

# An analysis of the relationship between airway resistance and spontaneous thoracic gas volume in asthmatic children

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*The relationship between airway conductance ( $G_A$ ) and spontaneous thoracic gas volume ( $V_{TG}$ ) was examined in a series of studies conducted on 10 asthmatic children. Our results showed no consistency in the degree of correlation of these measurements. Under the conditions in which our studies were performed, no significant changes in  $V_{TG}$  occurred after the administration of a Freon-generated bronchodilator aerosol, although there was substantial reduction in airway resistance. Therefore, no benefit was derived from making conductance or resistance measurements specific to thoracic gas volume. Changes in airway resistance in response to a bronchodilator appear to be related to the initial level of resistance.*

During the past decade there has been a rapid growth in technology for measuring pulmonary mechanics. Numerous methods have been devised to permit precise estimation of airway resistance under relatively normal physiologic conditions. The technique most widely used is the total body plethysmographic method of measuring airway resistance and thoracic gas volume as first described by DuBois and associates<sup>1</sup> in 1956.

Briscoe and DuBois<sup>2</sup> showed that a proportional inverse relationship exists between thoracic gas volume and airway resistance in individual subjects who voluntarily changed their lung volume over a wide range. As a consequence,

most workers correct airway resistance ( $R_A$ ) and conductance ( $\frac{1}{R} = G_A$ ) for changes in thoracic gas volume ( $V_{TG}$ ): specific airway resistance =  $R_A \times V_{TG}$ <sup>3, 4</sup> and specific conductance =  $G_A/V_{TG}$ .<sup>3</sup> However, there is still some dispute as to whether this relationship is constant<sup>5, 6</sup> or not.<sup>7, 8</sup>

The present investigation was an attempt to analyze the relationship between airway resistance and thoracic gas volume measurements in asthmatic children tested at spontaneous  $V_{TG}$  levels on numerous occasions over a period of several

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**TABLE I.** Physical characteristics, clinical index, and pulmonary functions of 10 asthmatic children

| Subject No. | Initials | Sex | Age | Race | Height (cm.) | Weight (Kg.) | Clin. index | PEFR              |                     |
|-------------|----------|-----|-----|------|--------------|--------------|-------------|-------------------|---------------------|
|             |          |     |     |      |              |              |             | Average (L./min.) | Predicted (L./min.) |
| 1           | N. C.    | F   | 10  | N    | 139          | 39           | 4           | 175               | 250                 |
| 2           | C. C.    | M   | 7   | C    | 115          | 20.4         | 4           | 110               | 205                 |
| 3           | D. G.    | M   | 9   | C    | 133          | 27.3         | 4           | 165               | 300                 |
| 4           | D. H.    | M   | 11  | C    | 139          | 30.3         | 4           | 220               | 350                 |
| 5           | D. J.    | M   | 12  | C    | 151          | 44.8         | 3           | 330               | 390                 |
| 6           | I. M.    | F   | 8   | N    | 124          | 27.5         | 4           | 180               | 180                 |
| 7           | C. A.    | F   | 12  | C    | 137          | 30.7         | 3           | 240               | 320                 |
| 8           | L. P.    | M   | 8   | C    | 128          | 23.4         | 3           | 180               | 245                 |
| 9           | R. W.    | M   | 11  | N    | 137          | 32.0         | 4           | 170               | 350                 |
| 10          | D. W.    | M   | 11  | N    | 130          | 32.5         | 4           | 145               | 350                 |

Clinical index: 1, seldom wheezes, no incapacitation; 2, occasional wheeze, minimal incapacitation; 3, frequent wheeze, frequent incapacitation; 4, continuous wheeze, frequent incapacitation.

PEFR = pulmonary expiratory flow rate.

months and to ascertain the need for correcting airway resistance or conductance measurements in evaluating the effects of bronchodilator aerosols.

## MATERIALS AND METHODS

Ten asthmatic patients from the Sunair Home for Asthmatic Children served as subjects. Pertinent information on them is shown in Table I. They all had had moderate to severe asthma since infancy.

$R_A$  and  $V_{Tg}$  were measured in a constant volume total body plethysmograph according to the method of DuBois and associates.<sup>1</sup> While the child was panting at a rate of 2 breaths per second, flow ( $\dot{V}$ ) and box pressure ( $P_b$ ) were displayed on a storage oscilloscope. A switch was thrown so that mouth pressure ( $P_m$ ) was plotted against  $P_b$ , and the shutter closed. The slopes of both curves were then read directly from the oscilloscope. Each subject underwent a training period to accustom himself to the box and the procedure required in the measurements. Determination of both airway resistance and thoracic gas volume were always made in triplicate and the results expressed as the mean of the three determinations. Airway resistance was corrected for the resistance of the pneumotachograph-interrupter system (0.5 cm.  $H_2O$  per liter per second). The investigations were carried out over a period of several months. The children were studied only when they were ambulatory and not experiencing severe respiratory distress. Nor were measurements made if they had received bronchodilator therapy within the previous 2 hours.

Response to bronchodilator aerosols was studied on two occasions in each of 10 children. After control measurements of airway resistance and thoracic gas volume were made, two inhalations, spaced one minute apart, of a Freon-generated aerosol containing 0.16 mg. of isoproterenol hydrochloride and 0.24 mg. of phenylephrine bitartrate per valve actuation\* were administered by one of the members of the technical staff. Fifteen minutes following the second inhalation, measurements of  $R_A$  and  $V_{Tg}$  were repeated. The results were compared to those obtained when a placebo aerosol was used.

In order to overcome any fear the children might have of the plethysmograph, a large drawing of the famous American cartoon character, "Snoopy," was placed on the door. It depicts Snoopy on his flying plethysmograph. He is saying, "Climb in, we're off to get the Red Baron." The children were soon calling the plethysmograph Snoopy and were eager to participate in the study. No anxieties were noted in any of the children.

\*Duo-Medihaler supplied by Riker Laboratories, Inc., Northridge, Calif. 91324.

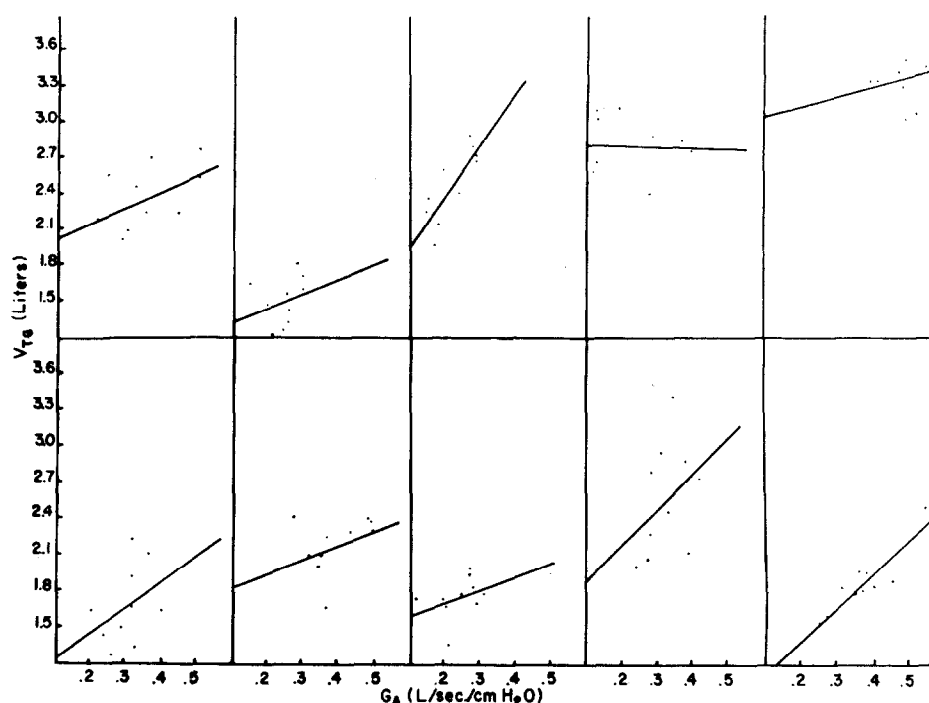


FIG. 1. Regression lines for correlation between airway conductance and spontaneous thoracic gas volume in 10 asthmatic children.

TABLE II. Coefficient correlation ratios for airway conductance and thoracic gas volume in 10 asthmatic children

| Subject No. | C intercept | m Slope | r     | p (for r) |
|-------------|-------------|---------|-------|-----------|
| 1           | 1.88        | 0.13    | 0.47  | > 0.1     |
| 2           | 1.19        | 1.19    | 0.29  | > 0.1     |
| 3           | 1.52        | 4.32    | 0.81  | < 0.01    |
| 4           | 2.81        | -0.09   | -0.40 | > 0.1     |
| 5           | 2.96        | 0.82    | 0.33  | > 0.1     |
| 6           | 1.01        | 2.12    | 0.38  | > 0.1     |
| 7           | 1.72        | 1.13    | 0.39  | > 0.1     |
| 8           | 1.47        | 1.12    | 0.37  | > 0.1     |
| 9           | 1.59        | 2.96    | 0.37  | > 0.1     |
| 10          | 0.83        | 2.75    | 0.90  | < 0.001   |

## RESULTS

Fig. 1 shows the relationship between airway conductance and thoracic gas volume measured on 10 occasions in each of the 10 children. Regression lines were computer drawn from the equation  $Y = mX + c$ . Coefficient correlation ratios calculated for each group (Table II) show no consistency in either degree of correlation, slope, or intercept. In only two instances were  $r$  values statistically significant.

Thoracic gas volume changes in response to the administration of a bron-

**TABLE III.** Effects of aerosols on thoracic gas volume in 10 asthmatic children

| Subject No. | Bronchodilator (BD) |          |         |          | Placebo   |               |
|-------------|---------------------|----------|---------|----------|-----------|---------------|
|             | Trial 1             |          | Trial 2 |          | (Trial 1) |               |
|             | Control             | After BD | Control | After BD | Control   | After placebo |
| 1           | 2,520               | 2,400    | 2,060   | 2,160    | 2,210     | 2,515         |
| 2           | 1,410               | 1,375    | 1,695   | 1,875    | 1,240     | 1,205         |
| 3           | 2,130               | 2,130    | 1,950   | 2,640    | 2,400     | 2,720         |
| 4           | 3,110               | 2,840    | 2,840   | 2,885    | 2,590     | 2,675         |
| 5           | 3,225               | 3,230    | 3,865   | 3,315    | 3,100     | 3,315         |
| 6           | 1,910               | 2,020    | 2,205   | 1,730    | 1,480     | 1,410         |
| 7           | 2,060               | 2,020    | 2,280   | 1,875    | 2,355     | 2,395         |
| 8           | 1,355               | 1,585    | 1,660   | 1,550    | 1,985     | 1,945         |
| 9           | 2,400               | 2,640    | 3,005   | 3,050    | 2,475     | 2,280         |
| 10          | 2,475               | 2,240    | 1,550   | 1,765    | 1,620     | 1,445         |
| Mean        | 2,245               | 2,248    | 2,311   | 2,285    | 2,146     | 2,190         |
| ± SD        | 622                 | 559      | 728     | 633      | 567       | 678           |
| t           | 0.0496              |          | 0.0869  |          | 0.1611    |               |
| p           | N.S.                |          | N.S.    |          | N.S.      |               |

SD = standard deviation; N.S. = not significant.

chodilator aerosol administered on two random occasions and a placebo are shown in Table III. A one-way analysis of variance revealed no statistically significant differences in the control values of thoracic gas volumes, and no changes were evident after the administration of either aerosol ( $F = 0.0999$ ).

A very pronounced decrease in airway resistance occurred following the administration of the bronchodilator aerosol (Table IV) with reductions of 34 and 33 per cent on the two trials. There was absolutely no difference in airway resistance measured before and after administration of the placebo aerosol. Table IV also contains data for the changes in specific airway resistance, conductance, and specific conductance. Correcting for lung volume had no influence on the analysis.

## DISCUSSION

In previous work of which we are aware, the relationship between airway resistance or conductance and thoracic gas volume was studied under conditions in which the patient or subject voluntarily adjusted his lung volume. We have attempted to examine the relationship between conductance and *spontaneous* thoracic gas volume of asthmatic children determined on numerous occasions over a period of several months, when the clinical symptoms were stabilized and the children were not experiencing severe respiratory distress. Analysis of our data (Table II) shows a correlation between  $G_A$  and  $V_{TG}$  in only 2 of the 10 patients. The relationship was not constant in any of the patients, in agreement with the interpretation of Sobol and associates.<sup>8</sup>

Our findings indicate that thoracic gas volume is not stable, as originally thought, but may vary over a rather large range even though resistance remains relatively unchanged. It is unlikely that these variations were artifacts produced by children breathing at higher than normal functional residual capacity (FRC), because the fluctuations occurred randomly throughout the study. Neither is it

TABLE IV. Four methods of expressing changes in airway dynamics in response to aeros

| Method          | No. | Bronchodila                |                           |            |
|-----------------|-----|----------------------------|---------------------------|------------|
|                 |     | Trial 1                    |                           |            |
|                 |     | Control<br>(mean $\pm$ SD) | After BD<br>Mean $\pm$ SD | $\Delta$ % |
| R <sub>A</sub>  | 10  | 3.8 $\pm$ 1.1              | 2.5 $\pm$ 0.8             | -34        |
| SR <sub>A</sub> | 10  | 8.7 $\pm$ 3.7              | 5.3 $\pm$ 1.3             | -39        |
| G <sub>A</sub>  | 10  | 0.28 $\pm$ 0.09            | 0.45 $\pm$ 0.15           | +61        |
| SG <sub>A</sub> | 10  | 0.13 $\pm$ 0.05            | 0.2 $\pm$ 0.05            | +54        |

likely that the high  $V_{TG}$  values we observed were related to trapped air. Differences in lung volumes when measured plethysmographically and by helium dilution have been reported<sup>9-11</sup> and are thought to be trapped air. Rodgers and co-workers<sup>10</sup> found that after use of a pressurized bronchodilator the plethysmographic  $V_{TG}$  decreased to that of the helium-measured FRC, indicating that the original differences in volume were due to noncommunicating or trapped air. However, in our studies no statistically significant reduction in  $V_{TG}$  occurred after the use of the pressurized bronchodilator aerosol (Table III), thus arguing against the presence of trapped air in these children.

The literature to date contains little information about plethysmographic measurements of airway resistance in children. Briscoe and DuBois<sup>2</sup> reported a mean  $R_A$  of 2.63 in 8 normal children, and Bachofen and associates<sup>12</sup> also found an  $R_A$  of 2.63 in 12 normal children. Our own data, which consist of sixty measurements of airway resistance in 10 asthmatic children, disclose a mean  $R_A$  of  $3.51 \pm 1.46$ . The range, which extends from 1.7 to 9.7, clearly shows that, even by a sensitive measurement, airway resistance can be normal in asthmatic children. This does not mean the lungs are normal; rather, it indicates the resistance of the large airways is in the normal range. There could still be considerable increased peripheral resistance which will not be detected with this technique. Peripheral resistance can cause air trapping due to collapse of bronchioles in which intraluminal pressure is less than alveolar pressure. Careful measurement of  $V_{TG}$  before and after a bronchodilator aerosol may uncover the presence of increased peripheral resistance. Thus bronchodilators may still be of value in reducing obstruction even though  $R_A$  is normal, though admittedly this is more likely to be the case in patients with chronic obstructive pulmonary disease. Finding  $R_A$  in the normal range should not be accepted alone as indicating an absence of obstructive disease.

Bronchodilator response is affected by a number of variables such as depth of inhalation, length of breath holding, positioning of the aerosol device in mouth, and position of tongue.\* If these are kept relatively constant, as was the case in this study, the response is related to the level of resistance, thus following the law of initial values.<sup>13</sup> This is illustrated in Fig. 2, which was computer drawn from our own data. Remarkable agreement was noted in the responses to

\*McIlreath, Busser, Strick, and Goldberg: Unpublished data.

treatment

| (BD)                       |                 |            | Placebo (Trial 1)          |                 |            |
|----------------------------|-----------------|------------|----------------------------|-----------------|------------|
| Trial 2                    |                 |            |                            |                 |            |
| Control<br>(mean $\pm$ SD) | After BD        |            | Control<br>(mean $\pm$ SD) | After placebo   |            |
|                            | Mean $\pm$ SD   | $\Delta$ % |                            | Mean $\pm$ SD   | $\Delta$ % |
| 3.6 $\pm$ 1.1              | 2.4 $\pm$ 0.6   | -33        | 3.6 $\pm$ 1.8              | 3.6 $\pm$ 1.8   | 0.0        |
| 8.1 $\pm$ 2.7              | 5.2 $\pm$ 1.2   | -36        | 7.7 $\pm$ 5.0              | 7.7 $\pm$ 4.5   | 0.0        |
| 0.29 $\pm$ 0.08            | 0.44 $\pm$ 0.11 | +52        | 0.33 $\pm$ 0.13            | 0.33 $\pm$ 0.12 | 0.0        |
| 0.14 $\pm$ 0.04            | 0.2 $\pm$ 0.05  | +43        | 0.16 $\pm$ 0.05            | 0.15 $\pm$ 0.05 | -6.0       |

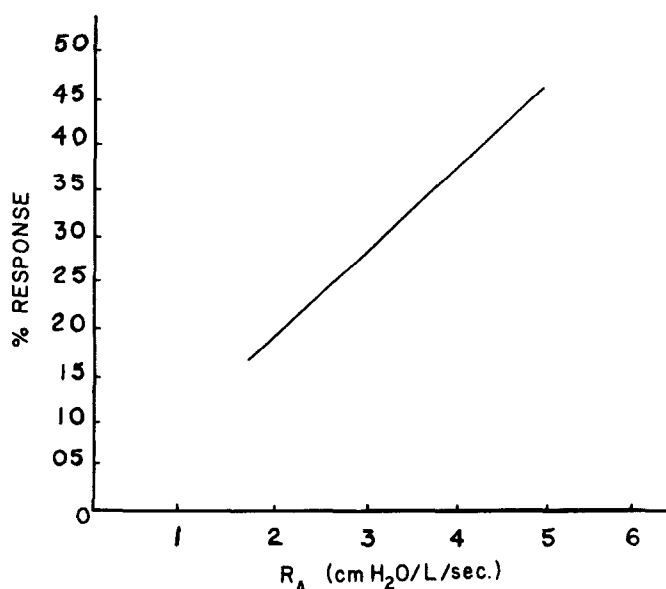


FIG. 2. The relationship between the initial level of airway resistance and response to a bronchodilator aerosol based on 60 measurements in 10 asthmatic children ( $r = 0.89$ ;  $p < 0.01$ ).

duplicate trials with a bronchodilator aerosol, but we found no benefit from correcting resistance or conductance measurements in evaluating the bronchodilator response. Sobol and co-workers<sup>14</sup> reported similar findings in adult asthmatic patients. However, this should not be construed as meaning the correction has no value. Cohen,<sup>4</sup> working with chronic obstructive pulmonary disease patients, found  $SR_A$  increased the discernment of bronchodilator changes.

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