ACUTE EFFECTS OF INHALATION OF CIGARETTE SMOKE ON PULMONARY MECHANICS

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ABSTRACT

The acute effects of the inhalation of cigarette smoke on pulmonary mechanics were studied in ten young adult men. The subjects were habitual cigarette smokers who had normal chest roentgenograms and had no history of respiratory disease.

Two popular brand cigarettes were smoked in succession by each subject and the smoke was inhaled every 30 - 60 seconds.

Forced expiratory volume, functional residual capacity, lung compliance and airflow resistance were measured before and immediately after smoking.

Lung compliance and airflow resistance were measured using the oesophageal balloon technique. Pressure-volume work loops were constructed from the transpulmonary pressure and tidal volume recordings. Elastic, resistive and total work per breath were calculated. Comparisons of mechanical properties of the lungs before and after smoking were made at strictly comparable rates and depths of breathing.

The one-half second forced expiratory volume was reduced by an insignificant amount after smoking.

Lung compliance was reduced by 17.8% after smoking and mechanical airflow resistance increased by 31%. The work per breath was increased by 37% as a result of the reduced compliance and increased airflow resistance.

The increased airflow resistance causes uneven ventilation which results in reduced dynamic compliance and increased elastic work of breathing.

It is concluded that the inhalation of cigarette smoke causes temporary impairment of pulmonary mechanics resulting in increased work of breathing.

PREFACE

The role of cigarette smoking in the aetiology and pathophysiology of chronic bronchitis, emphysema, and lung cancer is the subject of vigorous investigation at the present time. Despite the fact that evidence directly implicating cigarette smoking in the aetiology of these diseases is rapidly accumulating and despite many public pronouncements by the medical profession, the consumption of tobacco remains high and approximately 75% of men and 50% of women are habitual cigarette smokers in the United Kingdom.

While there are many reports comparing the pulmonary physiology of smokers to that of non-smokers, there are relatively few on the acute effects of cigarette smoking on pulmonary function.

Measurements of the mechanics of breathing especially the work of breathing, require expensive apparatus and present many analytical difficulties. The time-consuming and tedious nature of the analysis of the pressure-volume-flow relationships has greatly limited the extent to which these measurements have been employed.

The present study was designed to investigate the acute effects of cigarette smoking on the mechanics of breathing in healthy subjects, utilizing the oesophageal balloon technique for measurement of lung compliance and mechanical airflow resistance.

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INTRODUCTION

While this investigation was limited to a study of the acute effects of cigarette smoke inhalation on the mechanics of breathing, a brief review of the information available on the chronic effects of cigarette smoking on pulmonary mechanics will first be given as the latter are considered relevant to the present work.

CHRONIC EFFECTS OF SMOKING ON PULMONARY MECHANICS

Lung Volumes

One of the earliest reports on the comparison of pulmonary function of smokers with that of non-smokers was that of Turley and Harrison in 1932.[116] They measured vital capacity in 33 medical students and compared the results with vital capacity measurements in 42 non-smoking medical students. The mean vital capacity per square metre of body surface was 2.67 litres for the smokers and 2.64 litres for the non-smokers. They came to the conclusion that no significant difference existed between the two groups. They further reported no difference in ventilation between the two groups on moderate exercise. From these results they concluded that heavy smoking (20 or more cigarettes a day) for several years does not significantly diminish the respiratory efficiency in the performance of mild or moderately severe exercise.

Whitfield, Arnott and Waterhouse[121] studied the effects of smoking on lung volume in 1951. Measurements were made of vital capacity, residual volume and total lung capacity in 58 healthy males. They found a slightly reduced vital capacity and a more pronounced increase in residual volume and RV/TLC ratio in the smokers. These effects were found to be more evident in subjects whose recent consumption of tobacco had been high.

McKee[94] studied pulmonary function in 175 young men and made comparisons between non-smokers and smokers. He found no difference in vital capacity measurements between the two groups.

Blackburn, Brozek and Taylor[12] studied lung volumes in relation to smoking in 221 middle-aged males, mean age 52 years, in 1959. In this study the effects of age and body size were accounted for in the comparisons made between smokers and non-smokers. Vital capacity was smaller in each category of smokers and reached a statistically significant level for all smoking categories combined. Residual lung volume was larger in all categories of smokers but not consistently to statistically significant levels. The ratio of RV/TLC was significantly greater in smokers while total lung capacity was not significantly different between the groups. They further observed that in subjects who had stopped smoking the lung compartments were similar to the non-smokers and the RV/TLC ratio was significantly smaller than in the current smokers. They state that the differences in vital capacity,

residual volume and RV/TLC ratio were in the direction to be expected if smoking is a factor in producing a functional increase of airway resistance.

In 1960 Wilson et al. carried out a carefully controlled study comparing the pulmonary function of a group of non-smokers with that of a group of smokers.[123] Each group was comprised of 14 subjects, and the smokers had consumed 20 or more cigarettes daily for a mean period of eighteen years. The vital capacity and total lung capacity were significantly reduced in the smokers and the residual volume and RV/TLC ratio significantly increased.

Timed Vital Capacity and Maximum Breathing Capacity

In the group of young adults studied by McKee no differences in timed vital capacity or maximum breathing capacity were found and he came to the conclusion that ventilatory function is not impaired in young smokers when compared with non-smokers.[94]

In 1959 Higgins[58] carried out a survey of ventilatory function of smokers using an indirect maximum breathing capacity test. This measurement was defined as the three-quarters-second forced expiratory volume multiplied by 40. The study compared the results obtained in 65 non-smokers and 593 smokers. Non-smokers were found to record a higher mean maximum breathing capacity than the smokers, the difference, allowing for the size of the groups studied, being estimated at 9 litres per minute. There was no significant downward trend with increasing tobacco consumption among the smokers.

In the group studied by Wilson et al.[123] the forced expiratory volume and maximum breathing capacity were found to be significantly reduced in the smokers, the mean decrease in the 1-second forced expiratory volume being 22.45%.

An interesting joint study in pulmonary function was made in 1960 by Olsen of Denmark and Gilson of the United Kingdom.[97] They compared ventilatory capacity, in men, of a population sample from an agricultural area in the U.K. with a similar population sample from Denmark, paying particular attention to smoking habits. They found the mean maximum breathing capacity to be significantly higher in the Danish group, the difference not being explicable on the basis of differences in height, weight, density of population, or atmospheric pollution. There were, however, marked differences in smoking habits between the two groups. The Danish group contained more non-smokers and fewer cigarette smokers than the U.K. group. Furthermore, there was no difference in maximum breathing capacity between the two groups amongst the non-smokers.

Read and Selby[105] reported a study of ventilatory function of the lungs in relation to smoking, in 1961, using the Wright peak flow meter as their measurement of ventilatory function. This work was carried out in Sydney, Australia, which has a relatively unpolluted atmosphere as compared with many parts of Northern Europe. 302 subjects were assessed. They found that smoking, in the absence of symptoms, was

associated with a statistically significant lower ventilatory capacity, as determined by peak expiratory flow measurement. They further state that the results were not explicable on the basis of a simple quantitative effect of smoking on the bronchial mucosa, and postulate a genetic and environmental hypothesis to explain their findings. It should be noted, however, that no mention was made in their report as to how long each subject had abstained from smoking prior to the peak flow measurement.

NOTE ON THE PATHOLOGY OF CIGARETTE SMOKERS' LUNGS

It is reasonable to assume that there must be some pathological changes in the bronchial mucosa of cigarette smokers to account for 'smokers' cough', mucopurulent sputum production and the ventilatory disturbances which are so often present amongst habitual cigarette smokers.

Ballenger,[8] working at the Tissue Culture Laboratory of Northwestern University, Illinois, made a study of the experimental effects of cigarette smoke on human respiratory cilia. He demonstrated that cigarette smoke, in solution, from two cigarettes caused failure of the human ciliary mechanism in vitro. The failure of the ciliary mechanism was found to be irreversible if care was not taken to remove the 'smoked' basic salt solution very soon after its application to the bronchial mucosa. Ballenger suggests that paralysis of cilia in cigarette smokers results in a blanket of mucous forming on the bronchial mucosa, and that this mucous, with its contained foreign material is responsible for 'smokers' cough'.

Changes in the bronchial epithelium in relation to cigarette smoking were studied by Auerbach, Stout, Hammond and Garfenkel at the Veterans Administration Hospital, East Orange, New Jersey.[6,7] This work must rank as one of the most thorough and painstaking studies ever performed in the field of pulmonary pathology. 208 sections of tracheobronchial tree were made from each of 402 subjects. 22,110 sections from the total number were studied. This number, 22,110, represented one section for each of the 402 subjects for each of the 55 sections into which the tracheobronchial tree was divided.

The three principal types of epithelial changes recorded were:- Increase in number of cell rows; loss of cilia; and presence of atypical cells. Each of the three variables was found to increase greatly with the amount of cigarette smoking. In sections from non-smokers, the lesions found more often than not showed only one of the three types of change. The high incidence of loss of cilia and increased thickness of the bronchial epithelium observed in cigarette smokers in this study provides a substantial pathological basis for the abnormalities of ventilatory function already described.

A study of a similar nature of that of Auerbach et al. was made by Chang[19] who also observed increased thickness of bronchial epithelium and decreased average length of cilia in cigarette smokers.

ACUTE EFFECTS OF SMOKING ON PULMONARY MECHANICS

Lung Volumes and Spirometry

In addition to studying lung volumes in smokers as compared to non-smokers, McKee[94] measured vital capacity and maximum breathing capacity immediately after smoking a cigarette in 50 subjects. No significant changes in vital capacity or maximum breathing capacity occurred in these subjects, the mean vital capacity being 4.77 litres prior to smoking 1 cigarette and 4.83 litres immediately after smoking.

Bickerman and Barach[11] studied 27 healthy subjects, medical students and technicians, whose mean age was 31 years. The subjects habitually smoked between 5 and 20 cigarettes per day. All subjects had abstained from smoking on the day of the test and lung volumes and maximum voluntary breathing capacity were determined. These measurements were repeated following smoking 3 cigarettes at a leisurely pace and a ten minute rest period. The mean changes in lung volumes and maximum breathing capacity were small. The mean vital capacity was actually increased from 4.45 to 4.47 litres, and the maximum breathing capacity increased from 91.2 to 96.5 litres per minute. The residual volume increased from 1.7 to 1.8 litres. None of these changes were statistically significant and the individual results had no particular trend.

Rothfield, Biber and Bernstein[108] studied the acute effects of cigarette smoking on pulmonary function in 19 normal subjects. Vital capacity, timed vital capacity, maximum breathing capacity and functional residual volume showed no significant change after smoking 1 or 2 cigarettes.

Shapiro and Patterson[110] studied the effects of smoking and athletic conditioning on ventilatory mechanics. The subjects were healthy young seamen, mean age 27 years. 67 subjects were included in the group, 36 of whom were non-smokers, the remaining 31 subjects being cigarette smokers. Vital capacity, forced expiratory volume and maximum breathing capacity measurements were made before and after smoking two thirds of two standard-size popular brand cigarettes. The smokers had abstained from smoking at least four hours prior to testing. The smoking test was done on the non-smokers as well as the smokers. Many of the non-smokers exhibited side effects such as coughing, gagging, retching, and feelings of faintness. Some subjects in each group showed slightly impaired performance after smoking while others improved their performance slightly. The greatest variation was found in the maximum breathing capacity test but no significant trend was apparent. The authors also found that athletic conditioning was associated with an increased vital capacity and that chronic smoking was associated with a slightly reduced vital capacity.

In a recent study, Simonsson[112] studied the acute effect of cigarette smoking on the forced expiratory flow rate, using the 1-second forced expiratory volume as an index of forced expiratory flow rate. The subjects consisted of 7 men, mean age 20 years, and 9 women, mean age 28 years. All subjects had a normal chest X-ray and had no history of pulmonary or cardiac disease.

Forced vital capacity measurements were made before and after smoking 1 or 2 cigarettes of popular brand. Inhalation of each puff of smoke was a requisite for the series. The forced vital capacity measurements were made immediately after smoking and repeated after 45 to 60 minutes during which period smoking was not permitted. Thirteen of the 16 subjects showed a small decrease in the 1-second forced expiratory volume. The mean decrease for the group was 30 ml., or 1%. Simonsson applied a non-parametric statistical test and obtained a P value of less than 0.05. He concludes that this small change is significant and indicates that a small increase in airway resistance occurs as a consequence of cigarette smoke inhalation. He found no significant change in forced vital capacity after smoking. The mean value for the forced vital capacity was actually 20 ml. greater after smoking.

Lung Compliance and Airway Resistance

Eich, Gilbert and Auchinloss[40] reported, in 1957, a study of the acute effects of smoking on the mechanics of respiration in normal subjects and in subjects with chronic obstructive pulmonary emphysema. The control group consisted of 9 adults, mean age 39 years. Five of the nine had respiratory symptoms but had no evidence of emphysema, and the remaining 4 subjects had no pulmonary symptoms and were healthy. Measurements of compliance and airway resistance were made using the oesophageal balloon technique and the analysis of tracings made by established methods.[81, 92] (Although the authors use the term 'airway

resistance' in this study, their measurement was actually that of airflow resistance, as the oesophageal balloon technique measures pulmonary tissue resistance in addition to pure airway resistance.) No significant change in either compliance or airflow resistance occurred in any of the 9 subjects as a consequence of smoking one cigarette. The mean value for compliance (litres/cm. H_2O) was 0.444 before smoking and 0.407 after smoking. This small mean decrease was due to a large decrease in one of the 9 subjects, the other 8 subjects showing minimal changes. The mean value for airflow resistance (cm. H_2O/litre/sec.) was 3.82 prior to smoking and 3.79 after smoking. Four of the 9 subjects showed no change in airflow resistance, 2 subjects showed a small decrease, while 3 subjects had a small increase following smoking. The authors found a statistically significant increase in airflow resistance in the emphysematous patients, but no significant change in their compliance.

Attinger, Goldstein and Segal[2] reported on the acute effects of smoking on the mechanics of breathing in 20 normal subjects. Eleven subjects were smokers and nine were non-smokers. Measurements of compliance and airflow resistance were made using the oesophageal balloon technique before and after smoking 1 or 2 cigarettes. Compliance, mean inspiratory airflow resistance and mean expiratory airflow resistance were measured during quiet breathing and compliance also measured during hyperventilation. They found no statistical difference in these parameters for the group as a whole. One non-smoker and two smokers,

however, showed a marked increase in inspiratory mechanical resistance, while two smokers showed large increases in expiratory resistance. Only one non-smoker and one smoker showed a significant decrease in compliance following cigarette smoking. They concluded that while smoking had no significant effect on the mechanics of breathing for the group as a whole:

> these individual observations may indicate that in some instances smoking may have acute irritative effects upon the pulmonary mechanics in normal subjects, inducing some degree of unequal ventilation.

They also point out, from their data, that there was no statistically significant difference in the measured parameters of mechanics of breathing, in the control state, between the smokers and the non-smokers.

They mention, however, that this may have been due to the youth of the subjects studied, and the relatively small sample.

Motley and Kazman[88] of Los Angeles carried out an extensive study of pulmonary function before and after cigarette smoking in 141 subjects, who ranged in age from 24 to 70 years. Lung volumes, spirometry, blood gas exchange measurements and pulmonary compliance measurements were made before and after smoking two cigarettes. All measurements were not made in all subjects, however. Vital capacity and pulmonary compliance were measured before and after smoking in 41 subjects, 8 of whom were healthy and 33 had varying degrees of cardio-respiratory insufficiency as determined by complete pulmonary function studies. No significant change occurred in the mean values of vital

capacity before and after smoking, some subjects showing a decrease and others an increase. Six of the 8 normal subjects showed a decreased compliance after smoking, while one showed no change and the remaining subject showed a slightly increased value. In the 33 subjects with cardio-respiratory disease, 17 had a significant decrease in compliance after smoking, ten showed no significant alteration, and in 4 cases there was a significant increase. Elastic work of breathing (per minute) was calculated from the compliance results, during quiet breathing, the rate and depth being recorded: It was found to be increased in 4 of the 8 normal subjects while 4 had a decrease. In the group with cardio-respiratory impairment, 19 subjects had an increase in elastic work, 11 had a decrease, and 3 showed no change.

From these data, the authors concluded that decrease in pulmonary compliance was the only notable abnormality following smoking. Forced expiratory volume and airflow resistance were not included in their study.

In a recent publication, Nadel and Comroe[95] reported on the acute effects of inhalation of cigarette smoke on airway conductance in 36 normal subjects. Airway conductance (the reciprocal of airway resistance) was measured using the body plethysmograph technique[37] before and after the inhalation of cigarette smoke. Each subject inhaled 15 puffs of cigarette smoke during a period of 5 minutes. Many of the

non-smokers of the group were observed to cough and complain of nausea during the experiment. After smoking the cigarette the measurements of airway conductance and thoracic gas volume were made simultaneously and compared with the results obtained prior to smoking. Conductance/thoracic gas volume decreased in 31 of the 36 normal subjects, the mean decrease being 31%. The changes were highly significant ($P < 0.001$) and were similar for smokers and non-smokers. The changes were not severe enough to cause subjective symptoms of shortness of breath in any of the subjects. Repeated testing after smoking in 24 subjects showed that the response lasted from 10 to 80 minutes, the mean duration being 35 minutes.

If the subject puffed on a cigarette or smoked a cigar or pipe without inhaling appreciable amounts of smoke no significant change in conductance/thoracic gas volume ratio occurred. Inhalation of 0.5% isoproternol aerosol (bronchodilator) before smoking was found to prevent the increase in airway resistance, and to counteract the increase if given after cigarette smoking. Inhalation of 0.2% nicotine aerosol was found to produce no change in airway conductance, and variations in concentrations of nicotine in the inhaled smoke produced no significant difference in effect. In 5 subjects the smoke was filtered through charcoal to remove oxides of nitrogen and other volatile materials, and inhalation of this smoke led to the usual decrease in airway conductance. From these results the authors concluded that inhalation of cigarette

smoke causes a significant decrease in the conductance/thoracic-gas-volume ratio, and that this change is dependent neither on nicotine nor on oxides of nitrogen in cigarette smoke, and they suggest that the changes are related to inhalation of submicronic particles which are known to be present in large numbers in cigarette smoke.

Considering the rapidity of onset and the reversibility by isoproternol (which is both bronchodilator and vasodilator) they suggest further, that the response is due to bronchiolar constriction rather than to vascular congestion, mucus secretion or mucosal oedema, and postulate that the action is mediated by reflexes.

METHODS

SELECTION OF SUBJECTS

The subjects for the study fulfilled the following criteria:

1. Chronological age less than 40 years.
2. Habitual cigarette smokers who were accustomed to inhalation of cigarette smoke.
3. Absence of past or present history of respiratory illness or disability. Subjects who gave a history of regular or intermittent production of muco-purulent sputum were not accepted. The presence of 'morning cough' or 'smokers' cough' did not affect selection for this study.
4. Clinically in good health.
5. Chest X-ray within the preceding twelve months reported as normal.

This method of selection excluded subjects who did not effectively inhale cigarette smoke and the possibility of complication of the pulmonary function studies by old age or established cardiopulmonary disease was eliminated.

PERSONAL HISTORY

The history of cigarette smoking was obtained and recorded as the approximate average number of cigarettes smoked daily and the number of years smoking.

The age, height and weight of each subject were recorded.

APPARATUS AND TECHNIQUE

LUNG VOLUMES AND SPIROMETRY

The Godart Pulmotest, Model 1.A.7000, was used. (Figure 1)

Functional Residual Capacity

This was determined by the closed circuit helium technique.[9, 83] The patient was seated comfortably and allowed to adjust to the mouth-piece and spring nose-clip for at least five minutes. The measurement commenced at the end of a normal expiration, and readings were taken every 30 seconds. The point of equilibrium was determined by obtaining three consecutive identical concentrations of helium, and after a minimum period of ten minutes.

Expiratory Reserve Volume

This was obtained by having the patient expire maximally after a normal expiration, and the test was repeated until reproducible values (within 50 ml.) were obtained, the largest value being recorded.

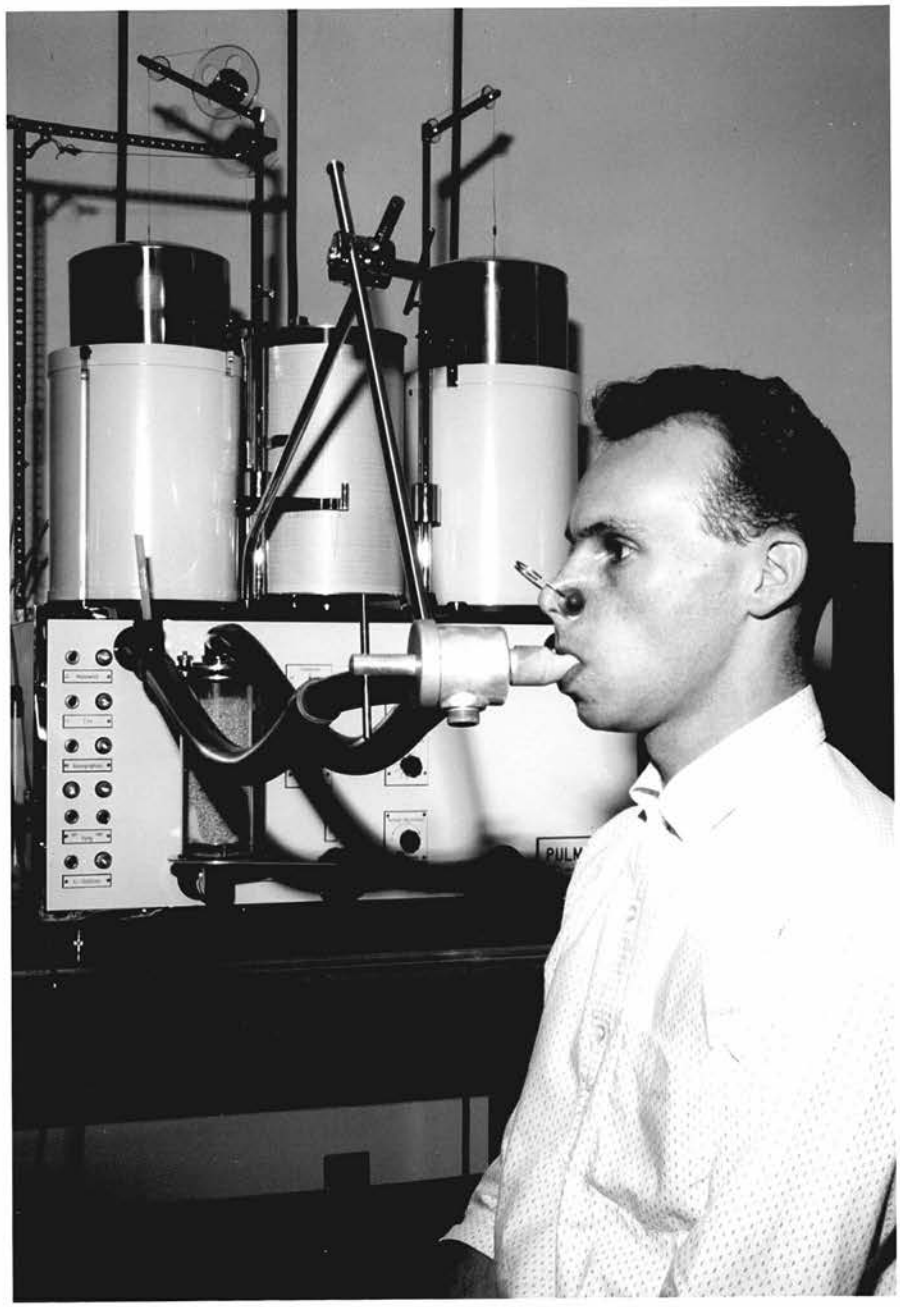
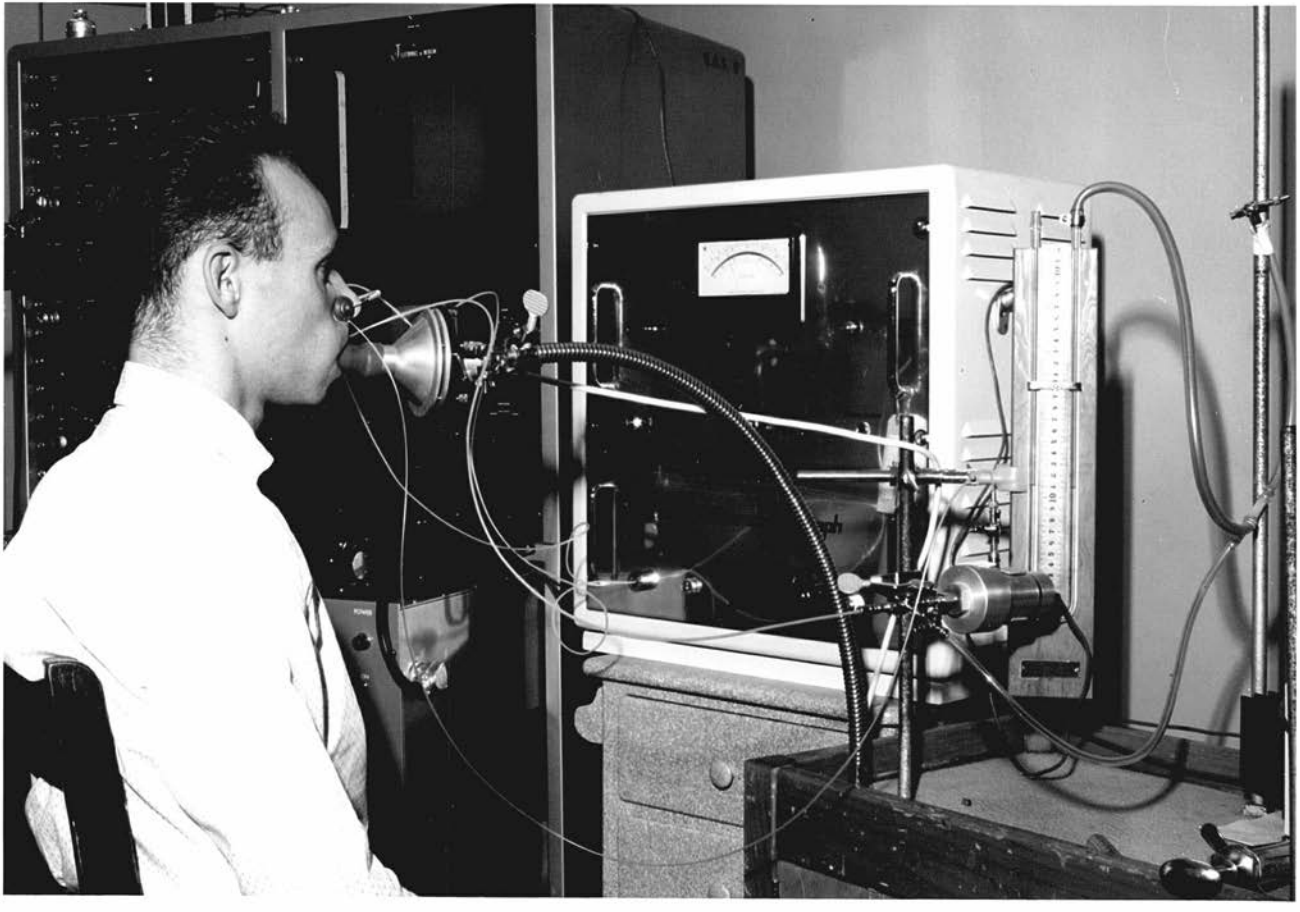


FIGURE 1

Photograph of the Godart Pulmotest



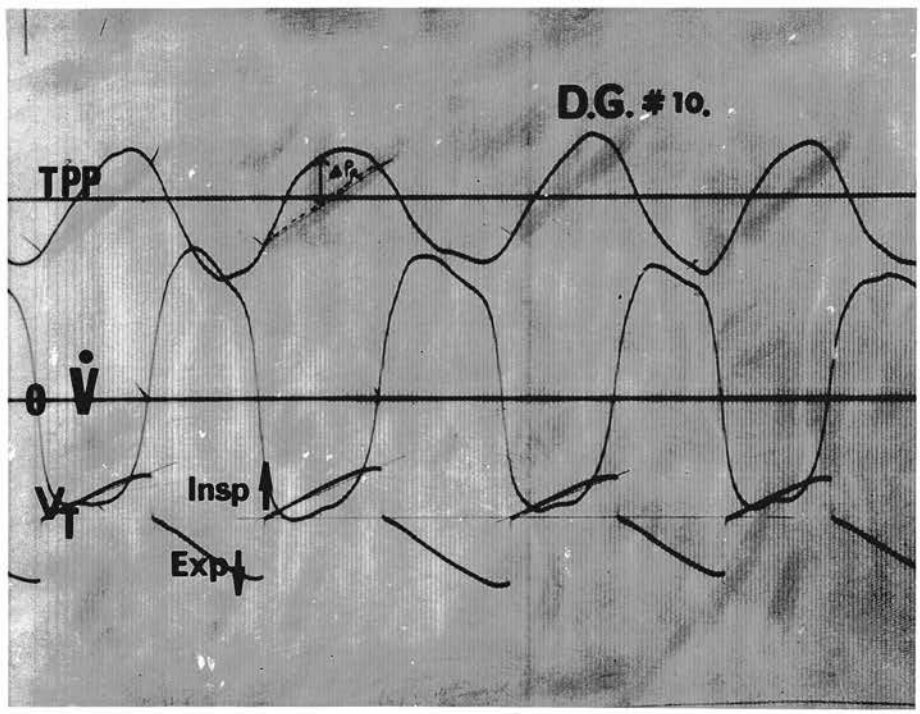


FIGURE 3

Photograph of Pressure-Volume-Flow Record

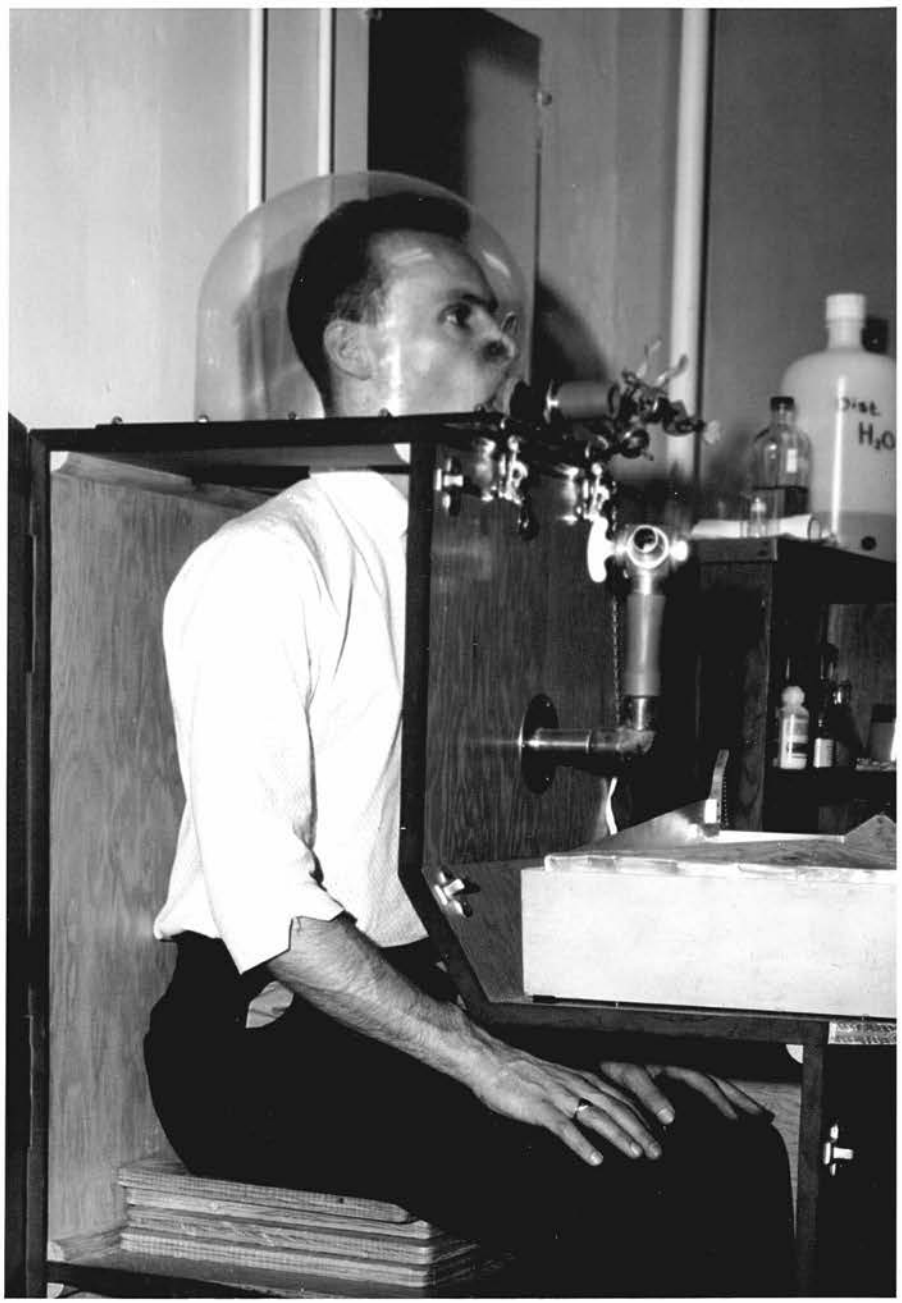


FIGURE 4

Photograph of the Body Plethysmograph

Residual Volume

The residual volume was obtained by subtracting the expiratory reserve volume from the functional residual capacity.

Forced Vital Vapacity and Forced Expiratory Volume$_{0.5 \text{ seconds}}$

This was measured by having the patient take a maximal inspiration and without hesitation to expire fully with maximal force. The total volume expired was the forced vital capacity (FVC). The test was repeated until reproducible values (within 50 ml.) were obtained and the largest value recorded. The volume obtained in the first one-half second of this procedure was the Forced Expiratory Volume$_{0.5 \text{ seconds}}$ ($FEV_{0.5}$) and here again reproducibility within 50 ml. was required and the largest volume recorded.[85] A minimum number of five readings was obtained.

Normal Values

The values of Kory and his group were used.[66] All gas volumes were measured at ambient temperature and pressure, saturated with water vapor (ATPS), and converted to body temperature and pressure saturated with water vapour (BTPS).

MECHANICS OF BREATHING

The apparatus used consisted of the Godart Pneumotachograph with volume-integrator, type GM-0577, a latex oesophageal balloon with attached polyethylene catheter, an Electronics for Medicine

Oscilloscope recorder, type DR-8, and a volume displacement body plethysmograph.[76]

Godart Pneumotachograph with Volume-Integrator (Figure 2)

The Godart Pneumotachograph is a device used to record instantaneous airflow to and from the lungs. The electronic volume-integrator, adapted to the output of the Pneumotachograph, delivers the respiratory volumes. These volumes are recorded simultaneously with the pneumotachogram.

The patient breathes into a flow-transducer. Across the centre of this manometer is stretched a wire gauze membrane. When gas flows past this membrane a pressure difference is set up from one side to the other. This mechanical signal is fed by means of two polyethylene tubes into a pressure receptor with transducer. These two tubes are transmitting the differential pressure at first to either side of a metal diaphragm. The movement of this diaphragm is sensed by a metal probe suspended within two coils. The inductance changes due to movements of the metal core are measured. The electrical signal thus produced is amplified in three stages with negative feedback and then detected by a phase sensitive rectifier and written by the recorder. This signal is also fed into a galvanometer provided with a scale calibrated in litres per minute at the front panel of the apparatus. Finally, this signal is transmitted into the volume integrator. The integrator comprises the

D.C. amplifier, which amplifies the signal of the Pneumotachograph. In the feedback of this amplifier there is an R.C. filter with sufficiently long R.C. time.

In this way the changing signal for rate of flow is registered, integrated and relayed as a static level, indicating the total volume of gas passed to and from the lungs.

The pneumotachograph was calibrated using the Godart Flowmeter, type 121, and found linear for flows up to 120 litres per minute, which was adequate for the present study.

The wire gauze screen requires meticulous cleansing after every patient as accumulation of mucous will seriously affect the results obtained. The screen was washed in alcohol regularly and carefully dried before use. The screen was heated to 38°C using the electrical heating spiral provided with the instrument.

The volume integration switch was used, at 'Position-2', whereby each inspiration and expiration is integrated separately. This type of integration is ideal for accurate measurements of work loops due to the difference between inspired and expired volumes per respiration cycle. The expiration volume was found to be 4% to 9% greater than the inspiration volume. By requesting the subject to breath at a constant rate, about twice his normal breathing rate, and using a metronome to facilitate this, a constant percentage increase of expired volume over

inspired volume could be obtained for each patient and correction of expired volume to ambient inspired volume accordingly made.

Oesophageal Balloon and Catheter

The oesophageal balloons used were kindly supplied by Dr. Milic-Emili of the Department of Physiology at the Harvard School of Public Health. The balloon is made of very thin latex and measures 10 cm. in length and 3.5 cm. in circumference. The balloon is sealed to a polyethylene catheter (internal diameter 1 m.m) with Pliobond adhesive. Small holes are present in the portion of the catheter inside the balloon, spirally arranged and at intervals of 0.5 cm. The end of the catheter inside the balloon is sealed and the tip of the balloon strengthened with Pliobond adhesive. Although these balloons are fragile they can be used on many occasions provided they are handled with care. Between experiments the balloon is maintained inflated with air to prevent sticking together of the walls. The smallest droplet of water, almost undetectible to the naked eye, if present in any portion of the tubing, can completely distort the pressure tracing. The balloon is lubricated with glycerine and passed into the oesophagus of the patient via the nostril. The length of the balloon is approximately one-third of the length of the oesophagus and the balloon is positioned to occupy the middle third of the oesophagus. Experiments have shown[84] that when a portion of the balloon is in the upper third of the oesophagus

misleading pressures are often obtained, and the lower third approximates closer to the atmospheric pressure than the middle third. The usual distance from the nostril to the junction of the middle and lower thirds of the oesophagus is 37 - 43 cm. The total length of the catheter was 85 cm. and measured markings were made on the tubing.

In this study the balloon was kept in the same position for all measurements before, during and after cigarette smoking so that while the position in the oesophagus varied slightly from one subject to another, it did not vary in the same subject and comparisons could be made before and after smoking without concern for the exact position of the balloon. The balloon is inserted in the flaccid state and the free end of the catheter attached to a three-way stopcock which had openings to the atmosphere and to a Statham differential pressure strain gauge transducer. A glass syringe with an easily gliding plunger was attached to the atmosphere opening of the stopcock. The patient performed several Valsalva manoeuvres until the balloon ceased to deliver air into the syringe. 5 ml. of air was then introduced into the balloon and the Valsalva manoeuvres repeated and the 5 ml. air recovered. 0.2 ml. of air was then introduced into the balloon and the stopcock turned to the strain gauge transducer. There are several reasons for this procedure. Firstly, the complete emptying of the balloon by suction with a syringe is inadvisable as this may induce adherence and creasing of the walls of the balloon. Secondly, it has been

found that 0.2 ml. of air gives realistic and reproducible values with this type of balloon.[84] If this balloon is used for studies of maximal respiratory effort, more air should be present in the balloon (0.4 - 0.6 ml.) due to compression of the air within the balloon. The introduction of 5 ml. air when the balloon is in place and subsequent withdrawal of 4.8 ml. serves to spread the surface of the balloon evenly to the wall of the oesophagus, as the balloon may have been twisted on its introduction in the flaccid state.

Calibration of the oesophageal pressure was carried out using a water manometer prior to each study.

Electronics for Medicine Oscilloscope Recorder Type DR-8 (Figure 2)

This recorder is very suitable for this type of work as continuous photography of the oscilloscope tracings is obtainable. The wide range of paper speeds (5 - 200 m.m. per second) and time-lines (0.004 - 1.0 seconds) is ideal for analysis of pressure - volume - flow relationships at different respiratory rates.

One of the main disadvantages of the use of the oesophageal balloon technique for accurate work is the fact that the heart beat is superimposed to a greater or lesser extent on the oesophageal tracing. It was found that with a paper speed of 5 or 10 m.m. per second the heart beat distorted the oesophageal pressure tracing irregularly from breath to breath. Using a very fast paper speed, 50 - 100 m.m. per second and especially

with a breathing rate of 40 - 60 per minute, smooth and more regular pressure tracings are obtained. While such a tracing is artificial insofar as the heart beat pressure fluctuations are smoothed out into the record, this is not a disadvantage when each patient is acting as his own control (before and after smoking), and the type of tracing obtained (Figure 3) greatly facilitated graphic expression and analysis. The sensitivity of the recorder was set so that 1 m.m. of volume deflection, represented 15 - 30 ml., 1 m.m. of pressure deflection represented 0.170 - 0.180 cm. water, and 1 m.m. of flow deflection represented 2.0 - 2.2 litres per minute, the precise values being determined in each case. With these settings accurate measurements can be made.

Body Plethysmograph

A volume displacement body plethysmograph of the type described by Mead[76] was used, (Figure 4). This apparatus consists of a chair-shaped plywood box with a 7-litre Krogh spirometer is its 'lap'. A linear transducer is attached to the spirometer and connected to the Electronics for Medicine Oscilloscope recorder. The volume events of respiration are readily recorded by allowing the subject to breathe room air. The 7-litre spirometer is adequate for vital capacity measurements. Suitable seat height for the individual subject is achieved using 3/4 inch plywood shims.

The apparatus was calibrated by running in a measured volume of water (usually 2 - 3 litres) and measuring the deflection obtained on the oscilloscope tracing.

The apparatus was used in the determination of change of functional residual capacity with different breathing patterns before and after cigarette smoking and also for forced expiratory volume measurements. Forced expiratory volume measurements can be made accurately with this system as the speed of response of the apparatus is more than adequate and the paper speed of the oscilloscope recorder can be set at 200 m.m. per second which is much faster than most spirometers.

PROCEDURE

The subject had abstained from smoking for at least one and a half hours prior to the study, and for longer in most instances. Lung volume studies were performed using the Godart Pulmotest as described. The subject was then placed in the body plethysmograph and allowed to become accustomed to the apparatus and breathing through the mouth-piece. Measurements of forced vital capacity, forced expiratory volume in the first half-second, and the inspiratory and expiratory reserve volumes were made. The subject was then asked to breathe at a constant rate, between 40 and 60 breaths per minute, a metronome being used to facilitate this manoeuvre. When the subject had selected a respiratory rate, within

the required range, which he could maintain for one to two minutes, the shift in the functional residual capacity was then recorded by means of a continuous tracing of the volume events from the plethysmograph.

This part of this procedure was repeated several times so that the subject became as familiar as possible with the requirement of regular fast breathing. The tidal volume aimed at was 450 - 650 ml. but higher tidal volumes were acceptable if the subject could best maintain a consistent reproducible rhythm at a higher tidal volume than 650 ml. The reasons for this choice of respiratory pattern will be described in the section on Analysis of Records.

The oesophageal balloon was then passed through the nostril in the manner described and the procedure of emptying the balloon and subsequent instillation of 0.2 ml. air carried out. The oesophageal balloon was secured in position with the aid of a spring nose clip and adhesive tape. The subject was then attached to the mouth-piece of the pneumotachograph. After becoming accustomed to the mouth-piece, the subject was asked to breathe at constant rate and depth, with the aid of the metronome, as described above. Continuous records of transpulmonary pressure, air flow and tidal volume were taken for 2 to 3 minutes. A quiet breathing period was then permitted for several minutes and rapid breathing records again obtained. The subject then rested quietly, detached from the mouth-piece, for several minutes;

the oesophageal balloon was maintained in the original position and the catheter remained attached to the differential pressure strain gauge transducer. The subject then commenced smoking a popular brand cigarette. (The brand of cigarette smoked in each instance is given in Appendix 1.) The smoke was inhaled regularly at a rate of approximately one inhalation every 30 - 60 seconds. The inhalations were observed throughout to ensure that the smoke was in fact inhaled and not merely puffed in and out of the mouth. (Cigarette smoke which is merely puffed in and out of the mouth is 'exhaled' in clearly visible clouds, whereas inhaled smoke is seen, on exhalation, to be more evenly distributed so that clouds of smoke are barely visible.) When the cigarette was smoked until three-quarters of an inch of tobacco remained, a second cigarette was lit and smoked in the same manner as the first. Some subjects smoked at varying rates, such as every 30 seconds for three or four inhalations and then every 60 seconds for several inhalations before resuming the faster inhalation rate. The exact number and rates of inhalation were not recorded but all subjects smoked two cigarettes, consecutively, with regular inhalations as described. The subject was then attached to the mouth-piece of the pneumotachograph and requested to breathe in a normal relaxed manner, and specifically instructed not to take any deep inspirations. After 1 - 2 minutes of quiet breathing the subject was then instructed to

gradually accelerate his breathing and to breathe with regular rate and depth at the rate between 40 and 60 breaths per minute which he had found most satisfactory prior to the cigarette smoking. Continuous tracings were obtained for at least two minutes. The subject was then placed in the body plethysmograph and the resting respiratory level recorded. Acceleration of breathing was again repeated and a continuous record obtained. Finally, forced vital capacity, forced expiratory volume, inspiratory and expiratory volumes were recorded. It will be noted that while the pneumotachograph records were commenced 2 minutes after the cessation of smoking, the plethysmograph records were not commenced until around 5 - 6 minutes after cessation of smoking. To compensate, as far as possible, for this time difference the subject was requested to inhale four or five times from a third cigarette immediately before entering the body plethysmograph and the recordings were commenced 2 minutes later. The oesophageal balloon was tested for possible leaks before and after each experiment by inflation with air and immersion in water.

ANALYSIS OF RECORDS - THEORY

The oesophageal balloon technique for the measurement of intrathoracic pressure has been an accepted method for the study of pulmonary mechanics since its introduction by Fry et al. in 1952.[52, 48-51, 73, 74, 78-81, 89-93, 113.]

The oesophageal - mouth pressure difference, or transpulmonary pressure, is obtained as described in the section on technique.

The difference in transpulmonary pressure between the beginning of inspiration and the end point of inspiration, measurements being made at these points of zero flow, gives a measurement of the elastic properties of the lungs when related to the inspired gas volume. When the transpulmonary pressure developed is divided by the inspired volume, the result obtained is called the elastance of the lungs. When the inspired volume is divided by the transpulmonary pressure developed, the result obtained is called the compliance of the lungs, which is the reciprocal of the elastance. In recent years it has become customary to use compliance rather than elastance.[26]

The usual units for compliance measurement are litres for volume, and cm. of water for transpulmonary pressure.

Despite the fact that lung compliance is a fundamental concept in any study of pulmonary mechanics, its use in clinical medicine has been on a very limited scale. There are several reasons for this. Firstly, the measurement requires special apparatus and the oesophageal balloon causes some inconvenience to the patient. Secondly, the range of normal values is wide and varies considerably from one laboratory to another.[26] In view of this wide normal range and considerable variation in absolute values, many clinicians hold that the measurement of lung compliance is of little or no practical importance. This is unfortunate. When the

reasons for the wide normal range and the variations from one laboratory to another are carefully considered and taken into account in the interpretation of results, it becomes apparent that pulmonary compliance is of real value in clinical physiology.

The apparently wide and varying normal ranges are readily explicable on both theoretical and technical grounds. The chief theoretical consideration is that compliance is directly related to the thoracic gas volume at the time of its measurement.[26] In normal subjects the thoracic gas volume is equal to the functional residual capacity which is readily obtainable. The position of the subject is also of importance in the measurement of compliance.[5] Compliance is lowest in the supine position and highest in the sitting position. The prone position compares with the sitting position while the head down and lateral are close to the supine position.[5]

Breathing therefore requires more effort, due to poorer intrapulmonary mixing and increased thoracic blood volume, when a supine or lateral position is assumed.[5,78] It is important that body position be designated when pulmonary function tests are reported.

The position and length of the oesophageal balloon greatly influence the compliance values. When the balloon is positioned wholly or partly in the upper third of the oesophagus, considerable variation occurs in the results obtained from time to time in the same individual.[84] The values obtained from the lower third are less than those from the

middle third as the intrathoracic pressure is closer to atmospheric in lower oesophagus.[77] Milic-Emili has found that least variation occurs from time to time, and when small changes are made in the position of the balloon, if the balloon is entirely or mostly in the middle third of the oesophagus, and no part of it is situated in the upper third.

The type of balloon used, the amount of air introduced, and the transducer employed all influence the results obtained.

The principles of the method of estimation of inspiratory and expiratory airflow resistance are well established[41, 81, 117] and are illustrated in Figure 5. The basic principle is that the shape of the transpulmonary pressure curve due to the compliance precisely follows the volume change. The residual pressure, when divided by the simultaneously occurring flow rate, gives a measure of airflow resistance.[77, 106, 107] The measurement of airflow resistance, for inspiration and expiration separately, by this method is time consuming and tedious, since a large number of breaths must be analysed to obtain a mean value which is reliable and takes into account the variability from breath to breath which can result from superimposition of the heart beat on the pressure tracing.

This method, however, has certain advantages over that of obtaining loops directly from the oscilloscope, where pressure and volume are plotted simultaneously. The chief disadvantage of the direct loop method is that it does not permit separate visualization of the two variables, so

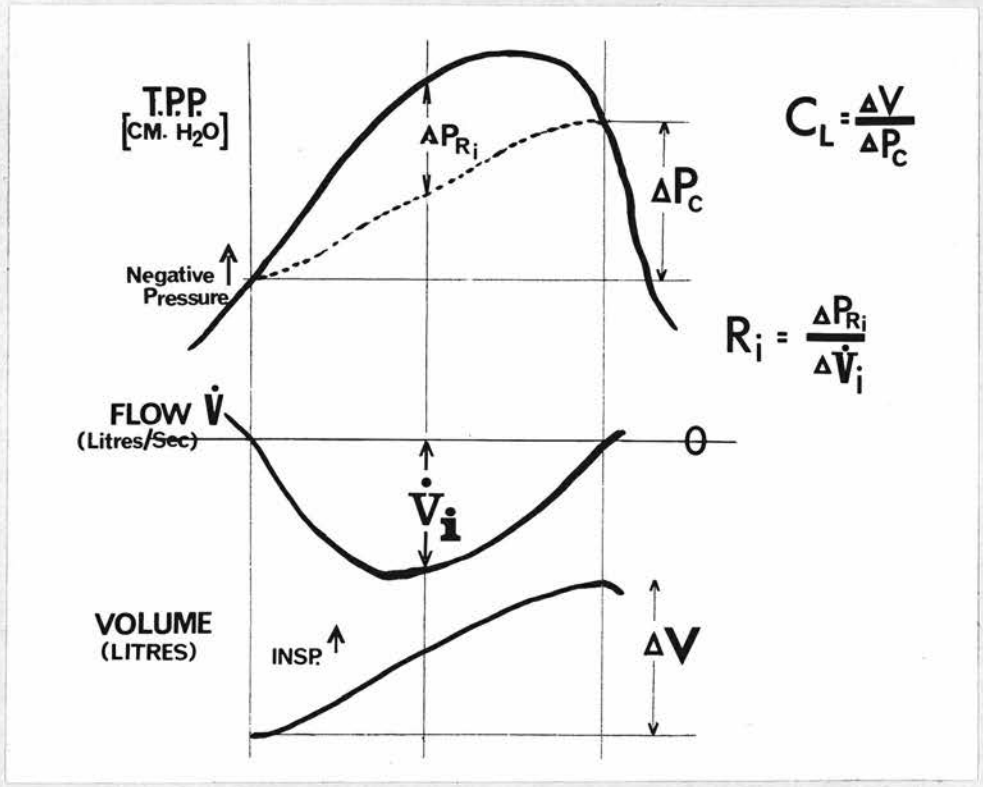


FIGURE 5

Diagram of Pressure-Volume-Flow Record

that an artefact of the pressure tracing due to temporary spasm of the oesophagus, which is readily identified from the continuous tracing, may be misinterpreted from the resultant respiratory loop. A further disadvantage of the direct method is that the loops do not close properly. This is due to the air warming within the lungs which causes the expiratory volume to be larger.

When, on the other hand, the variables are recorded separately, a factor can be used to convert the expired volume to the ambient air value and the loops close satisfactorily.

Airflow resistance can be measured at any point or points of the respiratory cycle. The measurement is usually made at or near peak flow to minimize error.[41, 81] Airflow resistance, as obtained using this technique, includes the 'tissue resistance' component[77, 117] and is not therefore a measure of pure airway resistance which can only be obtained by plethysmographic methods. The tissue component is small, however, in healthy individuals; furthermore, as has been described above, simultaneous measurement of lung compliance, respiratory rate and tidal volume are obtained by the oesophageal balloon - pneumotachograph method, whereas these measurements cannot readily be made simultaneously with airway resistance when the plethysmograph is employed. Another noteworthy consideration is that in the plethysmographic method the subject is required to pant, necessitating some training to produce reliable results, whereas a normal breathing pattern is adequate when the oesophageal balloon is used.

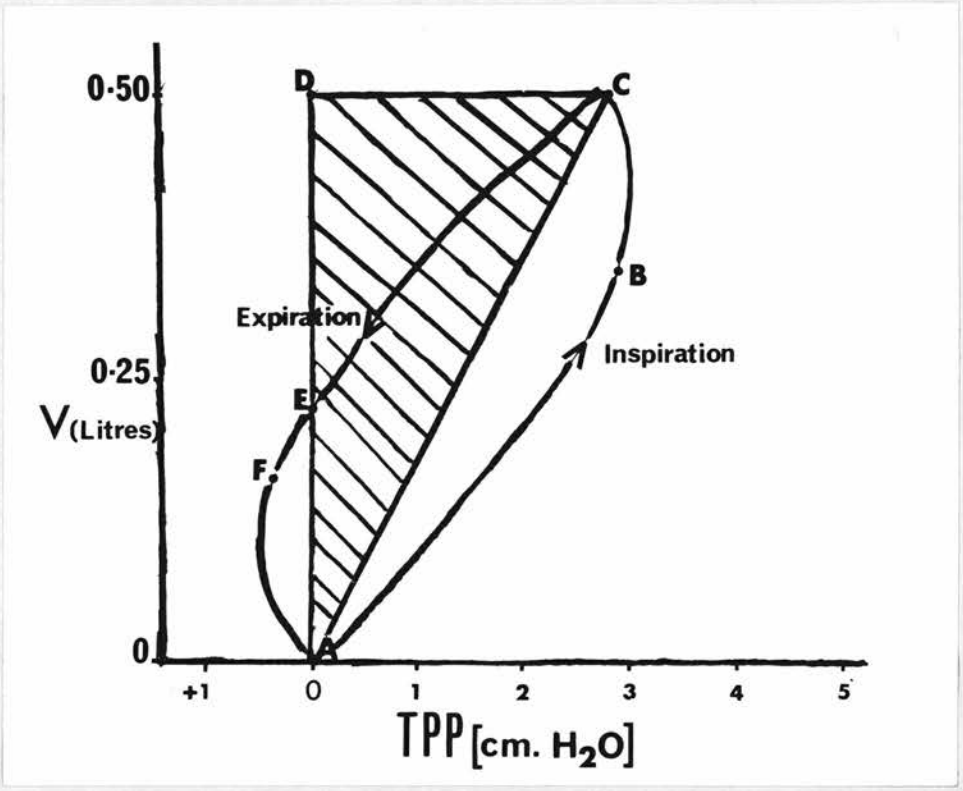


FIGURE 6

Diagram of Pressure-Volume Work Loop

Measurement of the work of breathing were made from the trans-pulmonary pressure and tidal volume records as described by McIlroy, Marshall and Christie.[92] The pressure-volume diagram obtained from this type of record is shown diagrammatically in Figure 6. With reference to this diagram, the work of breathing, per breath, is represented by the area ABCDEF. The work done on the lungs can be recorded in Kg - cm. (Kg - cm. is a suitable unit when measuring work per breath as opposed to work per minute, where Kg.m. is the unit commonly used). Area ACD represents the work done against elastic forces on inspiration, and the line AC is the 'compliance slope'. Area ABC is the work done against non-elastic or resistive forces on inspiration, and area CEFA the work required to overcome the resistive forces on expiration.

The area ACD, which is the elastic work of inspiration, is stored energy and is available for expiratory resistive work. Area CEA, which is the largest portion of expiratory resistive work, is therefore 'passive work'. This principle explains the fact that while inspiratory pulmonary work is active, the work done on the lungs during expiration is largely passive. In the diagram, a small portion of expiratory resistive work, area EFA, is not contained within the stored work area ACD, so that this portion of expiratory resistive work must be actively performed. The larger the area EFA becomes, the greater the amount of active expiratory resistive work. If the pulmonary compliance diminishes, the area ACD increases and the work loop is flatter. As airflow

resistance increases the area ABCFA widens and the work loop becomes fatter. During quiet breathing, resistive work is proportional to tidal volume, while elastic work due to its 'triangular area', is proportional to the square of the tidal volume.

Whereas slow deep breathing requires increased work per unit of time, due to a great increase in the elastic component, rapid shallow breathing reduces the total work per unit of time (for the same minute ventilation) but is associated with increased dead space ventilation. In normal subjects a compromise is achieved between these two extremes, and the usual manner of breathing is at a rate of around sixteen breaths per minute at a tidal volume of 500 ml. while the subject is at rest. Work of breathing measurements, as described above, refer only to work done on the lungs and do not include work done on the chest wall. Measurement of total work of breathing is difficult due, in part, to the fact that complete relaxation of the chest wall is not readily accomplished, even by trained subjects.

In the studies described herein, the work done on the lungs alone is evaluated.

ANALYSIS OF RECORDS - METHOD

As described in the section on Procedure, every subject was requested to breathe at a regular rate between 40 and 60 breaths per minute. The reasons for the selection of this type of respiratory pattern

were four in number, and while they are mentioned in the section on Technique, they are now given in detail:

1. As the study was designed to measure any acute changes in pulmonary mechanics which might occur following the inhalation of cigarette smoke, it was essential that the records obtained be as comparable as possible, so that any differences ascribed to smoking are valid, and cannot be attributed to variations in respiratory pattern which have no relation to the effects of cigarette smoke inhalation.

2. The cardiac impulse is often superimposed on the transpulmonary pressure tracing to a noticeable degree and on occasion may be so large as to render interpretation of the tracing very difficult or impossible. It was found that at a faster respiratory rate than normal the cardiac pulsation could often be made much less prominent and a smoother tracing, which was much more suitable for detailed analysis, was obtained. While this technique does not eliminate the effect of the cardiac pulsation on the results obtained, it is reproducible and therefore suitable for studies of acute changes in pulmonary mechanics in the same individual. Very small adjustments of the position of the oesophageal balloon within

the middle third of the oesophagus can often greatly reduce the cardiac interference. These adjustments were made in each subject, ensuring that the selected position of the balloon was maintained throughout the experiment.

3. Small changes in dynamic compliance are more readily detected at faster respiratory rates than normal, and a respiratory rate of 40 - 60 per minute was preferable to one of 15 - 20 per minute for this reason.
4. One of the few disadvantages of the pneumotachograph is that the expired volume is larger than the inspired volume due to warming of the inspired air by the subject's respiratory tract. At a faster respiratory rate than normal, this difference becomes smaller and more constant from breath to breath so that a factor can be calculated and the effect eliminated.

Each record was examined, sections of regular breathing pattern noted, and the respiratory rate measured. While many workers analyse 10 - 15 breaths for estimation of lung compliance and airflow resistance, at least 30 breaths were analysed in this study in an attempt to achieve as high a degree of accuracy as practicable, since precise measurement of any changes resulting from cigarette smoke inhalation was the aim of the study. Points of no airflow were marked on the record

of each variable and accuracy here was greatly enhanced by the fast paper speed and short time interval between the vertical time lines. The time intervals recorded were mostly 0.04 seconds and occasionally 0.01 seconds. At a respiratory rate of 50 per minute each breath was thus subdivided by the mechanical time lines into at least 30 segments. Compliance and airflow resistance measurements were made in accordance with the method described in the preceding section. The most time consuming part of the analysis was the separation of the transpulmonary pressure tracing into the elastic and non-elastic portions by fitting the volume tracing to the transpulmonary pressure tracing. This was done as exactly as possible by making measurements at frequent intervals throughout the respiratory cycle and not by simply fitting the volume pattern to the pressure tracing by free hand and visual judgement.

Any breath which contained an artefact in the pressure tracing, such as that caused by swallowing or oesophageal spasm, was deleted for purposes of calculation of mean values and another breath analysed in its place to maintain the 30 breath minimum.

After the measurements were made, any compliance value which deviated from the mean value by more than 0.015 for values above 0.1, and by more than 0.01 for values below 0.1 was deleted. This method of removal of individual breaths from the series, before final calculation of the mean, was arbitrary and based on experience in analysis of this

type of record in this laboratory. In the measurement of airflow resistance, any individual value which deviated from the mean by more than 0.25 cm. H_2O/litre/second was deleted.

For the construction of work loops from the transpulmonary pressure and volume tracings, at least four consecutive breaths, whose values for compliance and airflow resistance were close to the mean, were selected. If four such breaths could not be found then two sets of three consecutive breaths or three sets of two consecutive breaths were selected. In general, compliance was required to be within 0.005 litres/cm. H_2O of the mean and airflow resistance within 0.10 cm. H_2O/litre/sec. The loops were constructed on Keuffel and Esser graph paper which was ruled at m.m. intervals.

The compliance line and elastic work triangle were drawn as illustrated in Figure 6; these lines divided the work loop into the resistive segments already described. The area of each segment of each work loop was measured using the Keuffel and Esser Compensating Polar Planimeter, type 4236M, which is read directly in square centimetres to tenths. The work represented by each segment was calculated and recorded as Kg - cm. The mean values for total work and each of its components were calculated.

The comparison of work done before smoking to that required after smoking must be made at the same tidal volume. As it was not possible for the subject to achieve exactly the same tidal volume for each series

of breaths, the elastic and non-elastic components of work were calculated for the pre-smoking tidal volume. For elastic work the calculation was made by counting the appropriate number of squares to be added to or subtracted from the post-smoking value; this method was employed due to elastic work being proportional to the square of the tidal volume. In the case of resistive work, which is directly proportional to tidal volume, the calculation was made arithmetically.

For illustration, sample or mean representative loops were traced onto transparent plastic and photographed on a white background. (Figures 7 - 16)

FURTHER TECHNICAL CONSIDERATIONS

The relationship of compliance and airflow resistance to lung volume is important. For example, if the resting lung volume (FRC) increased after administration of a drug, then airflow resistance would be lower than it was prior to the administration, whether the drug had any bronchodilator effect or not; this is due to airflow resistance being inversely proportional to lung volume.

The FRC of each subject was measured at the same rate and depth of breathing at which measurements of compliance and airflow resistance were made; this ensured that any changes in compliance or airflow resistance, after smoking, could be interpreted with due attention to lung volume. One possible source of error here is that measurements of the functional residual capacity will not detect change in thoracic gas volume

if airway closure occurs. If such an error was in fact made, it must have been small and would not influence the conclusions drawn from this study. There are two reasons for disregarding this possible source of error. First, there was no change in vital capacity for the group. Had a significant degree of airway closure, with air trapping, occurred, the vital capacity would have been reduced by approximately the same amount. The only possible flaw in this argument is that, theoretically, air trapping could occur and the inspiratory capacity could increase simultaneously by a similar amount; this would mean that the total lung capacity had increased after cigarette smoking, with some of the increase as trapped air so that the vital capacity remained unchanged. This is extremely unlikely and can be discounted. The second reason for dismissing the possible source of error is based on observations made by Lovejoy et al.:[71] they found that administration of powerful bronchoconstrictors (Carbachol and aluminium dust) to normal subjects, in sufficient dosage to increase airway resistance threefold, produced only small increases in thoracic gas volume; the increase in the instance of Carbachol was barely significant at 0.52 litres, and was insignificant in the case of aluminum dust (0.23 litres).

In this study airflow resistance, after smoking, increased by 31%; in view of the unchanged vital capacity and Lovejoy's experiments it is a reasonable presumption that no significant air trapping occurred after smoking. Nevertheless, the results obtained for compliance and airflow

resistance are reported both as absolute measurements and as related to FRC. It will be shown statistically that the extremely small and inconsistent changes found in FRC after cigarette smoking do not in any way influence the conclusions reached.

It is interesting to note that subject D.G. had the largest increases in both airflow resistance and FRC, thereby demonstrating the same pattern of response to cigarette smoke as Lovejoy et al. found to powerful bronchoconstrictors. Finally, it is pointed out that if air trapping does in fact occur after cigarette smoking, its presence would increase rather than decrease the significance of the differences in compliance and airflow resistance found here.

STATISTICAL ANALYSIS OF RESULTS

Each subject served as his own control. For this reason the difference between the values before and after smoking is used as the statistic for analysis. This method, termed the paired t-test, involves calculating the standard deviation of the differences and then the standard error. The mean difference divided by the standard error gives the value of t and using 'two-tailed' t tables the P value is obtained for n - 1 degrees of freedom. The mean difference, standard error and P value for each measurement are shown in the tables of results.

RESULTS

The results are shown in Tables 1 to 7, diagrams of work loops obtained before and after smoking in each of the ten subjects are shown in Figures 7 to 16, and graphic representation of results is shown in Figures 17 - 23.

The age, height and weight, and smoking history of the subjects are shown in Table 1. The age range was 21 - 35 years, the average age being 27 years. All subjects smoked 10 or more cigarettes per day; duration of smoking ranged from 4 to 17 years, the mean duration being 9 years.

LUNG VOLUMES AND SPIROMETRY

Lung volumes and the half-second forced expiratory volume before and after smoking are shown in Tables 2 and 3.

TOTAL LUNG CAPACITY AND RESIDUAL VOLUME (Table 2)

The mean total lung capacity before smoking was 6.77 litres and the range was 6.17 - 7.92 litres. All values are within the normal range. The mean residual volume was 1.49 litres which corresponded to 24.5% of the total lung capacity and is normal. The highest residual volume was 2.04 litres (A.L.) which was 29% of this subject's total lung capacity. The RV/TLC ratio was less than 30% in all subjects, and none can be said to be abnormal.

FORCED VITAL CAPACITY (Table 2)

The mean FVC before smoking was 5.117 litres and the mean predicted value was 4.94 litres. In no subject was the FVC appreciably lower than the predicted value. The FVC exceeded the predicted value by an appreciable amount in two instances (R.K. and S.U.). Allowing for the normal individual variation in FVC, differences in technique and the geographical location of this study, the results are considered normal.

The mean value of the FVC after smoking was 5.119 litres, which is 0.002 litres higher than the value before smoking. No significant difference existed between the two means ($P > 0.9$).

HALF-SECOND FORCED EXPIRATORY VOLUME (Table 2; Figure 17)

The mean value before smoking was 3.118 litres which was slightly greater than the predicted value of 3.046 litres. None of the individual values varied greatly from the predicted value, showing that no appreciable degree of airway obstruction existed in any member of the group. The mean value after smoking was 3.017 litres, which is 0.027 litres less than the pre-smoking value. The standard error of the difference was 0.022 litres and the P value < 0.3 which is not statistically significant.

Seven of the ten subjects showed a decrease in $FEV_{0.5}$ after smoking, while two subjects (K.C. and S.J.) showed an increase. One subject (N.B.) recorded no change. Although the mean difference is not

statistically significant there is a trend towards reduced $FEV_{0.5}$ following smoking.

FUNCTIONAL RESIDUAL CAPACITY (Table 3)

The results obtained for functional residual capacity before and after smoking, at both normal and rapid respiratory rates are shown in Table 3.

At Normal Respiratory Rate

The mean value was 3.017 litres before smoking and 3.061 litres after smoking, there being no significant change ($P < 0.40$). One subject (D.G.) showed an increase of 350 ml., the largest change in the series. This subject was mainly responsible for the mean increase after smoking.

At Rapid Respiratory Rate

The mean value was 3.188 litres before smoking and 3.245 litres immediately after smoking. This slight increase following smoking is not statistically significant ($P < 0.2$). Six subjects showed an increase, three showed a slight decrease, and in one (J.C.) there was no change.

LUNG COMPLIANCE AND AIRFLOW RESISTANCE

Compliance and mechanical airflow resistance are shown in Tables 4 and 5 and Figures 18 - 21.

COMPLIANCE (Table 4; Figure 18)

The mean value was 0.135 litres/cm.H_2O before smoking and 0.111 litres/cm. H_2O after smoking. This decrease is statistically significant

($P < 0.02$). Seven of the subjects showed a decrease of greater than 0.01 and four of this group had a decrease of 0.02 or more. Three subjects (R.K., J.V.H. and A.L.) showed very small changes, two of them (J.V.H. and A.L.) having increased values (+0.007 and +0.004 respectively), while subject R.K. had a post-smoking value of only 0.001 less than the control value. The mean decrease was 17.8%.

AIRFLOW RESISTANCE (Table 4; Figure 20)

Inspiratory Resistance

The mean value was 2.04 (cm. H_2O/L./sec.) before smoking and 2.62 after smoking, the difference being statistically significant ($P < 0.05$). Eight subjects showed an increase while two (K.C. and J.V.H.) showed a slight decrease. The largest increase was obtained in subject D.G., resistance rising from 1.65 to 3.80, so that the post-smoking value was more than twice the control value. The mean increase for the series was 28.4%.

Expiratory Resistance

The mean value of 2.92 (cm. H_2O/L./sec.) rose to 3.88 after smoking, an increase of 32.9% and this was statistically significant ($P < 0.01$). Eight subjects showed an increase and two subjects (J.V.H. and A.L.) showed a small decrease. The mean post-smoking value of 3.88 is outside the normal range of 1.2 - 3.4 and indicates that a definite and abnormal expiratory airflow resistance had developed following cigarette smoke inhalation.

Mean Airflow Resistance

The mean airflow resistance, calculated literally as the mean of the inspiratory and expiratory values obtained, was 2.48 before smoking and 3.45 after smoking. This result is a statistically significant increase of 31% ($P < 0.01$). Eight of the subjects showed an increase, while two, (J.V.H. and A.L.), showed a small decrease.

COMPLIANCE RELATED TO FRC (Table 5; Figure 19)

Compliance was divided by FRC on each instance. The mean value was 0.0425 before smoking and 0.0344 after smoking, a statistically significant ($P < 0.02$) decrease of 0.0081. As the FRC changes were small and inconsistent it is not surprising that this procedure of relating the compliance to FRC does not alter the magnitude or significance of the difference obtained between the before and after smoking values.

CONDUCTANCE RELATED TO FRC (Table 5; Figure 21)

Conductance, the reciprocal of airflow resistance, was divided by the measured FRC. The mean value of 0.145 fell after smoking to 0.106, a decrease of 0.039 which is statistically significant ($P < 0.01$). Here again, due to the small and inconsistent changes in FRC, relating airflow resistance (as conductance) to FRC does not alter the magnitude or significance of the difference.

WORK OF BREATHING

Work per breath, before and after smoking, is shown in Tables 6 and 7, and the loop patterns and corresponding tidal volumes and

respiratory rates are shown for each subject in Figures 7 - 16. Graphical representation of the results is provided in Figures 22 and 23.

The work of breathing is here calculated as work per breath and not work per minute. This method was chosen because it permits visual comparison, as illustrated by the constructed loops; in any case work per minute is meaningless in this study as rate and depth of breathing were artificially selected. This measurement is valuable as it provides a composite picture of the actual mechanical changes occurring as a result of cigarette smoke inhalation. In this way, lung compliance, inspiratory and expiratory airflow resistance are brought together to form a meaningful concept. The unit of work is the Kg - cm. in all instances.

TOTAL WORK (Table 6; Figure 22)

The total work loop had a mean of 3.43 (Kg - cm.) before smoking and 4.69 after smoking, an increase of 1.26 which is statistically significant ($P < 0.01$). As no gross irregularities occurred in the loop patterns of any of these healthy subjects, either before or after smoking, it will be realised that the total work increase was in roughly the same proportion as the two measured variables (compliance and airflow resistance) which together form the loop. The portion of the increase in expiratory airflow resistance which remains inside the 'stored energy' compliance triangle does not appear in the total work loop. For this reason the measurements of elastic work and resistive work, as well as being recorded separately, were summed in each case to demonstrate

the actual effects of the cigarette smoke inhalation. This calculation emphasized that while some of the increase in resistive work is not actively performed by the subject, nevertheless, the increase encroaches upon the elastic reserve. The foregoing concept becomes important when there is decreased elastic reserve available as in patients who already have obstructive airway disease.

ELASTIC WORK (Table 6)

The mean value was 1.66 before smoking and 2.02 after smoking, a statistically significant increase of 0.36 ($P < 0.02$).

RESISTIVE WORK (Table 6; Figure 23)

The mean increases observed in inspiratory resistive work, expiratory resistive work, and total resistive work were all statistically significant.

The inspiratory resistive work increased from 1.15 to 1.58, an increase of 0.43, while the expiratory resistive work increased from 1.77 to 2.62, an increase of 0.85.

ELASTIC PLUS RESISTIVE WORK (Table 7)

The mean value of 4.58 increased to 6.24 after smoking, an increase of 1.66. It will be noted that this increase is greater than the actual increase in the total work loop by 0.40 kg - cm. As described above, the 0.40 Kg - cm. has been accommodated within the compliance triangle of the work loop and therefore does not have to be actively expended by the subject. Nevertheless, the total work loop increases

by 36.7%. This additional work means impairment of pulmonary mechanics has resulted from cigarette smoke inhalation.

NOTE

An account of the reproducibility of results for lung compliance and airflow resistance is given in Appendix 2.

The results obtained in two subjects for lung compliance and airflow resistance before and after 'puffing' on a cigarette, without inhalation, are given in Appendix 3.

TABLE 1 SUBJECTS STUDIED

	Subject	Age (yrs.)	Ht. (inches)	Wt. (lbs.)	Smoking History
1.	A.V.S.	32	64.5	135	10/day x 12 years
2.	J.C.	35	70	150	20/day x 17 years
3.	R.K.	21	68	151	10/day x 4 years
4.	K.C.	23	70	156	20/day x 6 years
5.	S.U.	27	68	179	25/day x 9 years
6.	J.V.H.	24	70.5	143	15/day x 7 years
7.	J.M.	27	69	151	25/day x 8 years
8.	A.L.	28	69.5	190	25/day x 12 years
9.	N.B.	30	68.5	183	20/day x 11 years
10.	D.G.	25	70.5	164	10/day x 5 years
	Mean	27.2	68.8	160.2	

TABLE 2

LUNG VOLUMES AND SPIROMETRY

	Subject	TLC (L.)	RV (L.)	$\frac{RV}{TLC} \times 100$	FVC Predicted (L.)	FVC B.S. (L.)	FVC A.S. (L.)	FVC Diff. (ml.)	$FEV_{0.5}$ Predicted (L.)	$FEV_{0.5}$ B.S. (L.)	$FEV_{0.5}$ A.S. (L.)	$FEV_{0.5}$ Diff. (ml.)
1.	A.V.S.	5.50	1.45	26.4	4.20	4.05	4.00	-50	2.71	2.58	2.42	-160
2.	J.C.	6.29	1.64	26.1	4.94	4.65	4.58	-70	2.93	2.87	2.81	-60
3.	R.K.	7.24	1.50	20.8	4.98	5.74	5.84	+100	3.15	3.71	3.69	-20
4.	K.C.	6.41	1.42	22.1	5.22	4.99	5.06	+70	3.21	3.12	3.22	+100
5.	S.U.	7.92	1.63	20.6	4.86	6.29	6.18	-110	3.02	3.86	3.89	+30
6.	J.V.H.	7.23	1.68	23.2	5.18	5.55	5.61	+60	3.18	3.03	3.00	-30
7.	J.M.	7.00	1.78	25.4	4.98	5.22	5.19	-30	3.06	3.26	3.25	-10
8.	A.L.	7.04	2.04	29.0	5.04	5.00	5.04	+40	3.07	3.02	2.97	-50
9.	N.B.	6.17	1.75	28.4	4.87	4.42	4.47	+50	2.98	2.21	2.21	-
10.	D.G.	6.85	1.59	23.2	5.16	5.26	5.22	-40	3.15	3.52	3.45	-70
	Mean	6.77	1.49	24.5	4.94	5.117	5.119	+02	3.046	3.118	3.091	-27
	S.E. $\bar{d}$							22.3				21.52
	P value							> 0.90				< 0.30

TLC = Total Lung Capacity
RV = Residual Volume
FVC = Forced Vital Capacity
$FEV_{0.5}$ = Forced Expiratory Volume in the first half-second

B.S. = Before Smoking
A.S. = After Smoking
Diff. = Difference between the before smoking and after smoking values.

TABLE 3 FUNCTIONAL RESIDUAL CAPACITY

Subject	Quiet Breathing			Rapid Breathing		
	B.S. (L.)	A.S. (L.)	Diff. (ml.)	B.S. (L.)	A.S. (L.)	Diff. (ml.)
1. A.V.S.	2.52	2.47	-50	2.81	2.78	-30
2. J.C.	3.00	3.01	+10	2.88	3.03	+150
3. R.K.	3.04	3.19	+150	3.24	3.24	-
4. K.C.	2.63	2.60	-30	2.86	2.78	-80
5. S.U.	3.12	3.00	-120	3.20	3.23	+30
6. J.V.H.	3.36	3.41	+50	3.48	3.51	+30
7. J.M.	3.13	3.16	+30	3.49	3.45	-40
8. A.L.	3.24	3.19	-50	3.42	3.47	+50
9. N.B.	3.29	3.40	+110	3.42	3.62	+200
10. D.G.	2.84	3.19	+350	3.08	3.34	+260
Mean	3.017	3.061	+44	3.118	3.245	+57
$S.E._{\bar{d}}$			42.4			35.1
P value			<0.40			<0.20

TABLE 4

COMPLIANCE* AND MECHANICAL AIRFLOW RESISTANCE**

SUBJECT	COMPLIANCE			INSP. AIRFLOW RESISTANCE			EXP. AIRFLOW RESISTANCE			MEAN AIRFLOW RESISTANCE		
	B.S.	A.S.	Diff.	B.S.	A.S.	Diff.	B.S.	A.S.	Diff.	B.S.	A.S.	Diff.
1. A.V.S.	0.123	0.106	-0.017	1.05	2.14	+1.09	2.96	3.96	+1.00	2.00	3.05	+1.05
2. J.C.	0.170	0.127	-0.043	1.70	2.18	+0.48	2.58	3.46	+0.88	2.14	2.86	+0.72
3. R.K.	0.100	0.099	-0.001	1.58	2.16	+0.58	2.40	3.88	+1.44	1.99	3.02	+1.03
4. K.C.	0.097	0.073	-0.024	1.67	1.56	-0.11	2.03	2.79	+0.76	1.85	2.17	+0.32
5. S.U.	0.129	0.108	-0.015	1.21	1.60	+0.39	2.41	3.11	+0.70	1.81	2.35	+0.54
6. J.V.H.	0.079	0.086	+0.007	3.26	3.04	-0.22	5.03	5.01	-0.02	4.14	4.02	-0.12
7. J.M.	0.242	0.180	-0.062	2.27	2.92	+0.65	2.39	3.01	+0.62	2.33	3.01	+0.54
8. A.L.	0.175	0.179	+0.004	1.48	1.57	+0.09	2.76	2.51	-0.25	2.12	2.04	-0.08
9. N.B.	0.076	0.056	-0.020	4.53	5.23	+0.70	5.00	6.88	+1.88	4.76	6.05	+1.29
10. D.G.	0.164	0.097	-0.067	1.65	3.80	+2.15	1.62	4.08	+2.46	1.63	3.94	+2.31
Mean	0.135	0.111	-0.024	2.04	2.62	+0.58	2.92	3.88	+0.95	2.48	3.25	+0.77
S.E. $\bar{d}$			0.0082			0.215			0.256			0.228
P value			<0.02			<0.05			<0.01			<0.01

*Compliance: -Litres/cm. H_2O.

**Mechanical Airflow Resistance (R.):- cm. H_2O/Litre/sec.

TABLE 5 COMPLIANCE AND CONDUCTANCE* RELATED TO FUNCTIONAL RESIDUAL CAPACITY

SUBJECT	COMPLIANCE FRC			CONDUCTANCE* FRC		
	B.S.	A.S.	Diff.	B.S.	A.S.	Diff.
1. A.V.S.	0.0438	0.0382	-0.0056	0.178	0.118	-0.060
2. J.C.	0.0590	0.0420	-0.0170	0.162	0.115	-0.047
3. R.K.	0.0310	0.0306	-0.0004	0.155	0.102	-0.053
4. K.C.	0.0339	0.0262	-0.0077	0.189	0.166	-0.023
5. S.U.	0.0386	0.0338	-0.0048	0.173	0.133	-0.040
6. J.V.H.	0.0227	0.0245	+0.0018	0.070	0.071	+0.001
7. J.M.	0.0695	0.0522	-0.0173	0.123	0.096	-0.027
8. A.L.	0.0512	0.0516	+0.0004	0.138	0.141	-0.003
9. N.B.	0.0222	0.0158	+0.0064	0.062	0.046	-0.016
10. D.G.	0.0530	0.0290	-0.0240	0.199	0.076	-0.123
Mean	0.0425	0.0344	-0.0081	0.145	0.106	-0.0390
S.E. $\bar{d}$			0.0026			0.0117
P value			<0.02			<0.01

*Conductance = Reciprocal of Mean Mechanical Airflow Resistance.

TABLE 6

WORK OF BREATHING

SUBJECT	TOTAL WORK			ELASTIC WORK			RESISTIVE WORK		
	B.S.	A.S.	Diff.	B.S.	A.S.	Diff.	B.S.	A.S.	Diff.
1. A.V.S.	6.76	10.29	+3.53	5.22	6.45	+1.23	4.71	8.47	+3.76
2. J.C.	1.73	2.42	+0.69	0.70	0.87	+0.17	1.57	2.22	+0.65
3. R.K.	3.17	4.35	+1.18	1.69	1.65	-0.04	2.62	4.09	+1.47
4. K.C.	2.45	3.04	+0.59	1.43	1.88	+0.45	1.94	2.48	+0.54
5. S.U.	2.75	3.60	+0.84	1.39	1.62	+0.23	2.39	3.19	+0.80
6. J.V.H.	2.95	2.91	-0.04	1.39	1.26	-0.13	2.58	2.60	+0.02
7. J.M.	3.12	4.27	+1.15	0.73	0.98	+0.25	2.96	4.12	+1.16
8. A.L.	2.11	1.95	-0.16	0.73	0.72	-0.01	1.96	1.75	-0.21
9. N.B.	6.81	8.75	+1.94	2.33	3.12	+0.79	6.32	8.20	+1.88
10. D.G.	2.41	5.35	+2.94	0.96	1.60	+0.64	2.15	5.09	+2.94
Mean	3.43	4.69	+1.26	1.66	2.02	+0.36	2.92	4.22	+1.30
S.E. $\overline{d}$			0.326			0.126			0.440
P value			<0.01			<0.02			<0.02

TABLE 7

WORK OF BREATHING

SUBJECT	INSP. RESISTIVE WORK			EXP. RESISTIVE WORK			ELASTIC + RESISTIVE WORK		
	B.S.	A.S.	Diff.	B.S.	A.S.	Diff.	B.S.	A.S.	Diff.
1. A.V.S.	1.18	2.28	+1.10	3.53	6.20	+2.67	9.93	14.92	+4.99
2. J.C.	0.56	0.84	+0.28	1.01	1.38	+0.37	2.26	3.10	+0.84
3. R.K.	1.02	1.39	+0.37	1.60	2.70	+1.10	4.32	5.75	+1.43
4. K.C.	0.80	0.77	-0.03	1.14	1.72	+0.58	3.36	4.36	+1.00
5. S.U.	0.77	1.04	+0.27	1.62	2.15	+0.53	3.78	4.81	+1.03
6. J.V.H.	1.03	0.98	-0.05	1.55	1.62	+0.07	3.97	3.86	-0.11
7. J.M.	1.50	2.04	+0.54	1.46	2.08	+0.62	3.69	5.10	+1.41
8. A.L.	0.67	0.66	-0.01	1.29	0.93	-0.36	2.69	2.47	-0.22
9. N.B.	2.91	3.34	+0.43	3.41	4.86	+1.45	8.65	11.32	+2.67
10. D.G.	1.08	2.50	+1.42	1.07	2.59	+1.52	3.11	6.69	+3.58
Mean	1.15	1.58	+0.43	1.77	2.62	+0.85	4.58	6.24	+1.66
S.E. $\bar{d}$			0.154			0.273			0.519
P value			<0.05			<0.02			<0.02

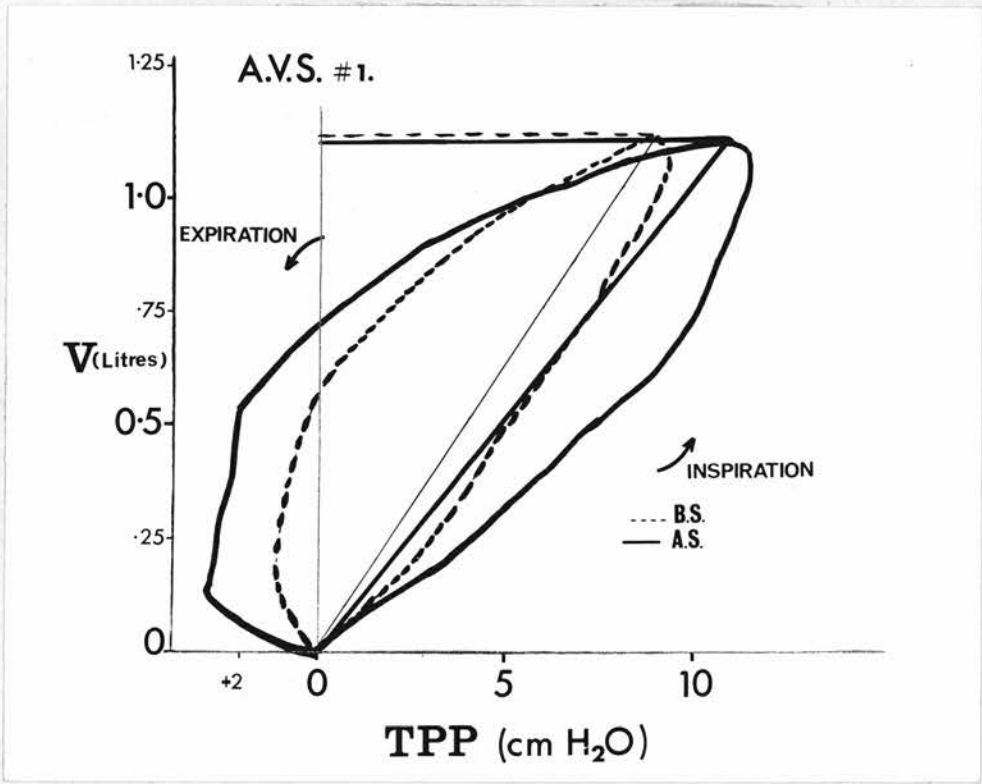


FIGURE 7

(In Figures 7 - 16, the work loop before smoking is represented by an interrupted line and the after smoking loop by a solid line.)

SUBJECT A.V.S. #1	B.S.	A.S.
Resp. rate/min.	39	38
Tidal Volume (ml.)	1,150	1,130
Total Work (Kg - cm.) (for 1,150 ml.)	6.76	10.29

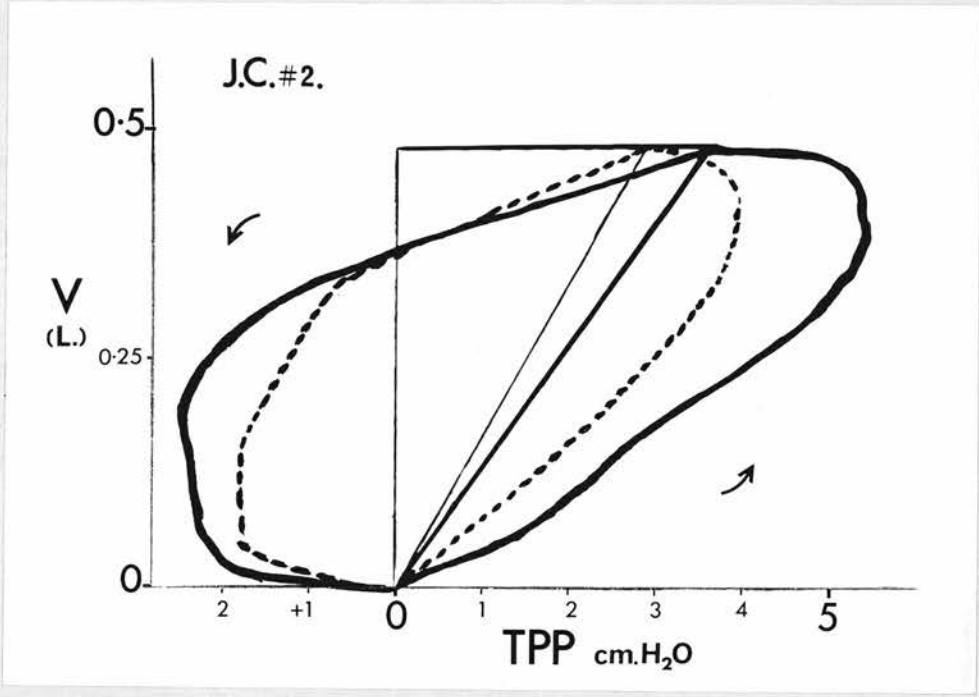


FIGURE 8

SUBJECT J.C. #2	B.S.	A.S.
Resp. rate/min.	62	60
Tidal Volume (ml.)	478	480
Total Work (Kg - cm.) (for 478 ml.)	1.73	2.42

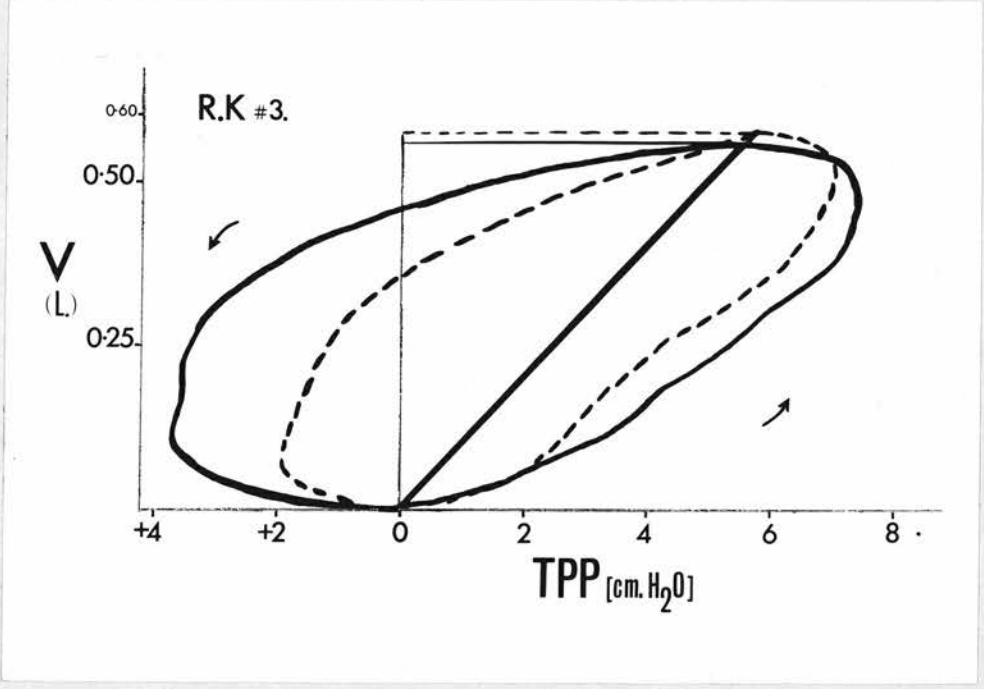


FIGURE 9

SUBJECT R.K. #3	B.S.	A.S.
Resp. rate/min.	60	60
Tidal Volume (ml.)	578	562
Total Work (Kg - cm.) (for 578 ml.)	3.17	4.35

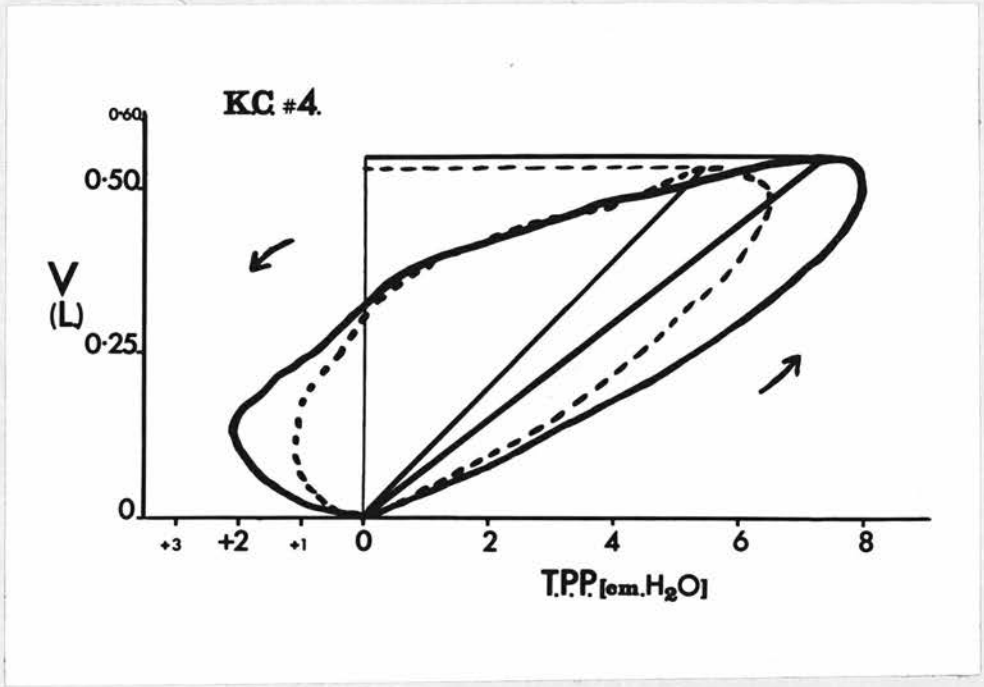


FIGURE 10

SUBJECT K.C. #4	B.S.	A.S.
Resp. rate/min.	55	54
Tidal Volume (ml.)	530	545
Total Work (Kg - cm.) (for 530 ml.)	2.45	3.04

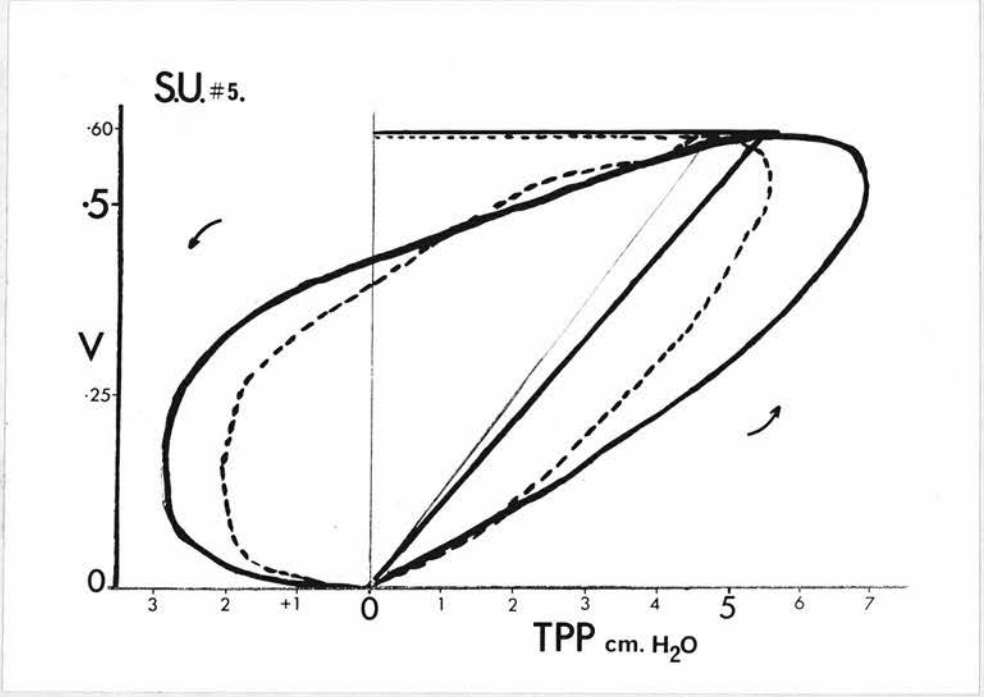


FIGURE 11

SUBJECT S.U. #5	B.S.	A.S.
Resp. rate/min.	60	58
Tidal Volume (ml.)	590	595
Total Work (Kg - cm.) (for 590 ml.)	2.76	3.60

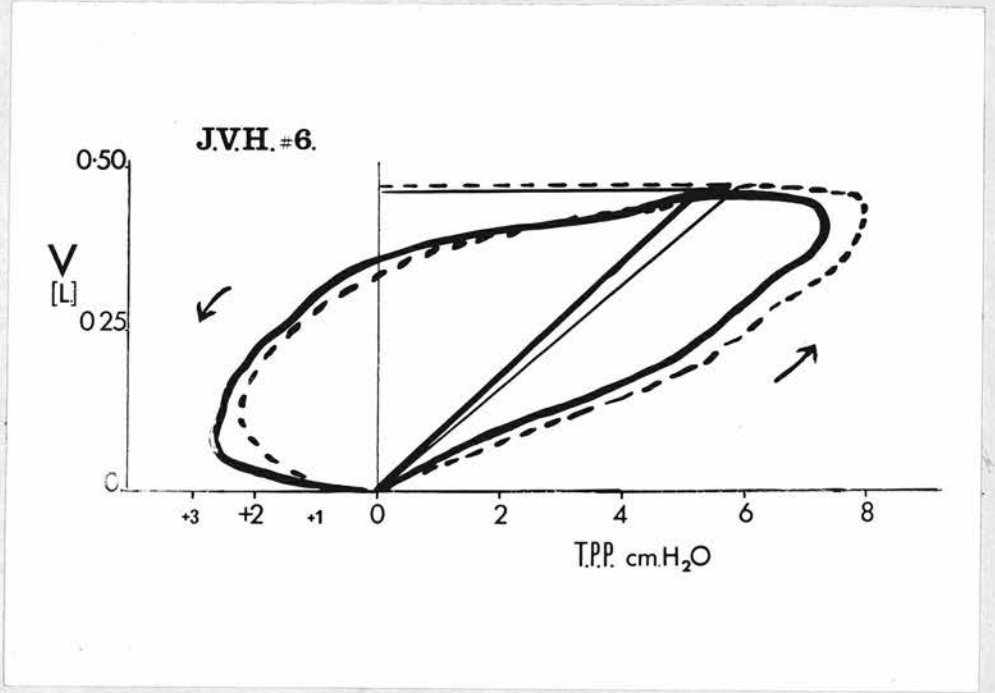


FIGURE 12

SUBJECT J.V.H. #6	B.S.	A.S.
Resp. rate/min.	49	50
Tidal Volume (ml.)	470	462
Total Work (Kg - cm.) (for 470 ml.)	2.95	2.91

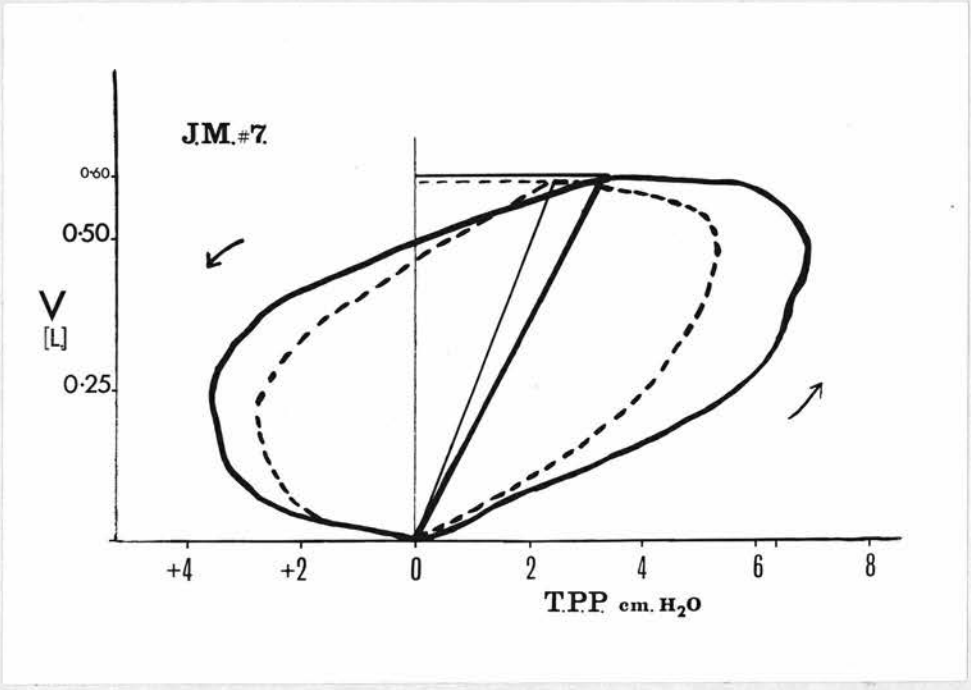


FIGURE 13

SUBJECT J.M. #7	B.S.	A.S.
Resp. rate/min.	58	57
Tidal Volume (ml.)	595	601
Total Work (Kg - cm.) (for 595 ml.)	3.12	4.27

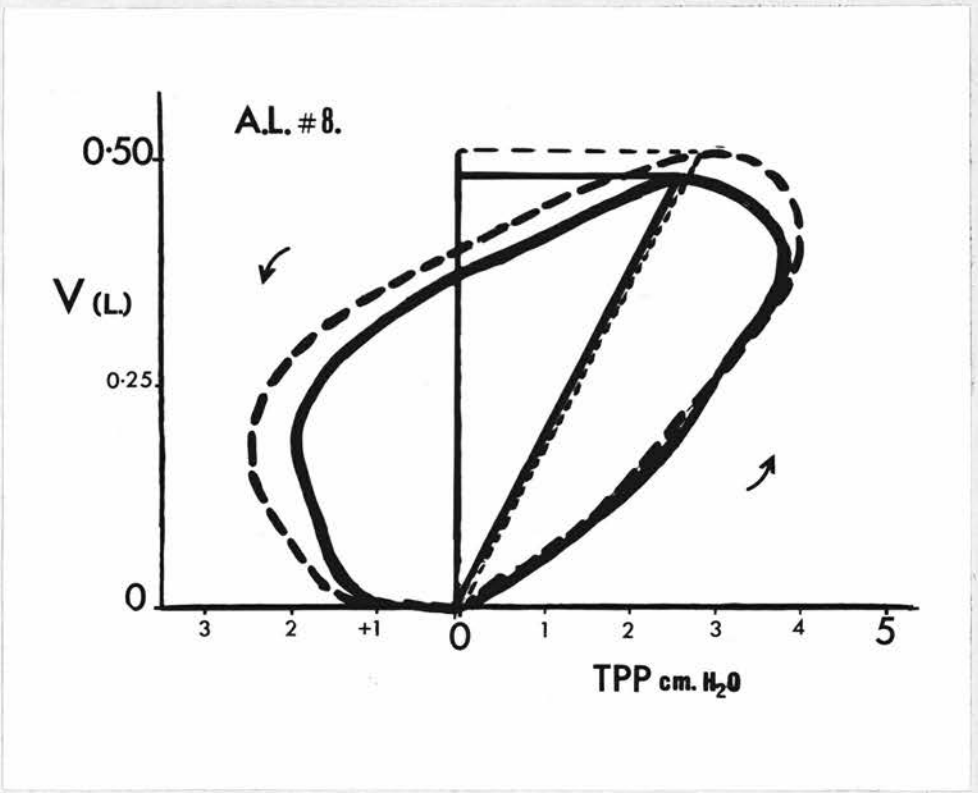


FIGURE 14

SUBJECT A.L. #8	B.S.	A.S.
Resp. rate/min.	54	54
Tidal Volume (ml.)	512	479
Total Work (Kg - cm.) (for 512 ml.)	2.11	1.95

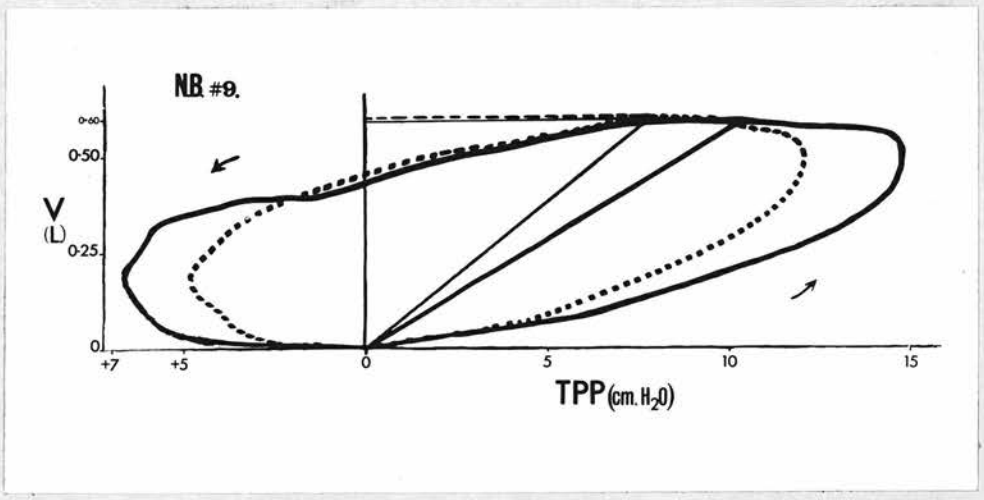


FIGURE 15

SUBJECT N.B. #9	B.S.	A.S.
Resp. rate/min.	58	59
Tidal Volume (ml.)	596	586
Total Work (Kg - cm.) (for 596 ml.)	6.81	8.75

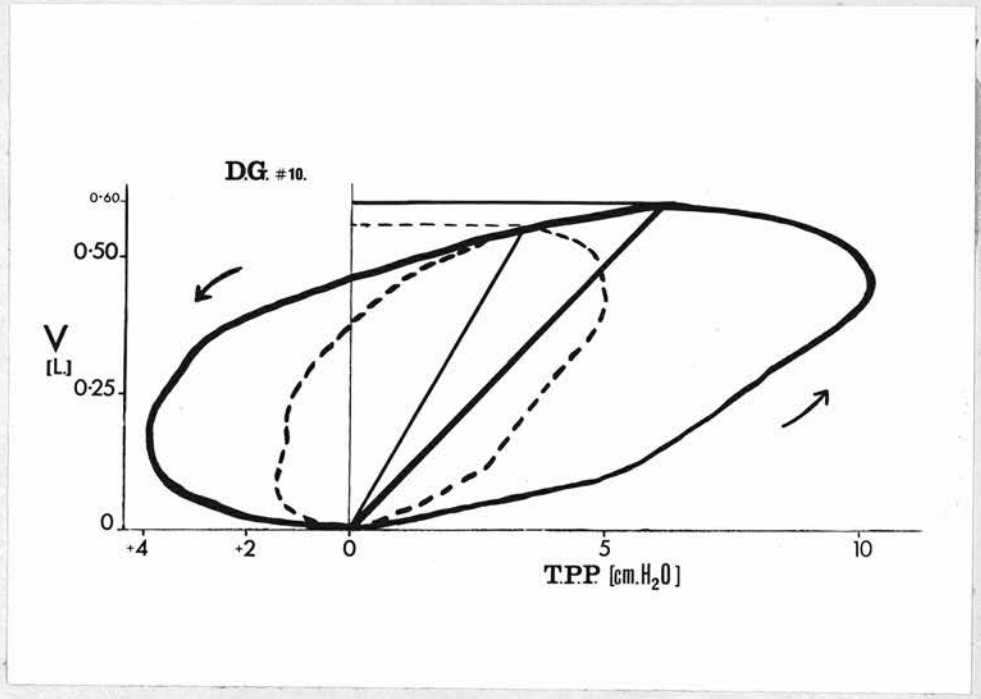


FIGURE 16

SUBJECT D.G. #10	B.S.	A.S.
Resp. rate/min.	59	61
Tidal Volume (ml.)	562	604
Total Work (Kg - cm.) (for 562 ml.)	2.41	5.35

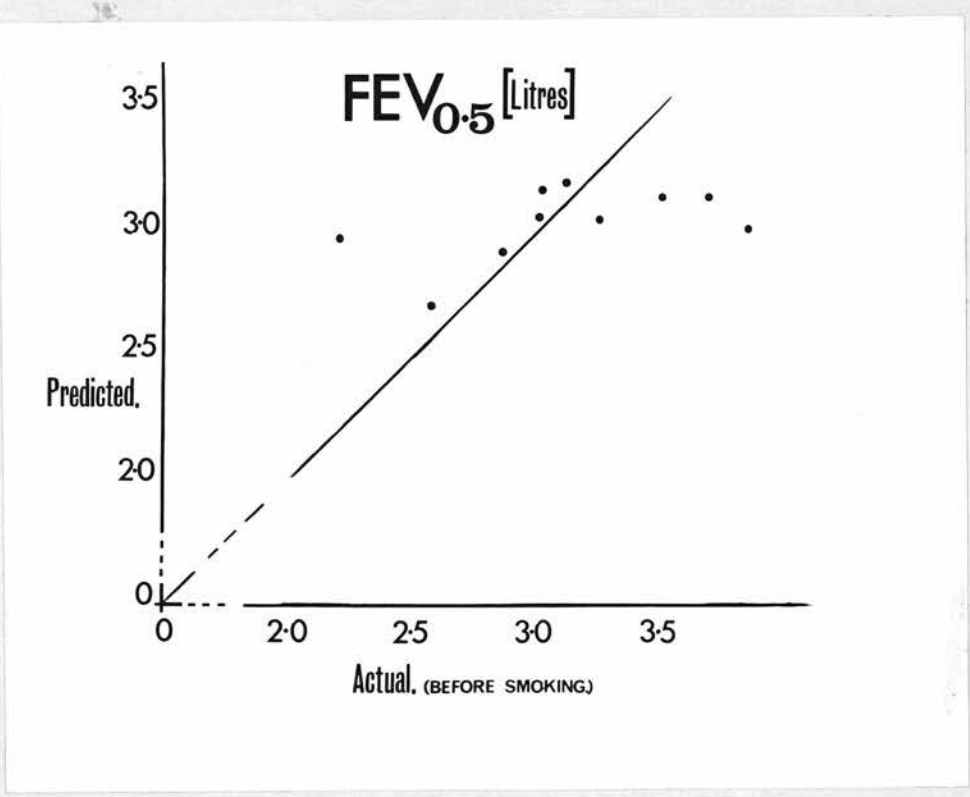


FIGURE 17

$FEV_{0.5}$ Predicted and Actual

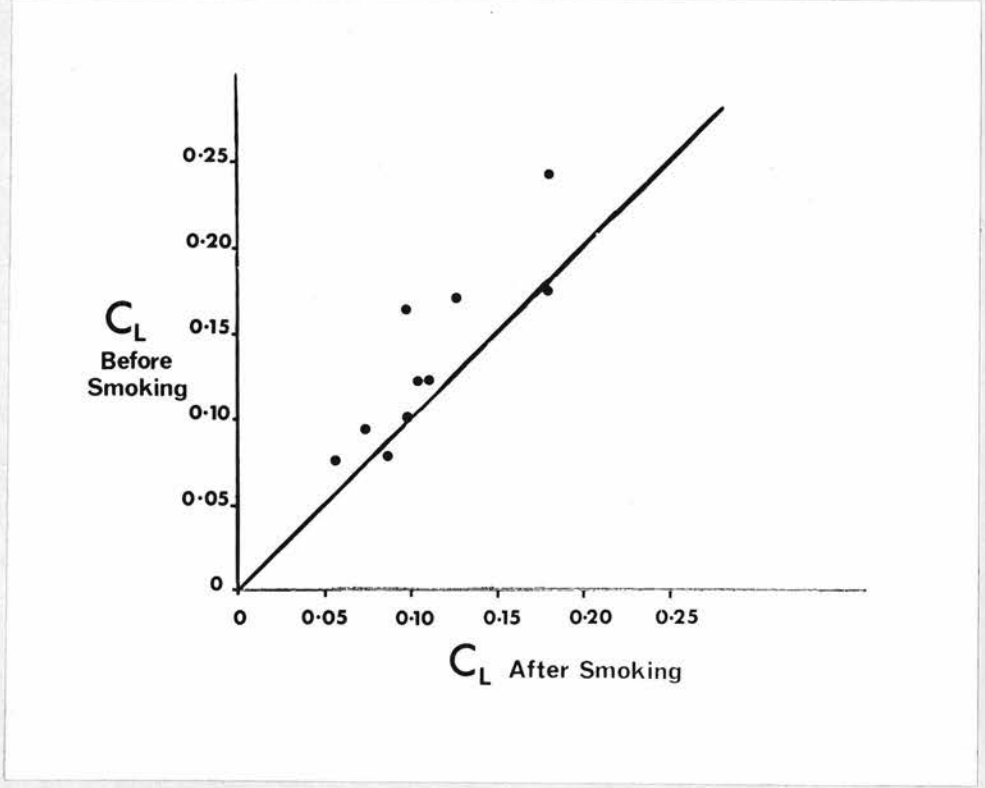


FIGURE 18

LUNG COMPLIANCE Before and After Smoking

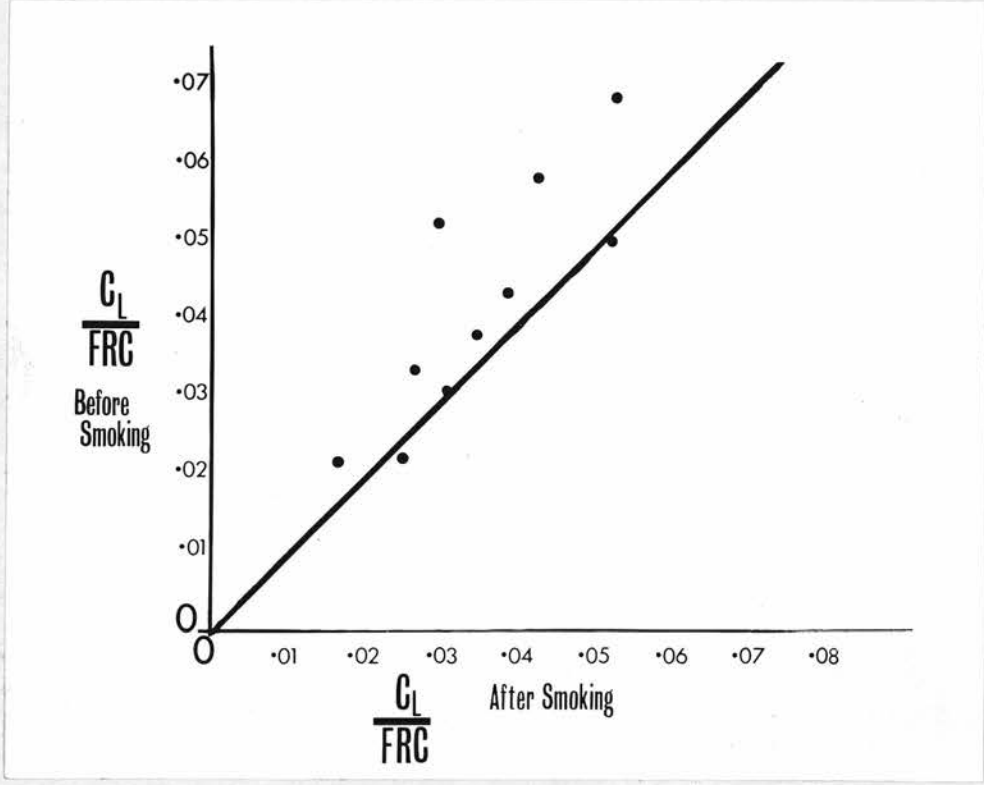


FIGURE 19

LUNG COMPLIANCE RELATED TO FRC
Before and After Smoking

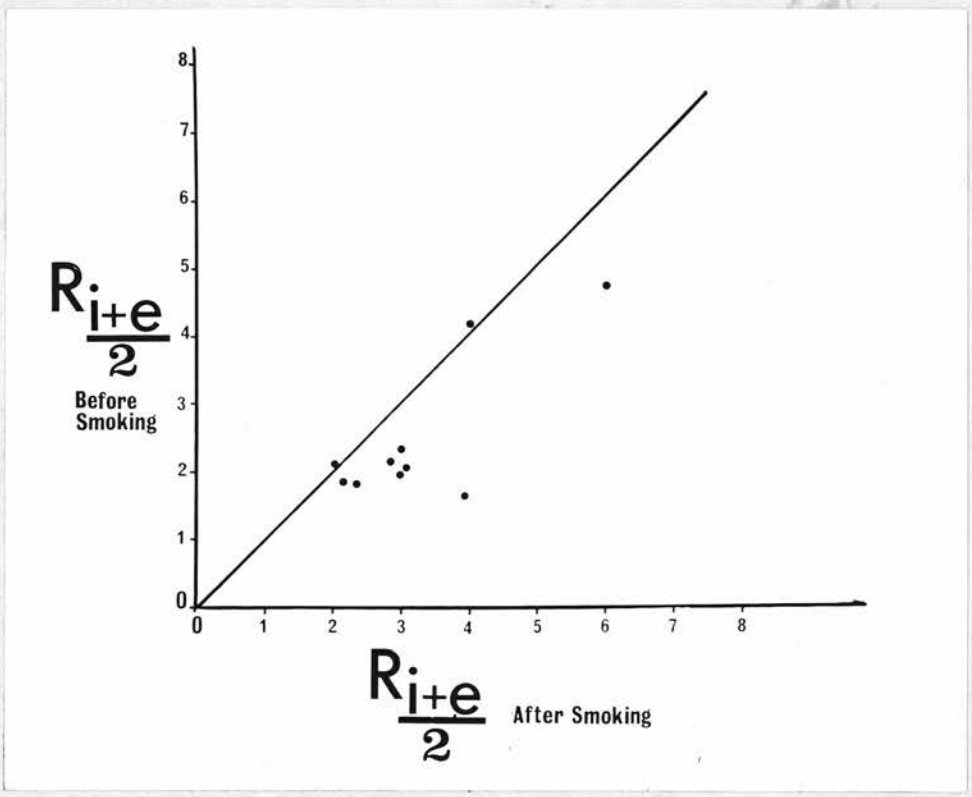


FIGURE 20

MEAN MECHANICAL AIRFLOW RESISTANCE
Before and After Smoking

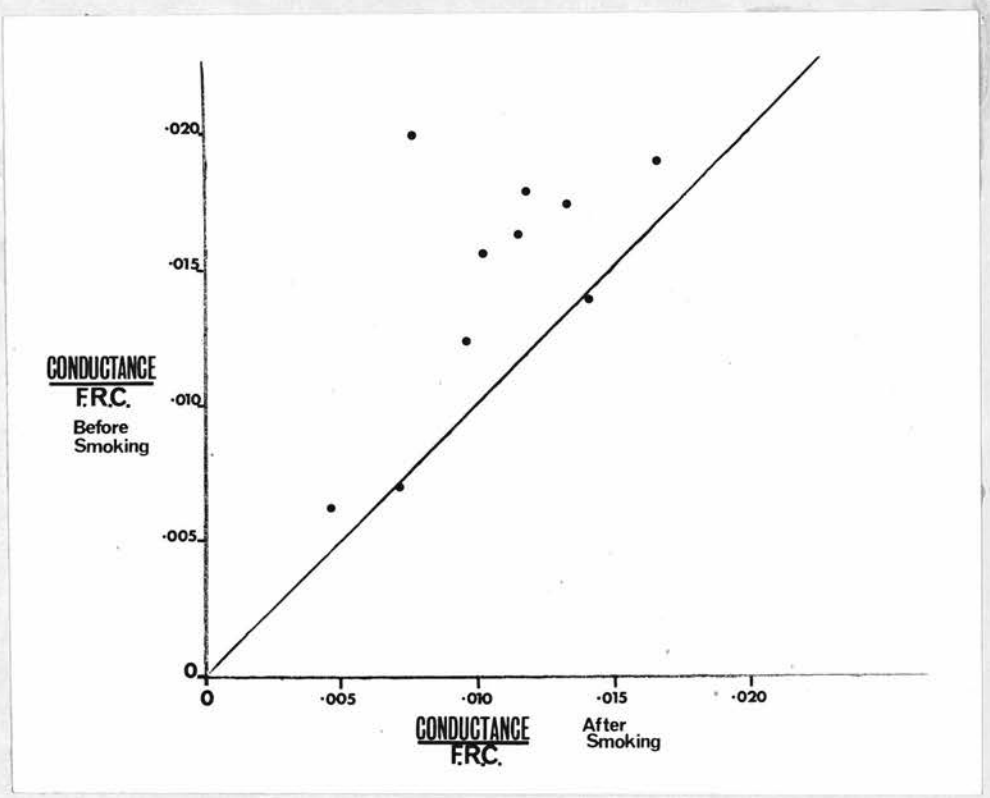


FIGURE 21

CONDUCTANCE RELATED TO FRC
Before and After Smoking

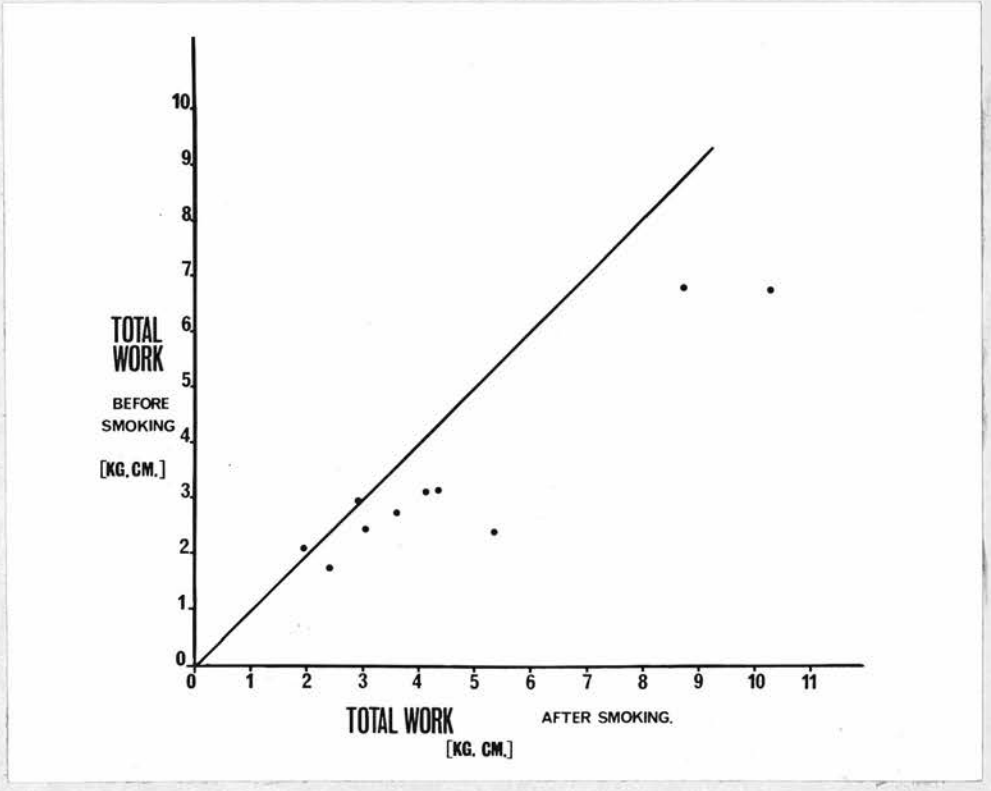


FIGURE 22

TOTAL WORK Before and After Smoking

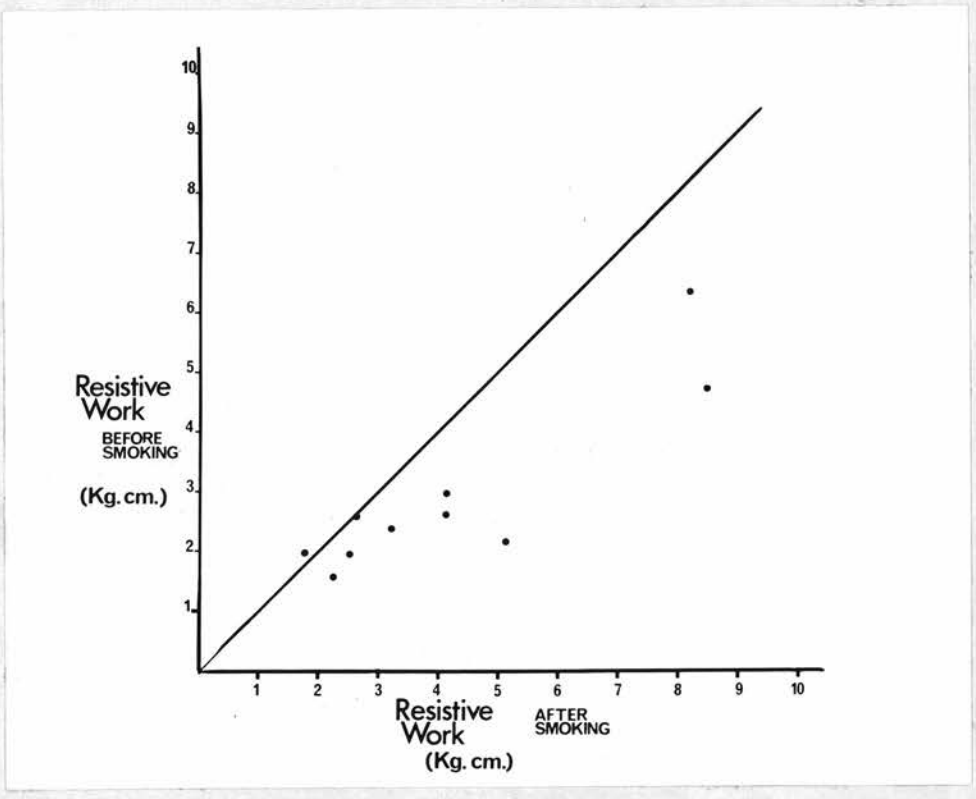


FIGURE 23

RESISTIVE WORK Before and After Smoking

RELATIONSHIP OF RESULTS OBTAINED TO NORMAL VALUES

Compliance and Airflow Resistance

An insufficient number of subjects has been studied in this laboratory to establish precise normal values for compliance and airflow resistance.

Normal values reported by N.R. Frank et al.[49] of the Harvard School of Public Health, Department of Physiology, for compliance and airflow resistance of young adults are:

Lung Compliance . . . . C_L = (0.00343 x height in cm.) −0.425
(L./cm. H_2O)

Range = 65 - 145% of C_L

Airflow Resistance . . . $R_{\frac{i+e}{2}}$ = 1.9
(cm. H_2O/L./sec.)

Range = 1.2 - 3.4

The oesophageal balloons used in the present study were supplied by Dr. Milic-Emili of the Harvard School and the technique employed was similar to that of Drs. Milic-Emili and Frank as verified by a visit to their laboratory. For these reasons, the values shown above are taken as the normal for the present study. Should there be a significant discrepancy in absolute values between the two laboratories, this is not important because this work is concerned with measurement of acute changes in pulmonary mechanics.

The Harvard laboratory values for compliance pertain to measurements at slow respiratory rates. When breathing is rapid, points of true zero flow are difficult to obtain and slightly lower values are usually obtained. In this study the respiratory rates were 40 - 60 per minute; this breathing pattern is probably responsible for the mean pre-smoking compliance (0.135 L./cm.H_2O) being slightly below the predicted normal for the group (0.171 L./cm. H_2O).

The pre-smoking values obtained for both compliance (0.135 L./cm. H_2O) and mean airflow resistance (2.48 cm. H_2O/L./sec.) are, however, within the normal range. The mean post-smoking expiratory airflow resistance (3.88 cm. H_2O/L./sec.) is the only value which can be said to be abnormal.

In normal subjects expiratory airflow resistance is equal to, or only slightly greater than, inspiratory resistance. In the subjects of this study, however, expiratory resistance exceeds inspiratory resistance by approximately 50%, before as well as after smoking, which suggests the presence of a minor physiological abnormality of their lungs.

The normal ranges of lung compliance and airflow resistance are seen to be wide, although they are narrowed when related to functional residual capacity.

The mean value for lung compliance when related to FRC, in adults, is 0.05 x FRC in litres, and the range of normal is (0.038 x FRC) - (0.070 x FRC).[49]

The mean value of compliance/FRC in the present subjects, before smoking, was 0.0425 which is within the normal range; after smoking, the mean value fell to 0.0344 which is slightly below the normal range.

Airflow resistance is inversely related to FRC and a satisfactory method of expressing the normal range is to relate the reciprocal of airflow resistance, which is referred to as conductance, directly to the FRC. There is no generally applicable normal range available in the literature for this measurement, although the mean value for a series of young adult males reported by Nadel and Comroe[95] was 0.21. Their measurement, however, was of pure airway resistance related to FRC and the value of 0.21 should therefore be higher than that obtained when airflow resistance, which includes tissue resistance, is used. The mean value of the airflow conductance related to FRC for this series, before smoking, was 0.145, which is lower than the 0.21 value of Nadel and Comroe. This difference is due partly to the tissue resistance and, presumably, partly to the differences in technique and subject material.

Work of Breathing

The work loop, while an excellent method of expressing lung compliance and airflow resistance in a meaningful manner, has the disadvantage of presenting complex factors which have to be taken into account in the establishment of normal values. This study is concerned with work per breath since the rate and depth of breathing were selected by the investigator.

Certain features of the work loop have been insufficiently appreciated by some authors. Specifically, that work per breath is not directly proportional to the volume of the breath; this is due to the fact that elastic work is proportional to the square of the tidal volume. An example will serve to emphasize this feature:- If an individual has a tidal volume of 500 ml. and the elastic work is 4 units, then the elastic work for a tidal volume of 1,000 ml. in this individual will be 16 units and not 8 units. Some authors measure work done on the lungs as 'work per litre-breath' and obtain this figure by dividing the work value obtained for the breath by the volume of the breath in litres.[21] It is apparent that this method is erroneous inasmuch as it does not take into account the described relationship of elastic work to tidal volume.

Another feature to be taken into account in the work per breath method is that resistive work is proportional to the speed of airflow so that it will vary with the rate of respiration.

For these reasons, if work per breath is to be used for comparison of individuals, or for comparison of pulmonary mechanics in the same individual under different circumstance (e.g. before and after cigarette smoke inhalation) both rate and depth of the breath must be included in the analysis and interpretation of results.

In this study the faster than normal rate of breathing is responsible for the resistive work being a greater proportion of the total than is normally the case on quiet breathing.

The method used in this study for comparing work of breathing before and after cigarette smoking takes these considerations into account.

Throughout this study work of breathing means work done on the lungs and does not take into account the work done on the chest wall.

DISCUSSION

The results obtained in this study show that inhalation of cigarette smoke causes increased work of breathing.

There are four similar reports (Attinger et al.;[2] Motley and Kuzman;[88] Eich et al.;[40] Nadel and Comroe[95]) concerned with the acute effects of cigarette smoke inhalation on lung compliance and airflow resistance; none deal with work of breathing. Nevertheless it is of value to compare this work with these related studies.

Attinger and co-workers[2] observed no significant alteration in lung compliance or airflow resistance after smoking two cigarettes. Several observations may be made on their technique and interpretation of results. It is not stated whether the subjects were required to inhale the cigarette smoke or not. In addition there was a fifteen minute delay between cessation of smoking and the post-smoking measurements. Their results on the twenty normal subjects studied, show that, following smoking, compliance fell in 13 subjects, inspiratory resistance increased in 14 subjects, and expiratory resistance increased in 14 subjects. In most subjects, however, the inspiratory and expiratory resistance changes were not in the same direction. They concluded that compliance and airflow resistance were not significantly altered by cigarette smoking but did not indicate the reasons for this conclusion.

Motley and Kuzman[88] studied compliance in normal subjects before and after smoking one cigarette. Inhalation was accomplished in this series by means of a smoking device. Compliance was observed to fall in six of the eight subjects, the mean decrease being 0.052 L/cm. H_2O. No measurements were made of airflow resistance in their study.

Eich and co-workers[40] studied the acute effects of cigarette smoking on lung compliance and airflow resistance in normal subjects and reported that no significant change occurred. Their technique warrants comment. No mention is made as to the requirement of inhalation of the cigarette smoke. No indication is given as to whether or not airflow resistance measurements were made at strictly comparable rates and depths of breathing. Furthermore, the functional residual capacity was not determined. It must be noted that their measurement of compliance was done using slow inspiration. This method gives a measurement of static rather than dynamic compliance.

Nadel and Comroe[95] measured airway resistance, by the plethysmographic method, before and after 15 inhalations of cigarette smoke. They observed an increase in 31 of 36 normal subjects, which averaged 31% and was statistically significant. They further observed, in the great majority of subjects, that the increased airway resistance fell to normal within one hour of cessation of smoking. They reported that the increase in airway resistance was unaffected by the nicotine contect of the cigarette, was not observed after injections of nicotine, and was unaffected by

removal of 'oxides of nitrogen and other volatile materials' from the inspired smoke. From these interesting studies they concluded that the submicronic particles known to be present in cigarette smoke[64, 67, 118] were responsible for the increased airway resistance.

They studied the effect of previous administration of isoproterenol on the experiment (cigarette-smoke induced airway resistance increase) and found that the increased airway resistance was prevented. They further observed that a deep inspiration after smoking, (taken 1 - 3 minutes prior to the measurement of airway resistance) resulted in no increase. From these observations and from the fact that the increase occurred rapidly and disappeared after one hour, they concluded that the mechanism was bronchiolar spasm. That a deep inspiration temporarily abolishes the cigarette smoke induced increase of airway resistance is of importance as a physiological phenomenon, and in the interpretation of spirometric studies after smoking. Widdicombe and Nadel believe this phenomenon to be reflex in nature.[61, 96, 122]

The fall in the half-second forced expiratory volume of 27 ml. in this study was not statistically significant. The after smoking volume, however, was reduced in seven subjects, unchanged in one and increased in only two instances. One of these two subjects showed an increase of 100 ml. which appreciably influences the mean value. Although forced expiratory volume is a measure of expiratory airway resistance it is also dependent to a large extent on voluntary effort. Furthermore, spirometers

cannot be read to a greater accuracy than 30 ml. However, the principal reason for the small change was probably the deep inspiration prior to measurement. Simonsson,[112] in a study of twenty subjects, observed a small reduction in the one-second forced expiratory volume after inhalation of cigarette smoke. The reduction was 30 ml., or 1%, which he considered statistically significant when a nonparemetric statistical test was used. This reduction does not compare with the measured increase in airflow resistance found in the present study. While the forced expiratory volume method suggests that increased airway resistance follows smoking, the method is inadequate. In a study of 67 subjects Shapiro and Patterson[110] reported a statistically insignifant reduction in forced expiratory volume following smoking. Similarly, Butler et al.[18] found no significant change after smoking . These results are comparable to the spirometric results obtained in the present study.

In this study the subjects were required to inhale the cigarette smoke. Comparisons of compliance and airflow resistance before and after smoking were made at strictly comparable rates and depths of breathing. The after smoking measurements were made within five minutes of cessation of smoking. Results were reported in relation to the functional residual capacity. The author considers all of these factors important but many of them were omitted from studies which report that cigarette smoking does not significantly influence pulmonary mechanics. Nadel and Comroe requested their subjects to inhale the cigarette smoke

and they measured functional residual capacity. Their results are similar to those reported here. They limited their study to measurement of airway resistance, however, and did not measure pulmonary compliance or work of breathing.

In this study dynamic compliance was significantly reduced following cigarette smoke inhalation while Eich and co-workers reported no change in the static pulmonary compliance following smoking.[40] Cigarette smoke causes reduced bronchial lumen, whether by bronchiolar spasm or by mucous secretion and oedema, as proven by the increased airway resistance. The fall in dynamic compliance, in the absence of change in static compliance, could be explained by the occurrence of uneven ventilation: Compliance remains unaltered in normal individuals up to respiratory rates of around 120 per minute, but in emphysema the compliance may fall greatly with increasing respiratory rate.[33, 101] The explanation of this phenomenon is based on the fact that unevenness of ventilation due to regional differences in airway resistance becomes exaggerated at rapid respiratory rates. (Figure 24) Static compliance is certainly the more fundamental measurement when considering the elastic properties of lungs, and dynamic compliance is in fact a combined measurement of elastic properties and airway resistance. Dynamic compliance, however, is a perfectly valid measurement, and a valuable one, provided the rate and depth of breathing are also reported. Furthermore, dynamic compliance is the effective

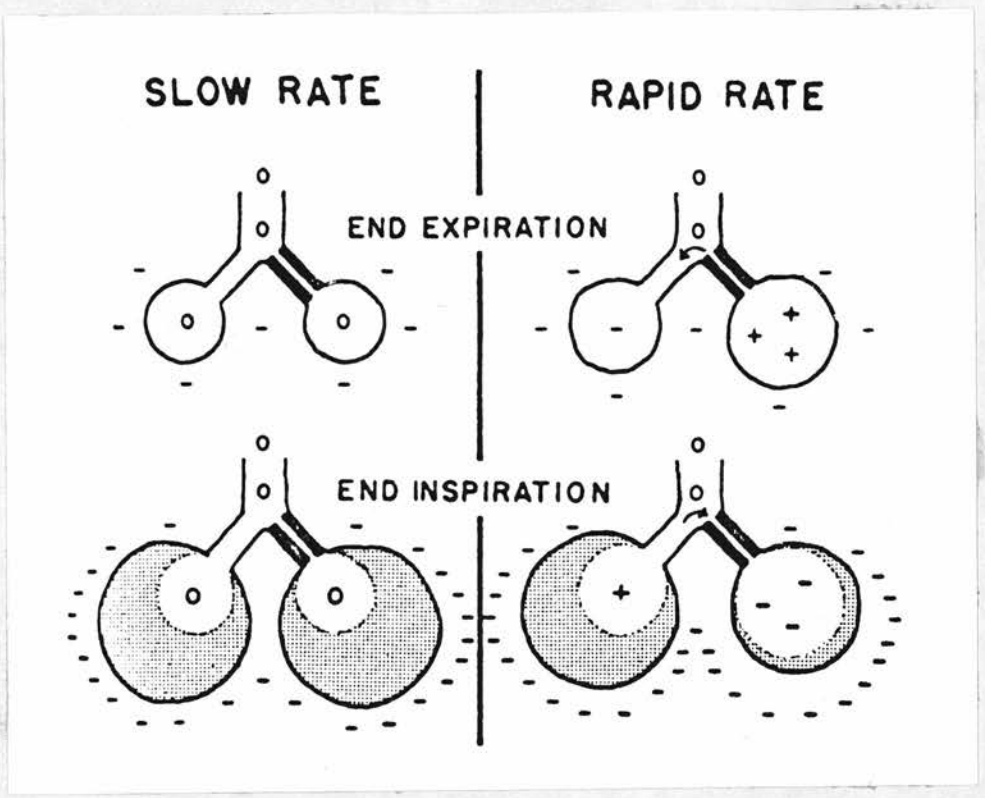


FIGURE 24. Diagram of 'Pendelluft'. From Otis et al.[101]

The figure is a schematic representation of a two-pathway system illustrating behaviour at slow and rapid rates. +, – and O indicate pressure relative to atmospheric. Shading indicates volume change. The two compliances are equal. The flow resistance of one pathway is greater than the other, and hence the time constant of the higher resistance pathway is greater. During very slow pressure cycling the impedances of the pathways are nearly equal, and hence the tidal volumes are about the same. The overall compliance is the sum of the individual compliances. At higher rates of cycling the impedance of the pathways depends increasingly on the pathway resistances, and the low resistive pathway receives more than one half of the total volume moved. The overall compliance in this case is less than at slow rates. At rapid rates the phase difference between the pathways becomes accentuated. At the end of inspiration, when flow has dropped to zero in the common path, the low time constant path is already expiring while the high time constant path is still inspiring. At the end of expiration gas is passing from the high to the low time constant pathway. As a result, the sum of the individual tidal volumes is greater than the overall tidal volume, the difference representing the volume of gas that passes back and forth between the two pathways ('pendelluft').

compliance and therefore more important in the assessment of dyspnoea.

It is concluded that the inhalation of cigarette smoke gives rise to a significant degree of uneven ventilation which is responsible for the observed decrease in dynamic compliance and increased elastic work of breathing. As the increase in airway resistance after smoking is slight compared to that found in emphysema, the amount of 'pendelluft' will be small.[101] (Figure 24)

Nadel and Comroe conclude that bronchiolar spasm is responsible for the increased airway resistance following smoking. While this may well be true,[70] it is not justifiable to dismiss other possibilities.

Paralysis of cilia, increased bronchial secretion and mucosal oedema are all known to occur following exposure of the bronchial mucosa to cigarette smoke in experimental animals.[8, 23, 30, 59] Increased sputum production and cough are characteristic clinical features of cigarette smokers.[39, 44-46, 58, 98, 102, 103, 123]

The fact that the increased airway resistance caused by cigarette smoke can be largely prevented by previous administration of isoproterend does not eliminate the possibility that mucous secretion and mucosal oedema may contribute to the increased airway resistance and decreased dynamic compliance following cigarette smoke inhalation. Bronchodilator agents may well act sufficiently powerfully in some regions of the lung to obscure the deleterious effects on pulmonary mechanics of mucosal

secretion and oedema in other regions. Furthermore, isoproterenol is known to cause some shrinkage of the oedematous mucosa. The forced expiratory volume was slightly reduced in this study, in that of Shapiro and Patterson, and in that of Simonsson. Until now this has been explained on the grounds that deep inspiration, prior to the measurement of forced expiratory volume, reflexly abolishes the cigarette smoke induced increase in airway resistance. However, the fact that a small reduction in forced expiratory volume is still obtained in the majority of instances means either that the inspiration does not completely remove the bronchiolar spasm or that some other factor such as mucosal secretion or oedema persists.

To this author it appears probable that mucosal secretion and/or oedema are partly responsible for the acute changes in pulmonary mechanics which follow cigarette smoke inhalation. The abnormalities of pulmonary mechanics which result from the inhalation of cigarette smoke are similar to those found in emphysema, namely increased air-flow resistance and uneven ventilation.

These abnormalities cause increased work of breathing - transient after smoking, permanent in emphysema.[32, 33, 46, 58, 72, 97, 105, 123]

The theory that the so called 'inert' submicronic smoke particles cause the increased airway resistance by direct irritation of the bronchial mucosa is supported by the work of Nadel and Comroe. Further investigation is required into the role of the other consistuents of tobacco smoke.[28, 29, 63]

It is well known that pipe and cigar smokers are not subject to the same incidence of lung cancer, emphysema and bronchitis.[34, 109, 114] The most likely explanation is that pipe and cigar smoke is not inhaled to any appreciable extent as it is more irritating to the bronchial mucosa.[109] It has been found that 'puffing' on a cigarette without inhaling the smoke into the lungs does not alter the mechanics of breathing.[40] This observation was made in the present study on two additional subjects, neither of whom were habitual cigarette smokers (Appendix 3). Attempts to study the effects of inhalation of cigarette smoke on pulmonary mechanics in non-smokers have been made.[95] First attempts at cigarette smoke inhalation are usually accompanied by untoward effects such as coughing, gagging and nausea, which influence the results of refined pulmonary function measurements. No reliance should be placed on these studies. Eich et al. and Attinger et al. failed to demonstrate any significant effect of the inhalation of cigarette smoke on the pulmonary mechanics of normal individuals but they did observe increased airway resistance and decreased compliance after smoking in patients who had chronic bronchopulmonary disease. The reasons for their failure to demonstrate the effects in normal individuals have already been discussed. That they were able to demonstrate decreased compliance and increased airway resistance in patients with bronchopulmonary disease suggests that the already deranged pulmonary mechanics were more subject to alteration than in the case of normal subjects. Most likely, the already

narrowed bronchi become further narrowed when irritated by cigarette smoke. The increase in airway resistance exaggerates the existing distribution defect resulting in a fall in dynamic compliance.

SUMMARY

The acute effects of the inhalation of cigarette smoke on pulmonary mechanics were studied in ten young adult men. The subjects were habitual cigarette smokers who had normal chest roentgenograms and had no history of respiratory disease.

Two popular brand cigarettes were smoked in succession by each subject and the smoke was inhaled every 30 - 60 seconds. Forced expiratory volume, functional residual capacity, lung compliance and airflow resistance were measured before and immediately after smoking. Pressure-volume work loops were constructed from the transpulmonary pressure and tidal volume recordings and elastic, resistive and total work per breath calculated.

Comparisons of mechanical properties of the lungs before and after smoking were made at strictly comparable rates and depths of breathing.

CONCLUSIONS

Inhalation of cigarette smoke causes temporary impairment of pulmonary mechanics resulting in increased work of breathing.

Airflow resistance is significantly increased resulting in increased resistive work of breathing.

The increased airflow resistance causes uneven ventilation which results in increased elastic work of breathing.

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APPENDIX 1

BRAND OF CIGARETTES SMOKED

	SUBJECT	BRAND	
1.	A.V.S.	Black Cat	Filter-Tip
2.	J.C.	Players Medium	Plain-Tip
3.	R.K.	Black Cat	Filter-Tip
4.	K.C.	Black Cat	Filter-Tip
5.	S.U.	Black Cat	Filter-Tip
6.	J.V.H.	Black Cat	Filter-Tip
7.	J.M.	Black Cat	Filter-Tip
8.	A.L.	Black Cat	Filter-Tip
9.	N.B.	Export "A"	Filter-Tip
10.	D.G.	Black Cat	Filter-Tip

Nicotine and Tar Content

The 1962 nicotine and tar content of the brands of cigarettes smoked were not available. The values for 1961 as reported by F.D. Snell* are:

Brand		Nicotine Content (mg)	Tar Content (mg)
Black Cat	Filter-Tip	2.1	21.3
Players Medium	Plain-Tip	2.4	27.7
Export "A"	Filter-Tip	2.7	26.2

These values represent average content per cigarette. The nicotine and tar content were determined by having the cigarette "smoked in a standard smoking apparatus which automatically puffs each cigarette in a manner that approximates human smoking as nearly as possible."* The cigarettes smoked in this study are representative of Canadian cigarettes insofar as tar and nicotine content are concerned.

Low nicotine and tar content cigarettes (e.g. 0.5 mg. nicotine; 1 mg. tar) are represented by a few popular brands only and none of this type were used in the present study. They were used in the study by Nadel and Comroe[95] where the nicotine and tar content were found to have no influence on the change in airway resistance after smoking.

*F.D. Snell Inc. Consulting Chemists. Tests made for the Reader's Digest. Canadian Edition, June, 1961.

APPENDIX 2

REPRODUCIBILITY OF RESULTS

Reproducibility of results for lung compliance and airflow resistance is important in this study where small changes were measured.

LUNG COMPLIANCE AND AIRFLOW RESISTANCE

Reproducibility of results for compliance and airflow resistance was tested in two subjects, measurements being made in the same manner as described in Method of Analysis of Records.

Tests for reproducibility must be made at the same rate of breathing. The tests were done before cigarette smoking.

The results obtained were:

Compliance

SUBJECT		RESP. RATE (breaths/min.)	C_L (mean of 30 breaths)
A.V.S.	1.	39	0.123
	2.	40	0.118
	3.	39	0.125
	4.	38	0.124
	5.	39	0.121
J.C.	1.	62	0.170
	2.	62	0.166
	3.	61	0.166
	4.	60	0.162
	5.	61	0.167

The largest difference between two individual determinations of compliance is 0.008 (L./cm. H_2O).

Any single series of 30 breaths can be said to give a compliance value within 0.04 of the mean. If the before smoking value deviated from the mean by 0.04 in one direction and the after smoking value deviated from the mean by 0.04 in the opposite direction this would give rise to an error of 0.08 in the calculation of the difference between the before and after smoking values. This maximum possible error of 0.08 is only one third of the observed difference for the series and therefore cannot explain the results obtained or influence the conclusions reached.

Airflow Resistance

SUBJECT		RESP. RATE (breaths/min.)	$R_{\frac{i+e}{2}}$ (mean of 30 breaths)
A.V.S.	1.	39	2.00
	2.	40	2.02
	3.	39	1.92
	4.	38	1.94
J.C.	1.	62	2.14
	2.	62	2.18
	4.	60	2.30

The above measurements of airflow resistance were made on the same series of breaths used for the compliance determinations. Only those series which exhibited the largest differences in compliance values were analysed for airflow resistance measurement.

The largest difference between individual determinations is 0.16 (cm. H_2O/L./sec.) so that any individual determination can be said to be within approximately 0.08 of the mean. The maximum possible error in measurement of the difference between pre-smoking and post-smoking values is therefore approximately 0.16. This error is small compared to the mean difference (0.77) obtained in this study.

APPENDIX 3

EFFECTS OF "PUFFING" ON A CIGARETTE ON COMPLIANCE AND AIRFLOW RESISTANCE

Measurements were made on two subjects before and after 'puffing' on a cigarette. The subjects did not inhale the cigarette smoke.

SUBJECT		C_L		$R_{\frac{i+e}{2}}$	
	Age	B.S.	A.S.	B.S.	A.S.
H.P.	32 years	0.164	0.166	1.65	1.68
L.F.	30 years	0.178	0.175	2.30	2.31

From these results it is concluded that 'puffing' on a cigarette has no appreciable effect on lung compliance or airflow resistance. Both subjects were non-smokers and experienced nausea and dizziness on attempting to inhale the cigarette smoke in the manner required for the smoke inhalation experiments, and the matter was not pursued further.

APPENDIX 4

GLOSSARY OF ABBREVIATIONS

TLC	Total Lung Capacity
RV	Residual Volume
FRC	Functional Residual Capacity
FVC	Forced Vital Capacity
$FEV_{0.5}$	Forced Expiratory Volume in the First Half-second
C_L	Lung Compliance
R	Mechanical Airflow Resistance
T.P.P.	Transpulmonary Pressure
V_T	Tidal Volume
$\dot{V}$	Gas volume/unit time
B.S.	Before Smoking
A.S.	After Smoking