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STUDIES ON THE REGISTRATION OF PROVOCATION TESTS FOR THE ETIOLOGICAL DIAGNOSIS OF BRONCHIAL ASTHMA

By

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The mechanics of breathing in bronchial asthma has been widely investigated (*Jeker, Wyss, McIlroy, Marshall, Scherrer et al., Attinger, Goldstein & Segal, Engström, Karlberg, Koch & Kraepelien, Colldahl, Nisell, Ripe & Svanborg*).

For the judgement of provocation tests it is of great value if use is made of an objective method for the registration of the changes in respiratory function that develop if the tests give positive results. If such methods are adopted it is possible to get a positive result with weaker antigen solutions than if one uses only the method of auscultation and records the degree of dyspnoea.

The registration can be made in different ways and some of these have been discussed by *Colldahl* (1959). The best methods seem to be those that involve the registration of intrapulmonary air mixing or flow resistance, since the registration in these cases can be made when the patient is breathing normally. Forced breathing in itself may provoke breathing difficulties in an asthmatic subject.

In earlier studies (1952) the registration of intrapulmonary air mixing was found to be a very good method for the objective registration of provocation tests, but as this method requires 4 to 10 minutes for each determination we have therefore turned our attention to the measurement of flow resistance to see if equally good results can be obtained by this

method, but in a shorter time. In particular we wished to study the more simple method for measuring the lung compliance and non-elastic respiratory resistance worked out by *Nisell & Ehrner* (1956 and 1958). With this method time-marked oesophageal pressure tidal volume curves are obtained.

At the Congress of Allergology in Paris, 1958, *Engström, Karlberg, Koch & Kraepelien* presented a paper describing a somewhat more complicated method of registering objectively respiratory resistance in provocation tests and reported that the results obtained by this method were good. At that time we also reported our findings with the method worked out by *Nisell & Ehrner* concerning the registering of respiratory resistance during provocation tests and these findings are now set out below in more detail.

We have studied 3 persons who in previous tests have been found to be sensitive to different antigens. These persons are:

1. T. S. Born 27.7.1927. Teacher. Suffers from hereditary allergy and has had asthma from childhood. Tests reveal a skin sensitivity as regards dust, moulds, animal dander and pollen. After inhalations of different antigens the patient experienced trouble from different kinds of moulds and horse dander but was not troubled by the inhalation of dust extracts.

2. G.B-W. Born 23.10.1938. A children's nurse. Has had asthmatic trouble since 1955 and attacks were brought on by animal contacts and dust. Skin tests showed skin sensitivity to dust extracts and extracts from different animal danders. After inhalation of dog and horse dander and dust extracts she had very mild asthmatic trouble.

3. L.B. Born 24.11.1909. Housewife. This patient has tuberculosis and asthma. Pneumothorax treatment was given on the right side between 1944 and 1950 and on the left side between 1950 and 1953. Since 1957 she has had periodic bouts of asthmatic breathing and skin tests showed a positive reaction to different moulds. After the inhalation of botrytis and mucor extract slight asthmatic breathing started.

METHODS

The provocation tests were performed in the following way and the patients were not suffering from asthmatic trouble before the tests:

A good nebuliser was used e.g. the model recommended by *Barach* or the spray de Vilbiss No. 40. The nebulisation was performed by compressed air and the patients first inhaled 1 ml of the pure solvent used for the extract in a period of about 10 minutes. If after inhalation of the solvent the patient felt no

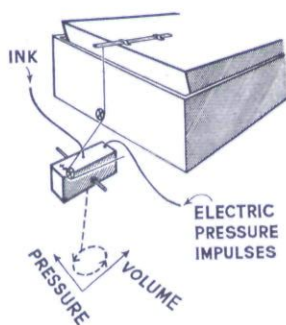


Fig. 1.

Diagram of apparatus for recording of the oesophageal pressure-tidal volume loops.

symptoms, the antigen solutions were inhaled. The first antigen solution inhaled was, as a rule, of the same strength as that which had given a positive result in a skin test. After each inhalation of an antigen solution the patient was examined by auscultation and determinations of vital capacity and pneumometer value as well as of resistance and compliance were made.

The mechanics of breathing was analysed as described previously (Nisell & Ehrner 1956). This method had the following main points: The respiratory pressure was recorded in the oesophagus with a Porges neoplex duodonal tube, charrier 10 or 12, to the end of which a thin latex balloon had been attached. The balloon had an effective length of 15 cm and a diameter of 8 mm. It communicated with the lumen of the tube via several perforations. Tube and balloon were advanced, without anaesthesia, through one nostril into the oesophagus until the tip was approximately 45 cm from the nostril. After complete collapse the balloon was filled with 1.5 to 2 ml of air. The pressure was recorded with a strain-gauge.

The subject breathed into a closed circuit which included a Krogh spirometer. Intra-oesophageal pressure tidal volume loops were recorded directly by a Mingo-graph ink jet, interrupted six times per second (fig. 1). (Supplied by AB Elema, Stockholm).

The respiratory flow ($\dot{V}$) was calculated from the tidal volume (V_T) and the duration of a complete respiratory cycle (t), $\dot{V} = 2V_T/t$. The resistance values were obtained as the 'width' resistance (R_W), (Nisell & Ehrner 1958), utilising the maximum sum of inspiratory and expiratory resistance pressure ($2P_R$) at one volume and assuming air flow to be approximately sine-wave in character: $R_W = P_{Rt}/\pi V_T$. The compliance was derived from the volume pressure relationship of a line between the curve points that indicated the beginning and the end of the tidal air. The oesophageal pressure fluctuation was the difference between the maximum and minimum pressures of the pressure-volume loop.

The number of loops from which each value was derived varied between 8 and 28.

Normal values with this method for compliance and resistance are as follows: The normal range of compliance during spontaneous breathing is 0.14 to 0.39 L(BTPS)/cmH₂O in males and 0.10 to 0.25 L/cmH₂O in females (Ehrner 1960). The normal range of resistance calculated from the width of the pressure-volume loop was about 0.8 to 3.7 cmH₂O/L(BTPS)/second.

The degree of dyspnoea was estimated from the subject's feeling of heaviness in the chest and ranged from 0-3. The auscultation findings for the degree of asthma were evaluated from 0 to 3, where 0 = normal breathing, $\frac{1}{2}$ = rhonchi without breathing difficulties and $1\frac{1}{2}$ = asthma of medium severity.

RESULTS

The effect on the appearance of the pressure-volume loop of asthma-inducing inhalation and subsequently of adre-

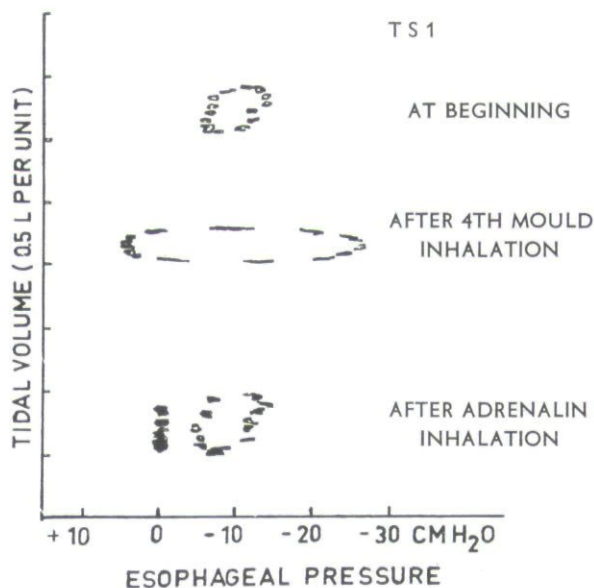


Fig. 2.

The appearance of the respiratory pressure-volume loop in some occasions during the first study on subject TS. One-sixth of a second intervals between consecutive dots on each curve. The vertical line of dots in the lowest represents zero pressure. The middle curve is obtained after induction of bronchial asthma.

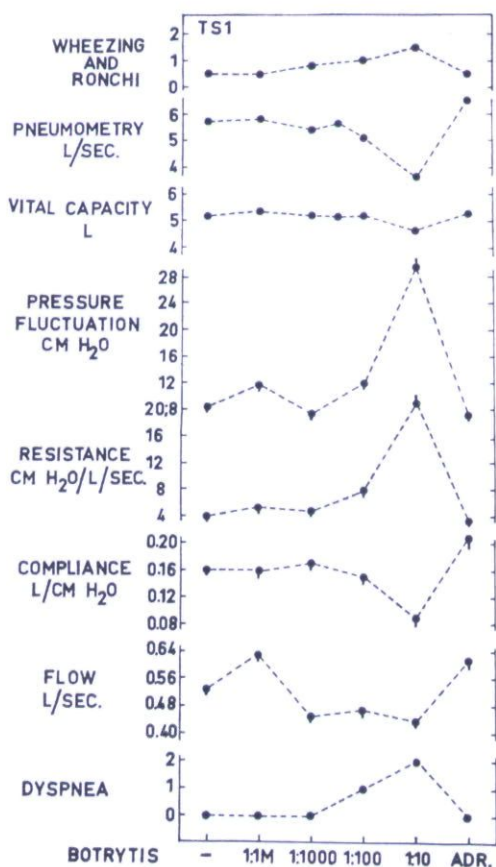


Fig. 3.

First study on subject TS (Date 21.5.58). Effects of inhalations of botrytis extracts in varying concentrations (1 M = 1,000,000) and of adrenaline (ADR). Each dot represents a mean value and its adhering vertical line the standard error of the mean. Approximately 15 minutes between consecutive values.

naline is shown in fig. 2. The pressure amplitude changed markedly.

The magnitudes of the oesophageal pressure fluctuation, respiratory resistance, compliance, flow, subjective dyspnoea etc. before and during the tests appear in figs. 3, 4, 5 and 6. An allergen inhalation of sufficient magnitude in a patient

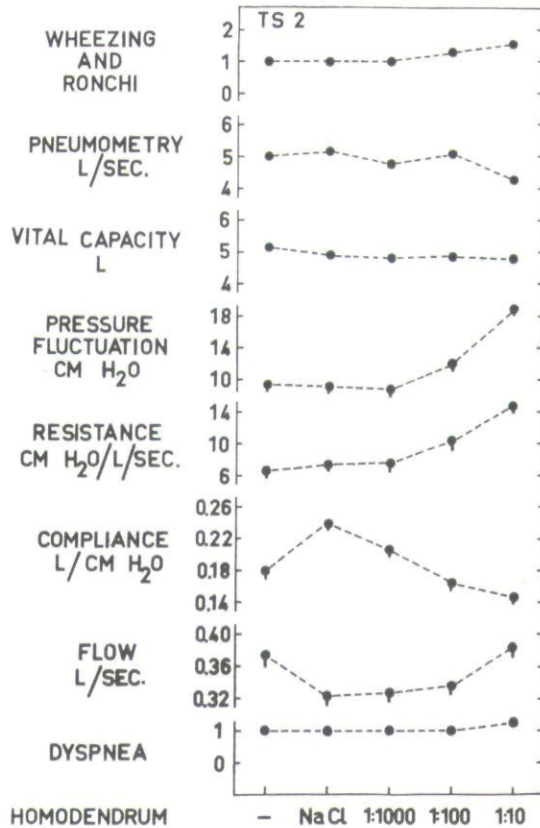


Fig. 4.

Second study on subject TS (Date 10.6.58). Effects of inhalations of physiological saline and of various homodendrum concentrations. See also legend of Fig. 3.

sensitive to this allergen is accompanied by an increase in pressure amplitude and in resistance and by a decrease in compliance.

The resistance and the amount of wheezing and rhonchi estimated by auscultation are in fig. 7 related to each other. An increase in one of them is, in general, accompanied by an increase in the other.

The pneumometer value was measured in two tests, figs. 3

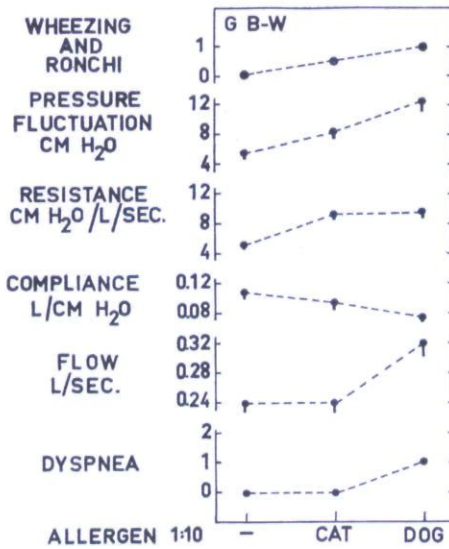


Fig. 5.

Study on subject G B-W. Inhalations of allergens (1:10) from cat and dog. Approximately half an hour between consecutive values. Inhalations were done not for etiological purposes but to obtain a bronchial reaction. See also legend of

Fig. 3.

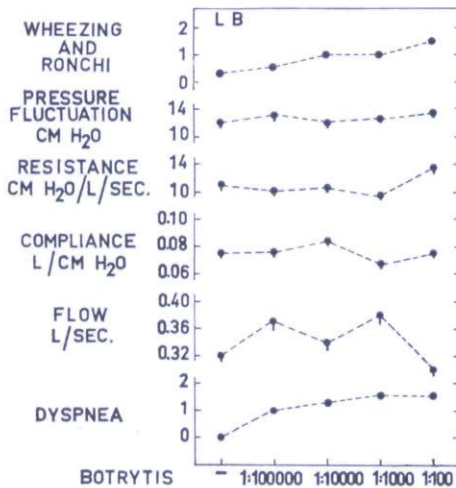


Fig. 6.

Study on subject LB. Inhalations of botrytis extracts in different concentrations. See also Legend of Fig. 3.

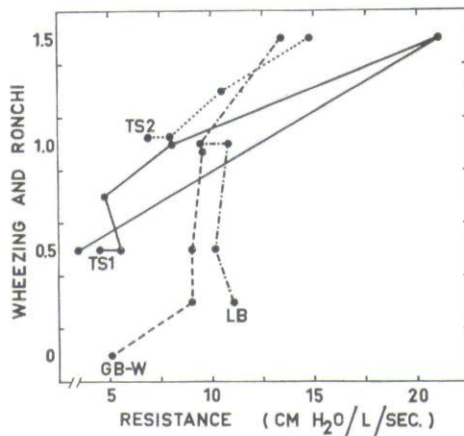


Fig. 7.

Respiratory resistance in relation to auscultatory estimation of wheezing and rhonchi before and after inhalation of antigen. Lowest dot furthest to the left of each curve indicates value before inhalation except in TS 1 where that dot is the state after adrenaline. The highest dot of curve indicates value after last antigen inhalation.

and 4. A change in the pneumometer value coincides with an opposite change in the resistance value.

In fig. 4 it will be seen that even before any significant change occurs in subjective breathing troubles (dyspnea), definite changes have already taken place in the pneumometer and resistance readings but not in vital capacity. In fig. 3 after the third inhalation of botrytis (in a concentration of 1 in 100) there was a clear change in pneumometer and resistance values but not yet in vital capacity and compliance. Marked changes in vital capacity and compliance occurred a little while later after the fourth and strongest inhalation (in a concentration of 1 in 10).

DISCUSSION

The correlations between dyspnoea and resistance or pressure amplitude (figs. 3, 4, 5 and 6), between the amount of abnormal sound and resistance and between the pneumometer value and resistance were, in general, apparently good. In the

individual cases, however, one factor changed frequently at an earlier stage without there having been any corresponding change in the other factor. For instance in figs. 5, 6 and 7, subjects LB and GB-W increased their wheezing and rhonchi with no change in resistance. After the last inhalation, however, the resistance in both cases was higher than at the beginning. In fig. 4 the resistance, pressure fluctuation, wheezing and rhonchi increased after the inhalation of homodrendrum (1 part in 100) with no change in breathing sensation, vital capacity and pneumometry. After inhalation of the strongest antigen solution (1 in 10) there is a change in pneumometry, resistance, compliance, dyspnoea, wheezing and rhonchi but not in vital capacity.

An objective and simultaneous registration of the different qualities enables a more precise judgement of the provocation test.

One point that should be emphasised here is that an objective registration of the test is not necessary in all cases, particularly not in those cases where an inhalation of antigen provokes an unmistakable asthmatic condition not noticeable by auscultation before the test or after the inhalation of the solvent only. But even in cases where the breathing sound is rough before the test started it is possible with a high degree of certainty to judge the result of the provocation just by following the changes in auscultation findings and the subjective condition of the patient during the test, as has been shown by *Colldahl* (1952).

But of course in all cases of provocation tests it is a valuable help also to have the test registered in an objective manner.

If an elevation of resistance or a decrease of the pneumometer reading develops during a provocation test, this can be considered positive even if the changes in dyspnoea and auscultation findings with the antigen concentrations used are not yet conclusive and had necessitated the inhalation of stronger antigen solutions to get clear results. On the other hand, if dyspnoea and auscultation findings are more pronounced after the inhalation of an antigen than after the inhalation of the

solvent for the antigen, this may be interpreted as a positive result even if there is no definite change yet in the objective method used. The reason for this may be that the inhalation of the antigen may provoke the secretion of mucus affecting the breathing sound without any simultaneous change in bronchial diameter. It is, however, best to continue with the antigen inhalations until a clear result is obtained both with the subjective and objective methods used.

A provocation of even slight bronchial asthma is, according to what is mentioned above, accompanied by an increase in resistance and pressure amplitude and a decrease in compliance, as appears from these studies and also from those of *Scherrer et al.* (1956). The simultaneous change in respiratory flow is not consistent. In the study of these patients we have found that pneumometry readings change earlier than vital capacity values during a provocation test and this is in agreement with the findings of *Colldahl* (1959). The value of pneumometry for registering provocation tests has clearly been shown by *Fuchs & Gronemeyer*.

SUMMARY

The investigation has shown that the measurement of respiratory resistance and pressure amplitude with the help of time-marked oesophageal pressure-volume curves is a good and sensitive method for the objective registration of provocation tests, though the calculation of the resistance from the obtained values takes some time. A change in resistance cannot therefore be seen instantly from the readings with the method used. The special advantage of the test, however, is that it can be performed when the patient is breathing normally and that several loops can be obtained in a short space of time.

The findings indicate that the correlation between dyspnoea, auscultation findings, pneumometry, vital capacity and resistance readings is, in general, good. On some occasions, however, there can be a discrepancy between the above mentioned registration methods, in that the rapidity with which significant

changes occur may vary between the different methods used. It is always valuable to have registered the changes that have occurred during a provocation test with different methods and to have obtained clear cut results with both objective and subjective tests.

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