). The effect of breathing frequency on pulmonary resistance was not great.[5]

TABLE VI

Changes in the mechanical characteristics of the lungs following an inhalation of aluminum powder, and repetition of the exposure to aluminum powder 85 minutes later *

Subject	Condition	Time	C_L	R_L	R_A	R_{tis}	FRC
		min.					*L.*
L. D.	Control	—	0.23	2.45	2.21	0.24	4.59
	Aluminum	0	0.18	3.54	3.08†	0.46	5.05
	3 L.	21	0.20	3.34	2.57	0.77	4.98
		56		2.63	2.28	0.35	4.65
		75	0.23	2.55	2.30	0.25	4.75
	Aluminum 3 L.	85	0.17	4.86	4.00†	0.86	4.74
	Dilator	98	0.18	2.06	1.32†	0.73	4.98

* Tachyphylaxis was not observed. A fine suspension was produced by elutriation into a 1 L. flask. The airflow was stopped. The subject then inhaled from the flask which had a small inlet vent. This was repeated three times. This way a measured volume (3 L.) of the fine suspension was inhaled.

† Values significantly greater or less than control value ($p < 0.05$).

Changes of thoracic gas volume were slight and inconsistent in direction, except in one case, R.A., after his marked response to inhalation of activated charcoal powder, when the vital capacity was significantly reduced. This may be attributed to complete obstruction of some airways with partial obstruction of others. The pulmonary tissue resistance changed experimentally in some subjects, but the physiological meaning of this change is difficult to interpret at present.

[5] Pulmonary resistances in Subject R.A. during panting and quiet breathing, respectively, were as follows: control, 1.64 vs. 2.57; after carbachol, 5.43 vs. 6.76; after dilator, 2.53 vs. 2.17. Comparable changes were observed on R.A. after charcoal and on L.D. after India ink, indicating that the changes of resistance were relatively independent of breathing frequency.

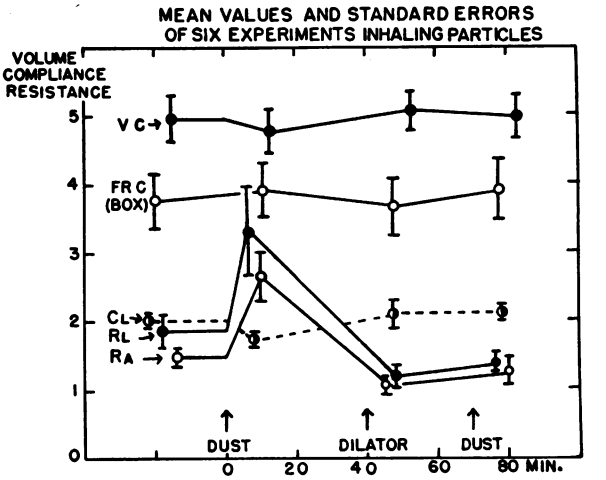

FIG. 4. STATISTICAL ANALYSIS OF THE GROUP OF EXPERIMENTS OF DUST INHALATION

Significant changes in airway resistance (R_A) and pulmonary resistance (R_L), plotted slightly apart to avoid overlap, are shown.

All subjects tested were capable of an "increased airway resistance" response. However the degree of response varied, and without numerous repetitions of the same dust on numerous subjects together with precise measurement of particle size and retention it is not possible to evaluate the

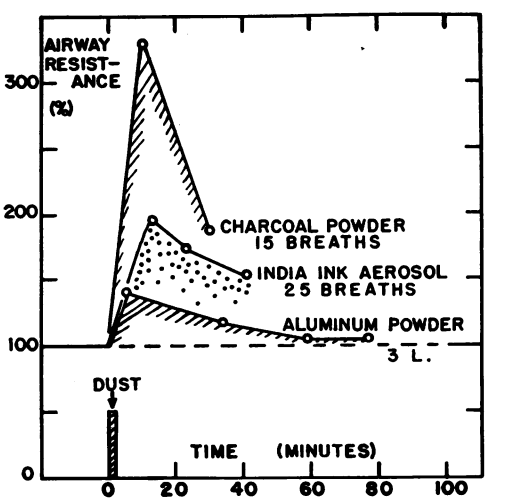

FIG. 5. TIME COURSE OF AIRWAY RESISTANCE CHANGES FOLLOWING INHALATION OF DUST PARTICLES FOR A ONE TO TWO MINUTE PERIOD

The number of breaths or volume inhaled are indicated. Numerical values are listed in Tables III and VI.

dose-response relationship. However, the pattern of the response was sufficiently uniform so that one might suspect that the different agents employed acted by a common but unidentified physiological mechanism.

SUMMARY

1. On five human subjects without chronic respiratory disease, measurements of pulmonary compliance, total pulmonary resistance (esophageal pressure method), airway resistance, pulmonary tissue resistance, and thoracic gas volume (plethysmographic methods) and of lung volume subdivisions (spirometric determinations) were made during a control period before inhalation of small quantities of carbachol micromicellar aerosols and of fine, chemically inert dust particles consisting of calcium carbonate powder, coal dust, activated charcoal powder, aluminum powder and aerosolized India ink.

2. After inhalation of these aerosols, the subjects usually showed a definite increase in airway resistance and pulmonary resistance and sometimes a slight decrease in lung compliance.

3. Sympathomimetic aerosols were administered a few minutes afterwards and the same measurements repeated. They showed that the resistance had fallen below the initial control value and the compliance had increased to the normal control value or had sometimes increased beyond the control value.

4. Following the administration of sympathomimetic aerosols, further inhalations of carbachol aerosol or of dust particles failed to raise the airway resistance above the initial control value and did not significantly reduce the lung compliance.

5. Fifteen to 30 minutes after taking 6 to 25 breaths of carbachol aerosol or of dust laden air, subdivisions of lung volume showed no significant change except in one of five subjects, who had a slight decrease in total lung capacity (mainly at the expense of the inspiratory capacity) on one occasion.

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